Biomedical Engineering

Department of Electrical Engineering
Short name: Biomedical Engineering

Addresses
Type of address: Postal address
Street: Elektrovej
Building: 349
Postal code: DK-2800
City: Kgs. Lyngby
Country: Denmark

Phone numbers
Phone: (+45) 4525 5832

Web addresses
Web: http://www.dtu.dk/centre/bme/English.aspx

E-mails
E-mail: jw@elektro.dtu.dk

Organisation profile

Education
Our group is responsible for the Medicine & Technology program, jointly offered by DTU and the University of Copenhagen, which aims at educating students to participate internationally in biomedical research and product development at universities, hospitals and in the industry.

Research
The Biomedical Engineering group researches in:

Ultrasound - hardware related implementation as well as imaging, flow estimation and ultrasound techniques

Magnetic Resonance Imaging

Signal Processing

Biomechanics and Biomedicine

Organisational unit: Section

Publications:

Accuracy and Precision of a Plane Wave Vector Flow Imaging Method in the Healthy Carotid Artery

The objective of the study described here was to investigate the accuracy and precision of a plane wave 2-D vector flow imaging (VFI) method in laminar and complex blood flow conditions in the healthy carotid artery. The approach was to study (i) the accuracy for complex flow by comparing the velocity field from a computational fluid dynamics (CFD) simulation to VFI estimates obtained from the scan of an anthropomorphic flow phantom and from an in vivo scan; (ii) the accuracy for laminar unidirectional flow in vivo by comparing peak systolic velocities from VFI with magnetic resonance angiography (MRA); (iii) the precision of VFI estimation in vivo at several evaluation points in the vessels. The carotid artery at the bifurcation was scanned using both fast plane wave ultrasound and MRA in 10 healthy volunteers. The MRA
geometry acquired from one of the volunteers was used to fabricate an anthropomorphic flow phantom, which was also scanned using the fast plane wave sequence. The same geometry was used in a CFD simulation to calculate the velocity field. Results indicated that similar flow patterns and vortices were estimated with CFD and VFI in the phantom for the carotid bifurcation. The root-mean-square difference between CFD and VFI was within 0.12 m/s for velocity estimates in the common carotid artery and the internal branch. The root-mean-square difference was 0.17 m/s in the external branch. For the 10 volunteers, the mean difference between VFI and MRA was -0.17 m/s for peak systolic velocities of laminar flow in vivo. The precision in vivo was calculated as the mean standard deviation (SD) of estimates aligned to the heart cycle and was highest in the center of the common carotid artery (SD = 3.6% for velocity magnitudes and 4.5° for angles) and lowest in the external branch and for vortices (SD = 10.2% for velocity magnitudes and 39° for angles). The results indicate that plane wave VFI measures flow precisely and that estimates are in good agreement with a CFD simulation and MRA.

**General information**

**State:** Published
**Organisations:** Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
**Authors:** Jensen, J. (Intern), Villagómez Hoyos, C. A. (Intern), Traberg, M. S. (Intern), Olesen, J. B. (Intern), Tomov, B. G. (Intern), Moshavegh, R. (Intern), Holbek, S. (Intern), Stuart, M. B. (Intern), Ewertsen, C. (Ekstern), Hansen, K. L. (Ekstern), Thomsen, C. E. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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A comparative study of methods for automatic detection of rapid eye movement abnormal muscular activity in narcolepsy

Objective: To evaluate rapid eye movement (REM) muscular activity in narcolepsy by applying five algorithms to electromyogram (EMG) recordings, and to investigate its value for narcolepsy diagnosis. Patients/methods: A modified version of phasic EMG metric (mPEM), muscle activity index (MAI), REM atonia index (RAI), supra-threshold REM EMG activity metric (STREAM), and Frandsen method (FR) were calculated from polysomnography recordings of 20 healthy controls, 18 clinic controls (subjects suspected with narcolepsy but finally diagnosed without any sleep abnormality), 16 narcolepsy type 1 without REM sleep behavior disorder (RBD), 9 narcolepsy type 1 with RBD, and 18 narcolepsy type 2. Diagnostic value of metrics in differentiating between groups was quantified by area under the receiver operating characteristic curve (AUC). Correlations among the metrics and cerebrospinal fluid hypocretin-1 (CSF-hcrt-1) values were calculated using linear models. Results: All metrics excluding STREAM found significantly higher muscular activity in narcolepsy 1 cases versus controls (p<0.05). Moreover, RAI showed high sensitivity in the detection of RBD. The mPEM achieved the highest AUC in differentiating healthy controls from narcoleptic subjects. The RAI best differentiated between narcolepsy 1 and 2. Lower CSF-hcrt-1 values correlated with high muscular activity quantified by mPEM, sMAI, iMAI, PEM and FR (p<0.05). Conclusions: This automatic analysis showed higher number of muscle activations in narcolepsy 1 compared to controls. This finding might play a supportive role in diagnosing narcolepsy and in discriminating narcolepsy subtypes. Moreover, the negative correlation between CSF-hcrt-1 level and REM muscular activity supported a role for hypocretin in the control of motor tone during REM sleep.
A Comparison Study of Vector Velocity, Spectral Doppler and Magnetic Resonance of Blood Flow in the Common Carotid Artery

Magnetic resonance phase contrast angiography (MRA) is the gold standard for blood flow evaluation. Spectral Doppler ultrasound (SDU) is the first clinical choice, although the method is angle dependent. Vector flow imaging (VFI) is an angle-independent ultrasound method. The aim of the study was to compare VFI- and SDU-estimated peak systolic velocities (PSV) of the common carotid artery (CCA) with PSV obtained by MRA. Furthermore, intra- and inter-observer agreement was determined. MRA estimates were significantly different from SDU estimates (left CCA: p

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Authors: Brandt, A. H. (Ekstern), Hansen, K. L. (Ekstern), Ewertsen, C. (Ekstern), Holbek, S. (Intern), Olesen, J. B. (Intern), Moshavegh, R. (Intern), Thomsen, C. (Ekstern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
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Automatic Detection of Cortical Arousals in Sleep using Bi-direction LSTM Networks

Cortical arousals are transient events that occur during sleep. Although they can occur naturally, arousals are often used to evaluate sleep-wake dysfunction. The gold standard for detecting arousals is visual inspection of polysomnography recordings. Manual annotation of arousals is time consuming and has been shown to have a high inter- and intra-scorer variation. This study proposes a method to fully automate detection of arousals using recent advances in machine learning.

Methods:
The proposed method in this study extracted features from electroencephalography (EEG), electrooculography (EOG) and chin electromyography (EMG) to compute a probability of arousals through a bi-directional long short-term memory neural network. The study used a dataset of 233 nocturnal PSGs of population-based samples from Wisconsin Sleep Cohort (WSC) and 30 nocturnal PSGs of clinical samples from the Stanford Sleep Cohort (SSC). The model was trained on 186 recordings from WSC and annotations from two scorers. The model was tested on 47 recordings from WSC and then compared to a set of 3 annotations from 9 independent scorers on 30 recordings from both cohorts by measure of Fleiss’ Kappa (level of agreement greater than chance).

Results:
The model obtained a precision of 0.79, a recall of 0.8 and F1-score of 0.79 on the 47 recordings from WSC. The model was robust to different sleep stages showing an F1-score of 0.71 ± 0.19, 0.8 ± 0.13, 0.89 ± 0.18 and 0.8 ± 0.17 (mean ± SD) for N1, N2, N3 and REM sleep, respectively. Preliminary results comparing the scorers show a Fleiss’ Kappa of 0.38 ± 0.12, while including the model predictions result in a Fleiss’ Kappa of 0.4 ± 0.1.

Conclusion:
Cortical arousals were detected automatically with the proposed algorithm with a high performance and robustness to different sleep stages. Preliminary results comparing nine independent scorers demonstrates a low inter-scorer reliability with a similar agreement to the model predictions.
Automatic Detection of Respiratory Events During Sleep Using Bidirectional LSTM Networks

Sleep apnea is a common sleep disorder, which involves cessation of breathing due to obstruction of the upper airway (obstructive) or due to suspension of ventilatory effort (central) during sleep. Currently, sleep apnea is diagnosed using polysomnography (PSG). Breathing events are manually scored by trained sleep technicians, however this is time-consuming, expensive, and prone to subjective interpretation. Thus, the aim of this study was to develop a fully automatic algorithm to detect respiratory events in sleep.

Methods:
Oxygen saturation, nasal pressure (transducer), oral airflow (thermistor), respiratory effort (RIP belts), and snoring signals were extracted from 2,366 PSGs from the Wisconsin Sleep Cohort (age: 59.7 ± 8.4, BMI: 31.6 ± 7.2 (mean±SD)). After filtering, sixteen features (time and frequency domain) were extracted from each signal using a sliding window of ten seconds with eight seconds overlap. Two models were developed based on bidirectional long short-term memory (bLSTM) neural networks: 1) a two-class model for classification of windows as “normal” or “event”, and 2) a four-class model for classification as “normal”, “obstructive”, “central”, or “mixed”. 1882 subjects were used for training; 249 subjects were used for validation. Preliminary results were obtained for a test set of 235 subjects.

Results:
With respect to the total number of events, the two-class model obtained precision of 0.740 and recall of 0.769. The four-class model obtained precision of 0.787, 0.205, and 0.100, and recall of 0.685, 0.190, and 0.0985, for obstructive, central, and mixed events, respectively. The Pearson correlation coefficient between annotated and predicted apnea hypopnea index (AHI) were 0.844 and 0.861 for the two-class and the four-class model, respectively.

Conclusion:
These results indicate that obstructive events can be reliably detected with a bLSTM network. However, the models had difficulties detecting central and mixed events correctly, which were present in a very limited number (1.5 % and 0.21 % of events). Future work includes improving the models for central and mixed event detection.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Stanford University, University of Wisconsin, Copenhagen University Hospital
Authors: Jacobsen, K. P. (Ekstern), Olesen, A. N. (Intern), Trap, L. (Ekstern), Peppard, P. E. (Ekstern), Sorensen, H. B. (Intern), Jennum, P. J. (Ekstern), Mignot, E. (Ekstern)
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Automatic, ECG-based detection of autonomic arousals and their association with cortical arousals, leg movements, and respiratory events in sleep

The current definition of sleep arousals neglects to address the diversity of arousals and their systemic cohesion. Autonomic arousals (AA) are autonomic activations often associated with cortical arousals (CA), but they may also occur in isolation in relation to a respiratory event, a leg movement event or spontaneously, without any other physiological associations. AA should be acknowledged as essential events to understand and explore the systemic implications of arousals. We developed an automatic AA detection algorithm based on intelligent feature selection and advanced machine learning using the electrocardiogram. The model was trained and tested with respect to CA systematically scored in 258 (181 training size/77 test size) polysomnographic recordings from the Wisconsin Sleep Cohort. A precision value of 0.72 and a sensitivity of 0.63 were achieved when evaluated with respect to CA. Further analysis indicated that 81% of the non-CA-associated AAs were associated with leg movement (38%) or respiratory (43%) events. The presented algorithm shows good performance when considering that more than 80% of the false positives (FP) found by the detection algorithm appeared in relation to either leg movement or respiratory events. This indicates that most FP constitute autonomic activations that are indistinguishable from those with cortical cohesion. The proposed algorithm provides an automatic system trained in a clinical environment, which can be utilized to analyse the systemic and clinical impacts of arousals.

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Continuous vital sign monitoring after major abdominal surgery—Quantification of micro events

Introduction: Millions of patients undergo major abdominal surgery worldwide each year, and the post-operative phase carries a high risk of respiratory and circulatory complications. Standard ward observation of patients includes vital sign registration at regular intervals. Patients may deteriorate between measurements, and this may be detected by continuous monitoring. The aim of this study was to compare the number of micro events detected by continuous monitoring to those documented by the widely used standardized Early Warning Score (EWS). Methods: Fifty patients were continuously monitored with peripheral arterial oxygen saturation (SpO2), heart rate (HR), and respiratory rate (RR) the first 4 days after
major abdominal cancer surgery. EWS was monitored as routine practice. Number and duration of events were analyzed using Fisher’s exact test and Wilcoxon rank sum test. Results: Continuous monitoring detected a SpO2 <92% in 98% of patients vs 16% of patients detected by EWS (P < .0001). Micro events of SpO2 <92% lasting longer than 60 minutes were found in 58% of patients by continuous monitoring vs 16% by the EWS (P < .0001). Fifty-two percent of patients had micro events of SpO2 <85% lasting longer than 10 minutes. Continuous monitoring found tachycardia in 60% of patients vs 6% by the EWS. Frequency of events for bradycardia, tachypnea, and bradypnea showed similar patterns. Conclusion: Very low SpO2 and tachycardia in post-operative patients are common and under-diagnosed by the EWS. Continuous monitoring can discover these micro events and potentially contribute to earlier detection and, potentially, result in prevention of clinical complications.
Curvilinear 3-D Imaging Using Row–Column Addressed 2-D Arrays with a Diverging Lens: Phantom Study

A double-curved diverging lens over the flat row–column-addressed (RCA) 2-D array can extend its inherent rectilinear 3-D imaging field-of-view (FOV) to a curvilinear volume region, which is necessary for applications such as abdominal and cardiac imaging. Two concave lenses with radii of 12.7 mm and 25.4 mm were manufactured using RTV664 silicone. The diverging properties of the lenses were evaluated based on simulations and measurements on several phantoms. The measured FOV for both lenses in contact with tissue mimicking phantom were less than 15% different from the theoretical predictions, i.e., a curvilinear FOV of 32°×32° and 24°×24° for the 12.7 mm and 25.4 mm radii lenses. A synthetic aperture imaging sequence with single element transmissions was designed for imaging down to 140 mm at a volume rate of 88 Hz. The performance was evaluated in terms of signal-to-noise ratio (SNR), FOV, and full-width-at-half-maximum (FWHM) of a focused beam. The penetration depths in a tissue mimicking phantom with 0.5 dB/(cm MHz) attenuation were 100 mm and 125 mm for the lenses with radii of 12.7 mm and 25.4 mm. The azimuth, elevation, and radial FWHM at 43 mm depth were (5.8, 5.8, 1)λ and (6, 6, 1)λ. The results of this study confirm that the proposed lens approach is an effective method for increasing the FOV, when imaging with RCA 2-D arrays.
Deep learning has seen significant progress over the last few years, especially in computer vision, where competitions such as the ImageNet challenge have been the driving factor behind many new model architectures far superior to humans in image recognition. We propose a novel method for automatic sleep staging, which relies on current advances in computer vision models eliminating the need for feature engineering or other transformations of input data. By exploiting the high capacity for complex learning in a state of the art object recognition model, we can effectively use raw PSG signals to detect and classify sleep stages in a robust and reliable way.

**Methods:**
A total of 2322 PSG studies from the Wisconsin Sleep Cohort were used in this study. Central and occipital EEG, left and right EOG, and chin EMG signals were extracted from all PSGs and subjected to initial pre-processing of zero-phase Butterworth bandpass filters with AASM-specified cutoffs. The raw signals were then segmented into 30 s epochs and fed as inputs to a novel deep neural network model based on the ResNet-50 architecture. The model was optimized over cross-entropy loss with respect to annotated scorings using the Adam optimizing algorithm and trained on a subset of 1858 PSGs. Hyperparameters were tuned using 40 iterations of random search in relevant hyperparameter intervals. Best performing model was selected based on performance measured by overall accuracy on a hold-out validation set of 232 PSGs.

**Results:**
Training accuracy, precision and recall were 84.93%, 97.42% and 97.02%, respectively. Evaluating on the validation set yielded an overall accuracy of 85.07% and overall precision/recall of 98.54% and 95.72%, respectively.

**Conclusion:**
Preliminary results indicate that state of the art deep learning models can effectively be used to classify sleep stages using untransformed PSG signals. We will perform further testing on independent datasets to enhance the model's utility.
Increasing the field-of-view of row-column-addressed ultrasound transducers: implementation of a diverging compound lens
The purpose of this work is to investigate compound lenses for row-column-addressed (RCA) ultrasound transducers for increasing the field-of-view (FOV) to a curvilinear volume region, while retaining a flat sole to avoid trapping air between the transducer sole and the patient, which would otherwise lead to unwanted reflections. The primary motivation behind this research is to develop a RCA ultrasound transducer for abdominal or cardiac imaging, where a curvilinear volume region is a necessity. RCA transducers provide 3-D ultrasound imaging with fewer channels than fully-addressed 2-D arrays (2N instead of N²), but they have inherently limited FOV. By increasing the RCA FOV, these transducers can be used for the same applications as fully-addressed transducers while retaining the same price range as conventional 2-D imaging due to the lower channel count. Analytical and finite element method (FEM) models were employed to evaluate design options. Composite materials were developed by loading polymers with inorganic powders to satisfy the corresponding speed of sound and specific acoustical impedance requirements. A Bi₂O₃ powder with a density of 8.9 g/cm³ was used to decrease the speed of sound of a room temperature vulcanizing (RTV) silicone, RTV615, from 1.03 mm/μs to 0.792 mm/μs. Using micro-balloons in RTV615 and a urethane, Hapflex 541, their speeds of sound were increased from 1.03 mm/μs to 1.50 mm/μs and from 1.52 mm/μs to 1.93 mm/μs, respectively. A diverging add-on lens was fabricated of a Bi₂O₃ loaded RTV615 and an unloaded Hapflex 541. The lens was tested using a RCA probe, and a FOV of 32.2° was measured from water tank tests, while the FEM model yielded 33.4°. A wire phantom with 0.15 mm diameter wires was imaged at 3 MHz down to a depth of 14 cm using a synthetic aperture imaging sequence with single element transmissions. The beamformed image showed that wires outside the array footprint were visible, demonstrating the increased FOV.
Modelling of ciprofloxacin killing enhanced by hyperbaric oxygen treatment in Pseudomonas aeruginosa PAO1 biofilms

Outline
In chronic lung infections by Pseudomonas aeruginosa (PA) the bacteria thrive in biofilm structures protected from the immune system of the host and from antibiotic treatment. Increasing evidence suggests that the susceptibility of the bacteria to antibiotic treatment can be significantly enhanced by hyperbaric oxygen treatment. The aim of this study is to simulate the effect of ciprofloxacin treatment in a PAO1 biofilm model with aggregates in agarose when combined with hyperbaric oxygen treatment. This is achieved in a reaction-diffusion model that describes the combined effect of ciprofloxacin diffusion, oxygen diffusion and depletion, bacterial growth and killing, and adaptation of the bacteria to ciprofloxacin. In the model, the oxygen diffusion and depletion use a set of parameters derived from experimental results presented in this work. The part of the model describing ciprofloxacin killing uses parameter values from the literature in combination with our estimates (Jacobs, et al., 2016; Grillon, et al., 2016). Micro-respirometry experiments were conducted to determine the oxygen consumption in the P. aeruginosa strain PAO1. The parameters were validated against existing data from an HBOT experiment by Kolpen et al. (2017). The complete oxygen model comprises a reaction-diffusion equation describing the oxygen consumption by using a Michaelis-Menten reaction term. The oxygen model performed well in predicting oxygen concentrations in both time and depth into the biofilm. At 2.8 bar pure oxygen pressure, HBOT increases the penetration depth of oxygen into the biofilm almost by a factor 4 in agreement with the scaling that follows from the stationary balance between the consumption term and diffusion term. Conclusion
In the full reaction-diffusion model we see that hyperbaric oxygen treatment significantly increases the killing by ciprofloxacin in a PAO1 biofilm in alignment with the experimental results from Kolpen et al. (Kolpen, et al., 2017; Kolpen, et al. 2016). The enhanced killing, in turn, lowers the oxygen consumption in the outer layers of the biofilm, and leads to even deeper penetration of oxygen into the biofilm.

General information
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Authors: Gade, P. A. V. (Ekstern), Olsen, T. B. (Ekstern), Jensen, P. (Ekstern), Kolpen, M. (Ekstern), Hoiby, N. (Ekstern), Henneberg, K. (Intern), Sams, T. (Intern)
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Non-invasive Estimation of Pressure Changes using 2-D Vector Velocity Ultrasound: An Experimental Study with In-Vivo Examples

A non-invasive method for estimating intravascular pressure changes using 2-D vector velocity is presented. The method was first validated on computational fluid dynamics (CFD) data, and with catheter measurements on phantoms. Hereafter, the method was tested in-vivo at the carotid bifurcation and at the aortic valve of two healthy volunteers. Ultrasound measurements were performed using the experimental scanner SARUS, in combination with an 8MHz linear array transducer for experimental scans and a carotid scan, whereas a 3.5MHz phased array probe was employed for a scan of an aortic valve. Measured 2-D fields of angle-independent vector velocities were obtained using synthetic aperture imaging. Pressure drops from simulated steady flow through six vessel geometries spanning different degrees of diameter narrowing, running from 20% – 70 %, showed relative biases from 0.35% to 12.06 %, depending on the degree of constriction. Phantom measurements were performed on a vessel with the same geometry as the 70% constricted CFD
model. The derived pressure drops were compared to pressure drops measured by a clinically used 4F catheter and to a finite element model. The proposed method showed peak systolic pressure drops of -3.0 kPa ± 57 Pa, while the catheter and the simulation model showed -5.4 kPa ± 52 Pa and -2.9 kPa, respectively. An in-vivo acquisition of 10 s was made at the carotid bifurcation. This produced eight cardiac cycles from where pressure gradients of -227 Pa ± 15 Pa were found. Lastly, the aortic valve measurement showed a peak pressure drop of -2.1 kPa over one cardiac cycle. In conclusion, pressure gradients from convective flow changes are detectable using 2-D vector velocity ultrasound.
Et nyudviklet peer review-system, der integrerer studenterdata, administration og grafiske procesoversigter, blev afprøvet i et obligatorisk bachelorkursus. Overensstemmelse mellem de studerende og hjælpelærernes kvantitative bedømmelser blev undersøgt for en relativt udfordrende opgave med 15 delspørgsmål. 49 studerende afleverede besvarelser. Efterfølgende blev hver besvarelse bedømt af tre medstuderende, svarende til at 735 delbesvarelser blev bedømt. Ud af disse var der enighed mellem studenterbedømmerne og hjælpelærerne i 480 tilfælde (65 %). I under 3,5 % af tilfældene var der total uenighed. Der var tendens til, at jo mere rigtigt en besvarelse blev bedømt, eller jo mere konkret svaret var, des mere enighed. En interviewundersøgelse hos de studerende viste stor opbakning til fremgangsmåden og viste også, at de studerende fandt det meget nyttigt at se andre studerendes besvarelser såvel som rettevejledningen. Afslutningsvis gives en række anbefalinger til processen og systemet.

**General information**

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Authors: Wilhjelm, J. E. (Intern), Prag, S. W. (Intern)
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BFI (2011): BFI-level 1
Probe development of CMUT and PZT row-column-addressed 2-D arrays

This paper presents the characterization of two prototyped fully integrated 62 + 62 row-column-addressed (RCA) 2-D transducer array probes, which are based on capacitive micromachined ultrasonic transducer (CMUT) and on piezoelectric transducer (PZT) technology, respectively. Both transducers have integrated apodization to reduce ghost echges and were designed with similar acoustical features i.e. 3 MHz center frequency, $\lambda/2$-pitch and 24.8 mm$^2$ × 24.8 mm$^2$ active footprint. The transducer arrays were assembled in a 3-D printed probe handle with electromagnetic shield and integrated electronics for driving the 128-channel coaxial cable to the scanner. The electronics were designed to allow all elements, both rows and columns, to be used interchangeably as either transmitters or receivers. The transducer characterization i.e. bandwidth, phase delay, surface pressure, sensitivity, insertion loss, and acoustical crosstalk, were based on several single element measurements, including pressure and pulse-echo, and were evaluated quantitatively and comparatively. The weighted center frequency was 3.0 MHz for both probes and the measured -6 dB fractional bandwidth was 109 ± 4% and 80 ± 3% for the CMUT and the PZT probe, respectively. The surface pressures of the CMUT and PZT were 0.55 ± 0.06 MPa and 1.68 ± 0.09 MPa, respectively, and the receive sensitivities of the rows (receiving elements) were 12.9 ± 0.7 μV/Pa and 13.7 ± 2.1 μV/Pa.

General information

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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Sound Technology, Inc., BK Ultrasound
Authors: Engholm, M. (Intern), Bouzari, H. (Intern), Christiansen, T. L. (Intern), Beers, C. (Ekstern), Bagge, J. P. (Ekstern), Moesner, L. N. (Ekstern), Diederichsen, S. E. (Intern), Stuart, M. B. (Intern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)
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Scopus rating (2017): SNIP 1.363 SJR 0.699 CiteScore 2.79
Web of Science (2017): Indexed Yes
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Real-time 2-D Phased Array Vector Flow Imaging

Echocardiography examination of the blood flow is currently either restricted to 1-D techniques in real-time or experimental off-line 2-D methods. This paper presents an implementation of transverse oscillation for real-time 2-D vector flow imaging (VFI) on a commercial BK Ultrasound scanner. A large field-of-view (FOV) sequence for studying flow dynamics at 11 frames per second (fps) and a sequence for studying peak systolic velocities (PSV) with a narrow FOV at 36 fps were validated. The VFI sequences were validated in a flow-rig with continuous laminar parabolic flow and in a pulsating flow pump system before being tested in vivo, where measurements were obtained on two healthy volunteers. Mean PSV from 11 cycles was 155 cm s\(^{-1}\) with a precision of ± 9.0% for the pulsating flow pump. In vivo, PSV estimated in the ascending aorta was 135 cm s\(^{-1}\) ± 16.9% for 8 cardiac cycles. Furthermore, in vivo flow dynamics of the left ventricle and in the ascending aorta were visualized. In conclusion, angle independent 2-D VFI on a phased array has been implemented in real-time, and it is capable of providing quantitative and qualitative flow evaluations of both complex and fully transverse flow.

General information

State: Accepted/In press
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, BK Ultrasound, Copenhagen University Hospital
Authors: Holbek, S. (Intern), Hansen, K. L. (Ekstern), Fogh, N. (Forskerdatabase), Moshavegh, R. (Intern), Olesen, J. B. (Intern), Bachmann Nielsen, M. (Ekstern), Jensen, J. A. (Intern)
Number of pages: 9
Reconstructing Dynamic Promoter Activity Profiles from Reporter Gene Data

Accurate characterization of promoter activity is important when designing expression systems for systems biology and metabolic engineering applications. Promoters that respond to changes in the environment enable the dynamic control of gene expression without the necessity of inducer compounds, for example. However, the dynamic nature of these processes poses challenges for estimating promoter activity. Most experimental approaches utilize reporter gene expression to estimate promoter activity. Typically the reporter gene encodes a fluorescent protein that is used to infer a constant promoter activity despite the fact that the observed output may be dynamic and is a number of steps away from the transcription process. In fact, some promoters that are often thought of as constitutive can show changes in activity when growth conditions change. For these reasons, we have developed a system of ordinary differential equations for estimating dynamic promoter activity for promoters that change their activity in response to the environment that is robust to noise and changes in growth rate. Our approach, inference of dynamic promoter activity (PromAct), improves on existing methods by more accurately inferring known promoter activity profiles. This method is also capable of estimating the correct scale of promoter activity and can be applied to quantitative data sets to estimate quantitative rates.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Novo Nordisk Foundation Center for Biosustainability, iLoop, Department of Biotechnology and Biomedicine, Regulatory Genomics, Technical University of Denmark
Authors: Kannan, S. (Ekstern), Sams, T. (Intern), Maury, J. (Intern), Workman, C. T. (Intern)
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Web of Science (2017): Indexed yes
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Web of Science (2015): Indexed yes
Scopus rating (2014): SJR 3.809 SNIP 1.154 CiteScore 3.84
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Respiratory variability of peak velocities in the common femoral vein estimated with vector flow imaging and Doppler ultrasound

Respiratory variability of peak velocities (RVPV) in the common femoral vein measured with ultrasound can reveal venous outflow obstruction. Pulse wave (PW) Doppler is the gold standard for venous velocity estimation of the lower extremities. PW Doppler measurements are angle dependent, whereas vector flow imaging (VFI) can yield angle-independent measures. The hypothesis of the present study was that VFI can provide RVPV estimations without the angle dependency of PW Doppler for an improved venous disease assessment. Sixty-seven patients with symptomatic chronic venous disease were included in the study. On average, VFI measured a lower RVPV than PW Doppler (VFI: 14.11 cm/s; PW: 17.32 cm/s, p=0.002) with a non-significant improved precision compared with PW Doppler (VFI: 21.09%; PW: 26.49%, p=0.08). In a flow phantom, VFI had improved accuracy (p < 0.01) and equal precision compared with PW Doppler. The study indicated that VFI can characterize the hemodynamic fluctuations in the common femoral vein.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Bechsgaard, T. (Ekstern), Hansen, K. L. (Ekstern), Brandt, A. H. (Ekstern), Moshavegh, R. (Ekstern), Forman, J. L. (Ekstern), Føgh, P. (Ekstern), Klitfod, L. (Ekstern), Bækgaard, N. (Ekstern), Lönn, L. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Web of Science (2015): Indexed yes
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Scopus rating (2014): SJR 1.054 SNIP 1.407 CiteScore 2.65
Web of Science (2014): Indexed yes
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ISI indexed (2013): ISI indexed yes
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Scopus rating (2011): SJR 0.952 SNIP 1.437 CiteScore 2.68
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BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.306 SNIP 1.572
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Scopus rating (2008): SJR 1.302 SNIP 1.301
Scopus rating (2007): SJR 1.091 SNIP 1.503
Ultrasound Open Platforms for Next-Generation Imaging Technique Development

Open platform (OP) ultrasound systems are aimed primarily at the research community. They have been at the forefront of the development of synthetic aperture, plane wave, shear wave elastography and vector flow imaging. Such platforms are driven by a need for broad flexibility of parameters that are normally pre-set or fixed within clinical scanners. OP ultrasound scanners are defined to have three key features including customization of the transmit waveform, access to the pre-beamformed receive data and the ability to implement real-time imaging. In this paper, a formative discussion is given on the development of OPs from both the research community and the commercial sector. Both software and hardware based architectures are considered, and their specifications are compared in terms of resources and programmability. Software based platforms capable of real-time beamforming generally make use of scalable graphics processing unit (GPU) architectures, whereas a common feature of hardware based platforms is the use of fieldprogrammable gate array (FPGA) and digital signal processor (DSP) devices to provide additional on-board processing capacity. OPs with extended number of channels (>256) are also discussed in relation to their role in supporting 3-D imaging technique development. With the increasing maturity of OP ultrasound scanners, the pace of advancement in ultrasound imaging algorithms is poised to be accelerated.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, University of Florence, University of Waterloo, University of Leeds
Authors: Boni, E. (Ekstern), Yu, A. C. H. (Ekstern), Freear, S. (Ekstern), Jensen, J. A. (Intern), Tortoli, P. (Ekstern)
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Vector Flow Imaging Compared with Pulse Wave Doppler for Estimation of Peak Velocity in the Portal Vein

The study described here investigated whether angle-independent vector flow imaging (VFI) technique estimates peak velocities in the portal vein comparably to pulsed wave Doppler (PWD). Furthermore, intra- and inter-observer agreement was assessed in a substudy. VFI and PWD peak velocities were estimated with from intercostal and subcostal views for 32 healthy volunteers, and precision analyses were conducted. Blinded to estimates, three physicians rescanned 10 volunteers for intra- and inter-observer agreement analyses. The precision of VFI and PWD was 18% and 28% from an intercostal view and 23% and 77% from a subcostal view, respectively. Bias between VFI and PWD was 0.57 cm/s (p = 0.38) with an intercostal view and 9.89 cm/s (p

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Authors: Brandt, A. H. (Ekstern), Moshavegh, R. (Intern), Hansen, K. L. (Ekstern), Bechsgaard, T. (Ekstern), Lönn, L. (Ekstern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
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Scopus rating (2010): SJR 1.306 SNIP 1.572
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Vector velocity ultrasound—a new ultrasound technique

- Vector flow techniques, with their many advantages over conventional Doppler techniques, are powerful alternatives for blood flow evaluation.
- Vector flow imaging can visualise complex flow; refine the classic flow parameters; and introduce new flow parameters and insonation windows.
- These factors will reduce operator dependency, improve the logistical work flow for users and the diagnostic accuracy for patients.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Lönn, L. (Ekstern), Jensen, J. A. (Intern), Olesen, J. B. (Intern), Nielsen, M. B. (Ekstern), Hansen, K. L. (Ekstern)
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Optimal pseudorandom sequence selection for online c-VEP based BCI control applications
Background: In a c-VEP BCI setting, test subjects can have highly varying performances when different pseudorandom sequences are applied as stimulus, and ideally, multiple codes should be supported. On the other hand, repeating the experiment with many different pseudorandom sequences is a laborious process. Aims: This study aimed to suggest an efficient method for choosing the optimal stimulus sequence based on a fast test and simple measures to increase the performance and minimize the time consumption for research trials. Methods: A total of 21 healthy subjects were included in an online wheelchair control task and completed the same task using stimuli based on the m-code, the gold-code, and the Barker-code. Correct/incorrect identification and time consumption were obtained for each identification. Subject-specific templates were characterized and used in a forward-step first-order model to predict the chance of completion and accuracy score. Results: No specific pseudorandom sequence showed superior accuracy on the group basis. When isolating the individual performances with the highest accuracy, time consumption per identification was not significantly increased. The Accuracy Score aids in predicting what pseudorandom sequence will lead to the best performance using only the templates. The Accuracy Score was higher when the template resembled a delta function the most and when repeated templates were consistent. For completion prediction, only the shape of the template was a significant predictor. Conclusions: The simple and fast method presented in this study as the Accuracy Score, allows c-VEP based BCI
systems to support multiple pseudorandom sequences without increase in trial length. This allows for more personalized BCI systems with better performance to be tested without increased costs.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark
Authors: Isaksen, J. L. (Ekstern), Mohebbi, A. (Ekstern), Puthusserypady, S. (Intern)
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.427 SNIP 1.136 CiteScore 3.32
Web of Science (2015): Indexed yes
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3-D Imaging using Row–Column-Addressed 2-D Arrays with a Diverging Lens: Phantom Study

A double-curved diverging lens over a flat row–column-addressed (RCA) 2-D array can extend its inherent rectilinear 3-D imaging field-of-view (FOV) to a curvilinear volume region, which is necessary for applications such as abdominal and cardiac imaging. A concave lens with radius of 12.7 mm was manufactured using RTV664 silicone. The diverging properties of the lens were evaluated based on measurements on several phantoms. The measured 6 dB FOV in contact with a material similar to human soft tissue was less than 15% different from the theoretical predictions, i.e., a curvilinear FOV of 32° × 32°. A synthetic aperture imaging sequence with single element transmissions was designed for imaging down to 14 cm at a volume rate of 88 Hz. The performance was evaluated in terms of signal-to-noise ratio (SNR), FOV, and full-width-at-half-maximum (FWHM). The penetration depth in a tissue mimicking phantom with 0.5 dB/(cm MHz) attenuation was 13 cm. The results of this study confirm that the proposed lens approach is an effective method for increasing the FOV, when imaging with RCA 2-D arrays.

Accuracy and Precision of Plane Wave Vector Flow Imaging for Laminar and Complex Flow In Vivo

In this study, a comparison between velocity fields for a plane wave 2-D vector flow imaging (VFI) method and a computational fluid dynamics (CFD) simulation is made. VFI estimates are obtained from the scan of a flow phantom, which mimics the complex flow conditions in the carotid artery. Furthermore, the precision of the VFI method is investigated under laminar and complex flow conditions in vivo. The carotid bifurcation of a healthy volunteer was scanned using both fast plane wave ultrasound and magnetic resonance imaging (MRI). The acquired MRI geometry of the bifurcation was used for fabricating an anthropomorphic flow phantom, which was also ultrasound scanned. The same geometry was used in a CFD simulation to calculate the velocity field. Results showed that similar flow patterns and vortices were estimated using CFD and VFI in the phantom. Velocity magnitudes were estimated with a mean difference within 15 %, however, it was 23 % in the external branch. For the in vivo scan, the precision in terms of mean standard deviation (SD) of estimates aligned to the cardiac cycle was highest in the center of the common carotid artery (SD 4.7° for angles) and lowest in the external branch and close to the vessel wall (SD 15.0° for angles).
Acute dosing of vortioxetine strengthens event-related brain activity associated with engagement of attention and cognitive functioning in rats

Studies of the antidepressant vortioxetine have demonstrated beneficial effects on cognitive dysfunction associated with depression. To elucidate how vortioxetine modulates neuronal activity during cognitive processing we investigated the effects of vortioxetine (3 and 10 mg/kg) in rats performing an auditory oddball (deviant target) task. We investigated neuronal activity in target vs non-target tone responses in vehicle-treated animals using electroencephalographic (EEG) recordings. Furthermore, we characterized task performance and EEG changes in target tone responses of vortioxetine vs controls. Quantification of event-related potentials (ERPs) was supplemented by analyses of spectral power and inter-trial phase-locking. The assessed brain regions included prelimbic cortex, the hippocampus, and thalamus. As compared to correct rejection of non-target tones, correct target tone responses elicited increased EEG power in all regions. Additionally, neuronal synchronization was increased in vehicle-treated rats during both early and late ERP responses to target tones. This indicates a significant consistency of local phases across trials during high attentional load. During early sensory processing, vortioxetine increased both thalamic and frontal synchronized gamma band activity and EEG power in all brain regions measured. Finally, vortioxetine increased the amplitude of late hippocampal P3-like ERPs, the rodent correlate of the human P300 ERP. These findings suggest differential effects of vortioxetine during early sensory registration and late endogenous processing of auditory discrimination. Strengthened P3-like ERP response may relate to the pro-cognitive profile of vortioxetine in rodents. Further investigations are warranted to explore the mechanism by which vortioxetine increases network synchronization during attentive and cognitive processing.
Adapted wavelet transform improves time-frequency representations: a study of auditory elicited P300-like event-related potentials in rats.

Objective. Active auditory oddball paradigms are simple tone discrimination tasks used to study the P300 deflection of event-related potentials (ERPs). These ERPs may be quantified by time-frequency analysis. As auditory stimuli cause early high frequency and late low frequency ERP oscillations, the continuous wavelet transform (CWT) is often chosen for decomposition due to its multi-resolution properties. However, as the conventional CWT traditionally applies only one mother wavelet to represent the entire spectrum, the time-frequency resolution is not optimal across all scales. To account for this, we developed and validated a novel method specifically refined to analyse P300-like ERPs in rats. Approach. An adapted CWT (aCWT) was implemented to preserve high time-frequency resolution across all scales by commissioning of multiple wavelets operating at different scales. First, decomposition of simulated ERPs was illustrated using the classical CWT and the aCWT. Next, the two methods were applied to EEG recordings obtained from prefrontal cortex in rats performing a two-tone auditory discrimination task. Main results. While only early ERP frequency changes between responses to target and non-target tones were detected by the CWT, both early and late changes were successfully described with strong accuracy by the aCWT in rat ERPs. Increased frontal gamma power and phase synchrony was observed particularly within theta and gamma frequency bands during deviant tones. Significance. The study suggests superior performance of the aCWT over the CWT in terms of detailed quantification of time-frequency properties of ERPs. Our methodological investigation indicates that accurate and complete assessment of time-frequency components of short-time neural signals is feasible with the novel analysis approach which may be advantageous for characterisation of several types of evoked potentials in particularly rodents.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, Aalborg University, H. Lundbeck A/S
Authors: Richard, N. (Ekstern), Laursen, B. (Ekstern), Grupe, M. (Ekstern), Drewes, A. (Ekstern), Graversen, C. (Ekstern), Sørensen, H. B. D. (Intern), Bastlund, J. (Ekstern)
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Main Research Area: Technical/natural sciences
Adaptive heart rate-based epileptic seizure detection using real-time user feedback

Automated seizure detection in a home environment has been of increased interest the last couple of decades. Heart rate-based seizure detection is a way to detect temporal lobe epilepsy seizures at home, but patient-independent algorithms showed to be insufficiently accurate due to the high patient-dependency of heart rate features. Therefore a real-time adaptive seizure detection algorithm is proposed here. The algorithm starts as a patient-independent algorithm, but gradually converges towards a patient-specific algorithm while more patient-specific data becomes available on-the-run. This is done by using real-time user feedback to annotate previously generated alarms, causing an immediate update to the used support vector machine classifier. Extra procedures are added to the updating procedure in order to cope with potential incorrect user feedback. The adaptive seizure detection algorithm resulted in an overall sensitivity of 77.12% and 1.24 false alarms per hour on over 2833 hours of heart rate data from 19 patients with 153 clinical seizures. This is around 30% less false alarms compared to the patient-independent algorithm. This low-complex adaptive algorithm showed to be able to deal well with incorrect user feedback, making it ideal for implementation in a home environment for a seizure warning system.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, KU Leuven, Roskilde Hospital
Authors: De Cooman, T. (Ekstern), Kjær, T. W. (Ekstern), Van Huffel, S. (Ekstern), Sørensen, H. B. D. (Intern)
Number of pages: 10
Advanced 3-D Ultrasound Imaging: 3-D Synthetic Aperture Imaging using Fully Addressed and Row-Column Addressed 2-D Transducer Arrays.

Compared with conventional 2-D ultrasound imaging, real-time 3-D (or 4-D) ultrasound imaging has several advantages, resulting in a significant progress in the ultrasound imaging instrumentation over the past decade. Viewing the patient’s anatomy as a volume helps physicians to comprehend the important diagnostic information in a noninvasive manner. Diagnostic and therapeutic decisions often require accurate estimates of e.g., organ, cyst, or tumor volumes. 3-D ultrasound imaging can provide these measurements without relying on the geometrical assumptions and operator-dependent skills involved in such estimations using 2-D scans. Although the detail resolution of ultrasound cannot compete with 3-D imaging modalities such as CT and MRI, the combination of patient safety by using nonionizing radiation, cost-effectiveness, portability, and real-time imaging ability makes ultrasound the preferred choice in many clinical applications. Real-time 3-D ultrasound imaging is still not as widespread in use in the clinics as 2-D ultrasound imaging. Two limiting factors have traditionally been the low image quality as well as low volume rate achievable with a 2-D transducer array using the conventional 3-D beamforming technique, Parallel Beamforming. The first part of the scientific contributions of this Ph.D. project demonstrate that 3-D synthetic aperture imaging achieves a better sensitivity and a higher volume rate than the parallel beamforming technique. Data were obtained using both Field II simulations and measurements with the ultrasound research scanner SARUS and a 3.8 MHz 1024 element 2-D transducer array. In all investigations, 3-D synthetic aperture imaging achieved a better resolution, lower side-lobes, higher contrast, and better signal to noise ratio than parallel beamforming. This is achieved partly because synthetic aperture imaging removes the limitation of a fixed transmit focal depth and instead enables dynamic transmit focusing. Particularly, synthetic aperture imaging could increase the achievable volume rate compared with parallel beamforming, to almost 50 times. Lately, the major ultrasound companies have produced ultrasound scanners using 2-D transducer arrays with enough transducer elements to produce high quality 3-D images. Because of the large matrix transducers with integrated custom electronics, these systems are extremely expensive. The relatively low price of ultrasound scanners is one of the factors for the widespread use of ultrasound imaging. The high price tag on the high quality 3-D scanners is limiting their market share.

Row-column addressing of 2-D transducer arrays is a low cost alternative to fully addressed 2-D arrays, for 3-D ultrasound imaging. Using row-column addressing, the number of transducer elements is dramatically reduced. This reduces the interconnection cost and removes the need to integrate custom electronics into the probe. Two downsides of row-column addressing 2-D arrays are its lower lateral resolution due to its one-way focusing compared with two-way focusing in fully addressed 2-D arrays and also the inherent forward-looking imaging field of view. In the second part of the scientific contributions of this Ph.D. project, row-column addressing of 2-D arrays was investigated to assess the possibilities and drawbacks associated with transducer arrays using this addressing scheme, when integrated into probe handles. For that reason, two in-house prototyped 62+62 row-column addressed 2-D array transducer probes were manufactured using capacitive micromachined ultrasonic transducer (CMUT) and piezoelectric transducer (PZT) technology. Based on a set of acoustical measurements the center frequency, bandwidth, surface pressure, sensitivity, and acoustical cross-talks were evaluated and discussed. The imaging quality assessments were carried out based on Field II simulations as well as phantom measurements. Moreover, an analysis on comparing the lateral resolution with a fully addressed array were presented. To improve the imaging sensitivity, spatial matched filter beamforming was used as well as delay-and-sum approach. An analysis on increasing the inherent forward-looking achievable field of view of a flat row-column addressed 2-D array by using a double curved row-column addressed 2-D array was presented. A delay-and-sum beamforming approach suitable for a double curved row-column addressed 2-D array was introduced. Due to challenges on manufacturing double curved 2-D arrays, using a diverging acoustical lens was proposed and its imaging abilities were evaluated based on Field II simulations and measurements. Thereby, the inherent imaging limitation with flat row-column addressed 2-D arrays was overcome by using a diverging lens. Overall, having a low channel count and a large field of view, offers the potential to fabricate arrays with large aperture sizes, which is important for abdominal scans. Thus by using a curved row-column addressed 2-D array, 3-D imaging with equipment in the price range of conventional 2-D imaging could be possible. The main part of the thesis consists of eight scientific papers submitted for international conferences and journals during the Ph.D. project.
A Methodology for Anatomic Ultrasound Image Diagnostic Quality Assessment

This paper discusses methods for assessment of ultrasound image quality based on our experiences with evaluating new methods for anatomic imaging. It presents a methodology to ensure a fair assessment between competing imaging methods using clinically relevant evaluations. The methodology is valuable in the continuing process of method optimization and guided development of new imaging methods. It includes a three phased study plan covering from initial prototype development to clinical assessment. Recommendations to the clinical assessment protocol, software, and statistical analysis are presented. Earlier uses of the methodology has shown that it ensures validity of the assessment, as it separates the influences between developer, investigator, and assessor once a research protocol has been established. This separation reduces confounding influences on the result from the developer to properly reveal the clinical value. The paper exemplifies the methodology using recent studies of Synthetic Aperture Sequential Beamforming tissue harmonic imaging.
A method to investigate the biomechanical alterations in Perthes' disease by hip joint contact modeling

Perthes' disease is a destructive hip joint disorder characterized by malformation of the femoral head in young children. While the morphological changes have been widely studied, the biomechanical effects of these changes still need to be further elucidated. The objective of this study was to develop a method to investigate the biomechanical alterations in Perthes' disease by finite element (FE) contact modeling using MRI. The MRI data of a unilateral Perthes' case was obtained to develop the three-dimensional FE model of the hip joint. The stress and contact pressure patterns in the unaffected hip were well distributed. Elevated concentrations of stress and contact pressure were found in the Perthes' hip. The highest femoral cartilage von Mises stress 3.9 MPa and contact pressure 5.3 MPa were found in the Perthes' hip, whereas 2.4 MPa and 4.9 MPa in the healthy hip, respectively. The healthy bone in the femoral head of the Perthes' hip carries additional loads as indicated by the increase of stress levels around the necrotic-healthy bone interface. Identifying the biomechanical changes, such as the location of stress and contact pressure concentrations, is a prerequisite for the preoperative planning to obtain stress relief for the highly stressed areas in the malformed hip. This single-patient study demonstrated that the biomechanical alterations in Perthes' disease can be evaluated individually by patient-specific finite element contact modeling using MRI. A multi-patient study is required to test the strength of the proposed method as a pre-surgery planning tool.
A New Wavelet-Based ECG Delineator for the Evaluation of the Ventricular Innervation

T-wave amplitude (TWA) has been proposed as a marker of the innervation of the myocardium. Until now, TWA has been calculated manually or with poor algorithms, thus making its use not efficient in a clinical environment. We introduce a new wavelet-based algorithm for the delineation QRS complexes and T-waves, and the automatic calculation of TWA. When validated in the MIT/BIH Arrhythmia database, the QRS detector achieved sensitivity and positive predictive value of 99.84% and 99.87%, respectively. The algorithm was validated also on the QT database and it achieved sensitivity of 99.50% for T-peak detection. In addition, the algorithm achieved delineation accuracy that is similar to the differences in delineation between expert cardiologists. We applied the algorithm for the evaluation of the influence in TWA of anticholinergic and antiadrenergic drugs (i.e., atropine and metoprolol) for healthy subjects. We found that the TWA decreased significantly with atropine and that metoprolol caused a significant increase in TWA, thus confirming the clinical hypothesis that the TWA is a marker of the innervation of the myocardium. The results of this paper show that the proposed algorithm can be used as a useful and efficient tool in clinical practice for the automatic calculation of TWA and its interpretation as a non-invasive marker of the autonomic ventricular innervation.
Aortic Valve Stenosis Increases Helical Flow and Flow Complexity: A Study of Intra-operative Cardiac Vector Flow Imaging

Aortic valve stenosis alters blood flow in the ascending aorta. Using intra-operative vector flow imaging on the ascending aorta, secondary helical flow during peak systole and diastole, as well as flow complexity of primary flow during systole, were investigated in patients with normal, stenotic and replaced aortic valves. Peak systolic helical flow, diastolic helical flow and flow complexity during systole differed between the groups (p < 0.0001), and correlated to peak systolic velocity (R = 0.94, 0.87 and 0.88, respectively). The study indicates that aortic valve stenosis increases helical flow and flow complexity, which are measurable with vector flow imaging. For assessment of aortic stenosis and optimization of valve surgery, vector flow imaging may be useful.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Hansen, K. L. (Ekstern), Møller-Sørensen, H. (Ekstern), Kjaergaard, J. (Ekstern), Jensen, M. B. (Ekstern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
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Automatic Atrial Fibrillation Detection: A Novel Approach Using Discrete Wavelet Transform and Heart Rate Variability

Early detection of Atrial Fibrillation (AF) is crucial in order to prevent acute and chronic cardiac rhythm disorders. In this study, a novel method for robust automatic AF detection (AAFD) is proposed by combining atrial activity (AA) and heart rate variability (HRV), which could potentially be used as a screening tool for patients suspected to have AF. The method includes an automatic peak detection prior to the feature extraction, as well as a noise cancellation technique followed by a bagged tree classification. Simulation studies on the MIT-BIH Atrial Fibrillation database was performed to evaluate the performance of the proposed method. Results from these extensive studies showed very promising results, with an average sensitivity of 96.51%, a specificity of 99.19%, and an overall accuracy of 98.22%.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, Cortrium ApS
Authors: Bruun, I. H. (Ekstern), Hissabu, S. M. S. (Ekstern), Poulsen, E. S. (Ekstern), Puthusserypady, S. (Intern)
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Automatic minimization of ocular artifacts from electroencephalogram: A novel approach by combining Complete Ensemble Empirical Mode Decomposition with Adaptive Noise and Renyi's Entropy

Ocular artifacts (OAs) are one of the major interferences that obscure electroencephalogram (EEG) signals. In this paper, a novel, completely automatic, adaptive and fast method that combines the Complete Ensemble Empirical Mode Decomposition with Adaptive Noise (CEEMDAN) and Renyi's Entropy (RE) is proposed for minimizing the OAs from corrupted EEG signals. The RE criterion is suggested to automatically select the Intrinsic Mode Functions (IMFs) to reconstruct the artifact minimized EEG signals. The scheme requires only a single channel OAs corrupted EEG recording and a reasonable computation time. The methods first evaluated on simulated OAs (one, two, and several blinks as well as saccadic eye movements) corrupted EEG signals and then extended to real EEG signals. The signal-to-noise ratio improvement (SNRimp) along with time and power spectral density (PSD) plots are used for evaluating the performance of the scheme. The method is compared to the one based on the CEEMDAN and manual choice of IMFs for OAs minimization from EEG. Results from extensive simulation studies clearly indicate the efficacy of the proposed scheme in automatically minimizing the OAs from the corrupted EEG signals.

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Authors: Guarascio, M. (Ekstern), Puthusserypady, S. (Intern)
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Automatic Segmentation of Vessels in In-Vivo Ultrasound Scans

Ultrasound has become highly popular to monitor atherosclerosis, by scanning the carotid artery. The screening involves measuring the thickness of the vessel wall and diameter of the lumen. An automatic segmentation of the vessel lumen, can enable the determination of lumen diameter. This paper presents a fully automatic segmentation algorithm, for robustly segmenting the vessel lumen in longitudinal B-mode ultrasound images. The automatic segmentation is performed using a combination of B-mode and power Doppler images. The proposed algorithm includes a series of preprocessing steps, and performs a vessel segmentation by use of the marker-controlled watershed transform. The ultrasound images used in the study were acquired using the bk3000 ultrasound scanner (BK Ultrasound, Herlev, Denmark) with two transducers “8L2 Linear” and “10L2w Wide Linear” (BK Ultrasound, Herlev, Denmark). The algorithm was evaluated empirically and applied to a dataset of in-vivo 1770 images recorded from 8 healthy subjects. The segmentation results were compared to manual delineation performed by two experienced users. The results showed a sensitivity and specificity of 90.41 ± 11.2 % and 97.93 ± 5.7 % (mean ± standard deviation), respectively. The amount of overlap of segmentation and manual segmentation, was measured by the Dice similarity coefficient, which was 91.25 ± 11.6 %. The empirical results demonstrated the feasibility of segmenting the vessel lumen in ultrasound scans using a fully automatic algorithm.

A Vector Flow Imaging Method for Portable Ultrasound Using Synthetic Aperture Sequential Beamforming

This paper presents a vector flow imaging method for the integration of quantitative blood flow imaging in portable ultrasound systems. The method combines directional transverse oscillation (TO) and synthetic aperture sequential beamforming to yield continuous velocity estimation in the whole imaging region. Six focused emissions are used to create a high-resolution image (HRI), and a dual-stage beamforming approach is used to lower the data throughput between the probe and the processing unit. The transmit/receive focal points are laterally separated to obtain a TO in the HRI that allows for the velocity estimation along the lateral and axial directions using a phase-shift estimator. The performance of the method was investigated with constant flow measurements in a flow rig system using the SARUS scanner and a 4.1-MHz linear array. A sequence was designed with interleaved B-mode and flow emissions to obtain continuous data acquisition. A parametric study was carried out to evaluate the effect of critical parameters. The vessel was placed at depths from 20 to 40 mm, with beam-to-flow angles of 65°, 75°, and 90°. For the lateral velocities at 20 mm, a bias
between -5% and -6.2% was obtained, and the standard deviation (SD) was between 6% and 9.6%. The axial bias was lower than 1% with an SD around 2%. The mean estimated angles were $66.70^\circ \pm 2.86^\circ$, $72.65^\circ \pm 2.48^\circ$, and $89.13^\circ \pm 0.79^\circ$ for the three cases. A proof-of-concept demonstration of the real-time processing and wireless transmission was tested in a commercial tablet obtaining a frame rate of 27 frames/s and a data rate of 14 MB/s. An in vivo measurement of a common carotid artery of a healthy volunteer was finally performed to show the potential of the method in a realistic setting. The relative SD averaged over a cardiac cycle was 4.33%.
BCB polymer based row-column addressed CMUT

This paper presents an inexpensive, low temperature and rapid fabrication method for capacitive micromachined ultrasonic transducers (CMUT). The fabrication utilizes the bonding and dielectric properties of the photosensitive polymer Benzocyclobutene (BCB). A BCB based row-column addressed CMUT with integrated apodization has been fabricated and characterized with initial impedance measurement. Furthermore, two linear BCB CMUT arrays have been fabricated with different bottom electrode designs and characterized acoustically. All the fabricated arrays have a center frequency of 2.5 MHz when immersed into water and a pull-in voltage of 75 V. Stability tests have showed a stable coupling coefficient of approximately 0.1 during 10 hours of biased operation. Acoustic measurements, with a hydrophone positioned 1 cm from the CMUTs, have showed a peak-to-peak pressure of 14 kPa.

Breathing disturbances without hypoxia are associated with objective sleepiness in sleep apnea

Determine if defining two subtypes of sleep-disordered breathing (SDB) events - with or without hypoxia - results in measures that are more strongly associated with hypertension and sleepiness. A total of 1,022 subjects with 2,112 nocturnal polysomnograms (PSGs) from the Wisconsin Sleep Cohort were analyzed with our automated algorithm, developed to detect breathing disturbances and desaturations. Breathing events were time-locked to desaturations,
resulting in 2 indices - desaturating (H-BDI) and non-desaturating (NH-BDI) events - regardless of arousals. Measures of subjective (Epworth Sleepiness Scale) and objective (2,981 multiple sleep latency tests from a subset of 865 subjects) sleepiness were analyzed, in addition to clinically relevant clinicodemographic variables. Hypertension was defined as BP ≥140/90 or antihypertensive use. H-BDI, but not NH-BDI, correlated strongly with SDB severity indices that included hypoxia (r=0.89, ps<0.001 with 3% ODI and AHI with 4%-desaturations). A doubling of desaturation-associated events was associated with hypertension prevalence, which was significant for ODI but not H-BDI (3% ODI OR=1.06, 95% CI=1.00-1.12, p

**General information**

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Stanford University, University of Wisconsin-Madison, University of Copenhagen
Authors: Koch, H. (Ekstern), Schneider, L. D. (Ekstern), Finn, L. A. (Ekstern), Leary, E. B. (Ekstern), Peppard, P. E. (Ekstern), Hagen, E. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern), Mignot, E. (Ekstern)
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Scopus rating (2004): SJR 1.401 SNIP 1.787
Scopus rating (2003): SJR 1.113 SNIP 1.441
Scopus rating (2002): SJR 1.193 SNIP 1.436
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Common Carotid Artery Flow Measured by 3-D Ultrasonic Vector Flow Imaging and Validated with Magnetic Resonance Imaging

Ultrasound (US) examination of the common carotid artery was compared with a through-plane magnetic resonance imaging (MRI) sequence to validate a recently proposed technique for 3-D US vector flow imaging. Data from the first volunteer examined were used as the training set, before volume flow and peak velocities were calculated for the remaining eight volunteers. Peak systolic velocities (PSVs) and volume flow obtained with 3-D US were, on average, 34% higher and 24% lower than those obtained with MRI, respectively. A high correlation was observed for PSV ($r = 0.79$), whereas a lower correlation was observed for volume flow ($r = 0.43$). The overall standard deviations were ±5.7% and ±5.7% for volume flow and PSV with 3-D US, compared with ±2.7% and ±3.2% for MRI. Finally, the data were reprocessed with a change in the parameter settings for the echo-canceling filter to investigate its influence on overall performance. PSV was less affected by the re-processing, whereas the difference in volume flow between 3-D vector flow imaging and MRI was reduced to -9%, and with an improved overall standard deviation of ±4.7%. The results illustrate the feasibility of using 3-D US for precise and angle-independent volume flow and PSV estimation in vivo.

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Curvilinear 3-D Imaging Using Row–Column-Addressed 2-D Arrays with a Diverging Lens: Feasibility Study
Constructing a double-curved row–column-addressed (RCA) 2-D array or applying a diverging lens over the flat RCA 2-D array can extend the imaging field-of-view (FOV) to a curvilinear volume without increasing the aperture size, which is necessary for applications such as abdominal and cardiac imaging. Extended FOV and low channel count of double-curved RCA 2-D arrays make 3-D imaging possible with equipment in the price range of conventional 2-D imaging. This study proposes a delay-and-sum beamformation scheme specific to double-curved RCA 2-D arrays and validates its focusing ability based on simulations. A synthetic aperture imaging sequence with single element transmissions is designed for imaging down to 14 cm at a volume rate of 88 Hz. Using a diverging lens with f-number of -1 circumscribing the underlying RCA array, the imaging quality of a double-curved λ/2-pitch 3 MHz 62+62 RCA 2-D array is investigated as a function of depth within a curvilinear FOV of 60°×60°. The simulated double-curved 2-D array exhibits the same full-width-at-halfmaximum values for a point scatterer within its curvilinear FOV at a fixed radial distance compared with a flat 2-D array within its rectilinear FOV. The results of this study demonstrate that the proposed beamforming approach is accurate for achieving correct time-of-flight calculations, and hence avoids geometrical distortions.

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Detection of Paroxysms in Long-Term, Single Channel EEG-Monitoring of Patients with Typical Absence Seizures.
Absence seizures are associated with generalized 2.5-5 Hz spike-wave discharges in the EEG. Rarely are patients, parents or physicians aware of duration or incidence of seizures. Six patients were monitored with a portable EEG-device over four times 24 hours to evaluate how easily outpatients are monitored and how well an automatic seizure detection algorithm can identify the absences. Based on patient-specific modeling, we achieved a sensitivity of 98.4% with only 0.23 false detections per hour. This yields a clinically satisfying performance with a positive predictive value of 87.1%. Portable EEG-Recorders identifying paroxystic events in epilepsy outpatients are a promising tool for patients and physicians dealing with absence epilepsy. Although the small size of the EEG-device, some children still complained about the obtrusive nature of the device. We aim at developing less obtrusive though still very efficient devices e.g. hidden in the ear canal or below the skin.
Diagnostic value of sleep stage dissociation as visualized on a 2-dimensional sleep state space in human narcolepsy

Type 1 narcolepsy (NT1) is characterized by symptoms believed to represent Rapid EyeMovement (REM) sleep stage dissociations, occurrences where features of wake and REM sleep are intermingled, resulting in a mixed state. We hypothesized that sleep stage dissociations can be objectively detected through the analysis of nocturnal Polysomnography (PSG) data, and that those affecting REM sleep can be used as a diagnostic feature for narcolepsy. A Linear Discriminant Analysis (LDA) model using 38 features extracted from EOG, EMG and EEG was used in control subjects to select features differentiating wake, stage N1, N2, N3 and REM sleep. Sleep stage differentiation was next represented in a 2D projection. Features characteristic of sleep stage differences were estimated from the residual sleep stage probability in the 2D space. Using this model we evaluated PSG data from NT1 and non-narcoleptic subjects. An LDA classifier was used to determine the best separation plane. This method replicates the specificity/sensitivity from the training set to the validation set better than many other methods. Eight prominent features could differentiate narcolepsy and controls in the validation dataset. Using a composite measure and a specificity cut off 95% in the training dataset, sensitivity was 43%. Specificity/sensitivity was 94%/38% in the validation set. Using hypersomnia subjects, specificity/sensitivity was 84%/15%. Analyzing treated narcoleptics the specificity/sensitivity was 94%/10%. Sleep stage dissociation can be used for the diagnosis of narcolepsy. However the use of some medications and presence of undiagnosed hyposomnolence patients impacts the result.
Directional Transverse Oscillation Vector Flow Estimation

A method for estimating vector velocities using transverse oscillation (TO) combined with directional beamforming is presented. In Directional Transverse Oscillation (DTO) a normal focused field is emitted and the received signals are beamformed in the lateral direction transverse to the ultrasound beam to increase the amount of data for vector velocity estimation. The approach is self-calibrating as the lateral oscillation period is estimated from the directional signal through a Fourier transform to yield quantitative velocity results over a large range of depths. The approach was extensively simulated using Field IIpro and implemented on the experimental SARUS scanner in connection with a BK Medical 8820e convex array transducer. Velocity estimates for DTO are found for beam-to-flow angles of 60, 75, and 90, and vessel depths from 24 to 156 mm. Using 16 emissions the Standard Deviation (SD) for angle estimation at depths ranging from 24 to 104 mm are between 6.01 and 0.93 with a mean SD of 2.8. The mean relative SD for the lateral velocity component is 9.2% and the mean relative bias -3.4% or 4 times lower than for traditional TO. The approach also works for deeper lying vessels with a slight increase in SD to 15.7%, but a maintained bias of -3.5% from 126 to 156 mm. Data for a pulsating flow has also been acquired for 15 cardiac cycles using a CompuFlow 1000 pump. The relative SD was here 7.4% for a femoral artery waveform.

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Economy, Movement Dynamics, and Muscle Activity of Human Walking at Different Speeds

The complex behaviour of human walking with respect to movement variability, economy and muscle activity is speed dependent. It is well known that a U-shaped relationship between walking speed and economy exists. However, it is an open question if the movement dynamics of joint angles and centre of mass and muscle activation strategy also exhibit a U-shaped relationship with walking speed. We investigated the dynamics of joint angle trajectories and the centre of mass accelerations at five different speeds ranging from 20 to 180% of the predicted preferred speed (based on Froude speed) in twelve healthy males. The muscle activation strategy and walking economy were also assessed. The movement dynamics was investigated using a combination of the largest Lyapunov exponent and correlation dimension. We observed an intermediate stage of the movement dynamics of the knee joint angle and the anterior-posterior and mediolateral centre of mass accelerations which coincided with the most energy-efficient walking speed. Furthermore, the dynamics of the joint angle trajectories and the muscle activation strategy was closely linked to the functional role and biomechanical constraints of the joints.

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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.034 SNIP 1.597 CiteScore 5.3
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.163 SNIP 1.554 CiteScore 4.75
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.998 SNIP 1.57 CiteScore 4.06
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.531 SNIP 0.962 CiteScore 2.44
Electrophysiological dynamics of covert and overt visual attention.

Attention is a key neural function for choosing certain information to receive more processing than others. Attention is allocated either by directly looking at the target (overt) or without eye movement towards the target (covert). The current study was designed to extract relevant features by using steady-state visual evoked potentials (SSVEP) task. SSVEP task was presented to subjects at the same time that the electroencephalography (EEG) signals were recorded by the scalp electrodes. Subjects were instructed to respond to a certain stimulus by pressing a button. This way attention was measure in continuous manner. Results showed that the amplitude of SSVEP frequencies is higher in overt than covert attention. This indicates that by overt attention events are registered with larger power. However, exploring the harmonics of frequencies showed that covert attention generates larger 2nd harmonic (e.g. 12Hz) than the 1st harmonic (e.g. 6Hz). This pattern was not observed in overt attention. We suggest that covert attention increases the non-linearity in the visual system. Results from the source analysis showed that SSVEP signals are extracted from the primary visual cortex in overt attention. However, when covert attention is allocated to SSVEPs, frequencies are extracted from parietal and frontal areas. This shows that covert attention recruits higher cognitive function. To test how SSVEPs are represented in higher brain areas, we conducted an invasive multi-unit recording from rhesus monkeys. Monkeys were trained to perform similar SSVEP task. Recording was done from somatosensory (S1) and motor (M1) cortices. Results showed that the neuronal ring rates in S1 and M1 not only increased selectively to attended icker stimulus, but also they were highly synchronized. Moreover, some SSVEP frequencies was enhanced in single neurons. These results showed, for the rst time, that visual attention to repetitive stimuli is able to regulate neuronal activities in S1 and M1 regions.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen Center for Health Technology, Copenhagen University Hospital
Authors: Ordikhani-Seyedlar, M. (Intern), Puthusserypady, S. (Intern), Kjaer, T. W. (Ekstern), Siebner, H. R. (Ekstern), Sørensen, H. B. D. (Intern)
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Electrophysiological dynamics of covert and overt visual attention.
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Energy Based Clutter Filtering for Vector Flow Imaging
To obtain accurate blood flow velocity estimates it is important to remove the clutter signal originating from tissue. Conventionally, the clutter signal has been separated from the blood signal based on the difference of their spectral frequencies. However, this approach is not enough for obtaining vector flow measurements, since the spectra overlaps at high beam-to-flow angles. In this work a distinct approach is proposed, where the energy of the velocity spectrum is used to differentiate among the two signals. The energy based method is applied by limiting the amplitude of the velocity spectrum function to a predetermined threshold. The effect of the clutter filtering is evaluated on a plane wave (PW) scan sequence in combination with transverse oscillation (TO) and directional beamforming (DB) for velocity estimation. The performance of the filter is assessed by comparison of the velocity estimates of the proposed filter against a conventional moving average clutter filter. The effect of tissue motion is investigated using a Field II simulation of a straight vessel with moving wall, while the direct effect of the filter on the velocity estimates is evaluated on a CFD model of a carotid bifurcation with a fixed vessel wall. The results show that the proposed filter outperformed the moving average during moving vessel wall conditions, where standard deviations from the velocity magnitudes and angles were kept consistently below 6% and 6°.
compared to 63% and 48◦ on the moving average filter. The results on the CFD showed that on non-moving conditions
the velocity estimates had minor statistical differences with errors on the magnitude of -7.95±10.1% and angles of
0.15±6.65◦ for the proposed filter compared to -5.83±9.08% and -0.12±4.48◦.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
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Electronic versions:
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Source: PublicationPreSubmission
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Evaluation of New Ultrasound Techniques for Clinical Imaging in selected Liver and Vascular Applications
This Ph.D. project is based on a longstanding collaboration between physicists and engineers from the Center of Fast
Ultrasound Imaging (CFU) at the Technical University of Denmark and medical doctors from the department of Radiology
at Rigshospitalet. The intent of this cooperation is to validate new ultrasonic methods for future clinical use. Study I
compares two B-mode ultrasound methods: the new experimental technique Synthetic Aperture Sequential Beamforming
combined with Tissue Harmonic Imaging (SASB-THI), and a conventional technique combined with THI. While SASB
reduces the amount of data transformation, thus enabling wireless transmission, THI can improve resolution and image
contrast, and creates fewer artifacts. Thirty-one patients with verified liver tumors were scanned and recordings with and
without visible pathology were performed. Subsequently, eight radiologists evaluated blinded to information about the
technique, which B-mode images they preferred, as well as detection of pathology. Evaluation showed that the techniques
were preferred equally and tumor could be detected equally well.

Study II deals with the ability of vector flow imaging (VFI) to monitor patients with arteriovenous fistulas for hemodialysis
for upcoming stenosis. VFI is an angle-independent method for determining blood flow direction and velocity. Volume can
be determined by integrating the velocity profile multiplied by the cross-sectional area. Nineteen patients were monitored
monthly over a period of six months, and VFI estimates were compared with the reference ultrasound dilution technique
(UDT). VFI volume flow values were not significantly different from UDT and had a better precision. Concordance between
VFI and UDT was high when large volume flow changes (greater than 25%) occurred between dialysis sessions. However,
the methods could not be regarded as interchangeable. Study III deals with VFI's ability to determine peak velocity in the portal vein. The commonly used ultrasound method for this is spectral Doppler, which is known to
overestimate peak velocity when the angle between the blood vessel and the beam is more than 70 degrees; this
overestimation becomes even larger when the angle becomes
larger. VFI can determine the peak velocity angle independently. Thirty-two healthy volunteers were scanned with spectral
Doppler and VFI with two portal vein scan positions (intercostal and subcostal). The study showed that VFI estimates the
same peak velocity as spectral Doppler. Furthermore, VFI has better precision and can estimate the same peak velocity
with a scan position, where spectral Doppler cannot. Finally, inter- and intraobserver agreement is higher for VFI. All three
studies indicate that the techniques can be used in the clinic and probably will be part of everyday practice in the near
future.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging,
Copenhagen University Hospital
Authors: Brandt, A. H. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern), Hansen, K. L. (Ekstern), Hemmsen, M. C.
(Intern)
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Evaluation of respiratory motion correction in PET/CT using a 3D printed phantom

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Authors: Vilsbøll, J. H. (Intern), S. W. Hasler, H. (Ekstern), Duchstein, L. D. L. (Ekstern), Wilhjelm, J. E. (Intern), Lonsdale, M. N. (Ekstern)
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Experimental performance assessment of the sub-band minimum variance beamformer for ultrasound imaging
Recent progress in adaptive beamforming techniques for medical ultrasound has shown that current resolution limits can be surpassed. One method of obtaining improved lateral resolution is the Minimum Variance (MV) beamformer. The frequency domain implementation of this method effectively divides the broadband ultrasound signals into sub-bands (MVS) to conform with the narrow-band assumption of the original MV theory. This approach is investigated here using experimental Synthetic Aperture (SA) data from wire and cyst phantoms. A 7 MHz linear array transducer is used with the SARUS experimental ultrasound scanner for the data acquisition. The lateral resolution and the contrast obtained, are evaluated and compared with those from the conventional Delay-and-Sum (DAS) beamformer and the MV temporal implementation (MVT). From the wire phantom the Full-Width-at-Half-Maximum (FWHM) measured at a depth of 52 mm, is 16.7 μm (0.08λ) for both MV methods, while the corresponding values for the DAS case are at least 24 times higher. The measured Peak-Side-lobe-Level (PSL) may reach ~41 dB using the MVS approach, while the values from the DAS and MVT beamforming are above ~24 dB and ~33 dB, respectively. From the cyst phantom, the power ratio (PR), the contrast-to-noise ratio (CNR), and the speckle signal-to-noise ratio (sSNR) measured at a depth of 30 mm are at best similar for MVS and DAS, with values ranging between ~29 dB and ~30 dB, 1.94 and 2.05, and 2.16 and 2.27 respectively. In conclusion the MVS beamformer is not suitable for imaging continuous targets, and significant resolution gains were obtained only for isolated targets.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Heriot-Watt University, University of Edinburgh
Authors: Diamantis, K. (Ekstern), Greenaway, A. H. (Ekstern), Anderson, T. (Ekstern), Jensen, J. A. (Intern), Sboros, V. (Ekstern)
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BFI (2016): BFI-level 1
Fast Plane Wave 2-D Vector Flow Imaging Using Transverse Oscillation and Directional Beamforming

Several techniques can estimate the 2-D velocity vector in ultrasound. Directional beamforming (DB) estimates blood flow velocities with a higher precision and accuracy than transverse oscillation (TO), but at the cost of a high beamforming load
when estimating the flow angle. In this paper, it is proposed to use TO to estimate an initial flow angle, which is then refined in a DB step. Velocity magnitude is estimated along the flow direction using cross-correlation. It is shown that the suggested TO-DB method can improve the performance of velocity estimates compared to TO, and with a beamforming load, which is 4.6 times larger than for TO and seven times smaller than for conventional DB. Steered plane wave transmissions are employed for high frame rate imaging, and parabolic flow with a peak velocity of 0.5 m/s is simulated in straight vessels at beamto-flow angles from 45 to 90. The TO-DB method estimates the angle with a bias and standard deviation (SD) less than 2, and the SD of the velocity magnitude is less than 2%. When using only TO, the SD of the angle ranges from 2 to 17 and for the velocity magnitude up to 7%. Bias of the velocity magnitude is within 2% for TO and slightly larger but within 4% for TO-DB. The same trends are observed in measurements although with a slightly larger bias. Simulations of realistic flow in a carotid bifurcation model provide visualization of complex flow, and the spread of velocity magnitude estimates is 7.1 cm/s for TO-DB, while it is 11.8 cm/s using only TO. However, velocities for TO-DB are underestimated at peak systole as indicated by a regression value of 0.97 for TO and 0.85 for TO-DB. An in vivo scanning of the carotid bifurcation is used for vector velocity estimations using TO and TO-DB. The SD of the velocity profile over a cardiac cycle is 4.2% for TO and 3.2% for TO-DB.

General information
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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering, Department of Information Technology, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Jensen, J. (Intern), Villagómez Hoyos, C. A. (Intern), Stuart, M. B. (Intern), Ewertsen, C. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 2.94 SJR 1.183 SNIP 1.447
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.73 SJR 0.986 SNIP 1.402
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.814 SNIP 1.494 CiteScore 2.43
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.088 SNIP 1.627 CiteScore 2.18
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.872 SNIP 1.496 CiteScore 2.18
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.802 SNIP 1.479 CiteScore 1.87
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.733 SNIP 1.325 CiteScore 1.95
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Fast Plane Wave Imaging

This PhD project investigates and further develops methods for ultrasound plane wave imaging and blood flow estimation with the objective of overcoming some of the major limitations in conventional ultrasound systems, which are related to low frame rates and only estimation of velocities along the ultrasound beam. The first part of the contribution investigates the compromise between frame rate and plane wave image quality including the influence of grating lobes from a λ-pitch transducer. A method for optimizing the image quality is suggested, and it is shown that the frame rate can be increased by a factor of three without loss of image quality for a particular λ/2-pitch transducer, when compared to a λ-pitch transducer. The second part presents a method for high frame rate 2-D vector flow imaging. The method was validated in simulations and measurements, and it is shown that angles can be estimated with a bias and standard deviation less than 2°, and the velocity magnitude can be estimated with a bias and standard deviation less than 4 % over a large range of beam-to-flow angles. The vector flow method was also investigated under laminar and complex flow conditions in the carotid arteries in ten healthy volunteers. Complex flow patterns were measured in an anthropomorphic flow phantom and showed good agreement with the velocity field simulated using computational fluid dynamics. The last part of the contribution investigates two clinical applications. Plane wave imaging was used for slow velocity flow estimation in the human placenta, which made it possible to map the vessel resistance in several fetal arteries. Finally, vector flow imaging was used for volume flow estimation in patients undergoing dialysis. The sources of error related to the volume flow estimation were investigated, making it possible to compensate for the errors. The developed techniques for plane wave imaging using high frame rates and/or estimation of 2-D vector flow may give the clinicians new tools for assessing the health of blood vessels and aid while examining patients with cardiovascular and organ diseases.

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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering
Authors: Jensen, J. (Intern), Jensen, J. A. (Intern), Stuart, M. B. (Intern)
Number of pages: 210
Flexible Method for the Automated Offline-Detection of Artifacts in Multi-Channel Electroencephalogram Recordings

Electroencephalogram (EEG) signal quality is often compromised by artifacts that corrupt quantitative EEG measurements used in clinical applications and EEG-related studies. Techniques such as filtering, regression analysis and blind source separation are often used to remove these artifacts. However, these preprocessing steps do not allow for complete artifact correction. We propose a method for the automated offline-detection of remaining artifacts after preprocessing in multi-channel EEG recordings. In contrast to existing methods it requires neither adaptive parameters varying between recordings nor a topography template. It is suited for short EEG segments and is flexible with regard to target applications. The algorithm was developed and tested on 60 clinical EEG samples of 20 seconds each that were recorded both in resting state and during cognitive activation to gain a realistic artifact set. Five EEG features were used to quantify temporal and spatial signal variations. Two distance measures for the single-channel and multi-channel variations of these features were defined. The global thresholds were determined by three-fold cross-validation and Youden's J statistic in conjunction with receiver operating characteristics (ROC curves). We observed high sensitivity of 95.5%±4.8 and specificity of 88.8%±2.1. The method has thus shown great potential and is promising as a possible tool for both EEG-based clinical applications and EEG-related research.
High-frame-rate Imaging of a Carotid Bifurcation using a Low-complexity Velocity Estimation Approach

In this paper, a 2-D vector flow imaging (VFI) method developed by combining synthetic aperture sequential beamforming and directional transverse oscillation is used to image a carotid bifurcation. Ninety-six beamformed lines are sent from the probe to the host system for each VFI frame, enabling the possibility of wireless transmission. The velocity is estimated using a relatively inexpensive 2-D phase-shift approach, and real-time performance can be achieved in mobile devices. However, high-frame-rate velocities can be obtained by sending the data to a cluster of computers. The objective of this study is to demonstrate the scalability of the method’s performance according to the needs of the user and the processing capabilities of the host system. In vivo measurements of a carotid bifurcation of a 54-year-old volunteer were conducted using a linear array transducer connected to the SARUS scanner. The velocities were estimated at a rate of 134 independent frames per second (FPS) to reveal complex flow patterns. A peak frame rate of 2140 FPS can be obtained by generating the images recursively. VFI images are shown during the systolic phase revealing the formation of a vortex in the internal carotid artery. The peak systolic velocity from a range gate in the common tract was 0.76 m s⁻¹ with a standard deviation (SD) of 6.1%. The mean velocity profile was calculated from the same range gate with an average SD of 7.86%.

How fast is a collective bacterial state established?

Bacteria in a biofilm colony have the capacity to monitor the size and growth conditions for the colony and modify their phenotypical behaviour to optimise attacks, defence, migration, etc. The quorum sensing systems controlling this involve production and sensing of diffusive signal molecules. Frequently, quorum sensing systems carry a positive feedback loop which produces a switch at a threshold size of the colony. This all-or-none switch can be beneficial to create a sudden attack, leaving a host little time to establish a defence. The reaction-diffusion system describing a basal quorum sensing loop involves production of signal molecules, diffusion of signal molecules, and detection of signal molecules. We study the ignition process in a numerical solution for a basal quorum sensor and demonstrate that even in a large colony the ignition travels through the whole colony in a less than a minute. The ignition of the positive feedback loop was examined in different approximations. As expected, in the exact calculation the ignition was found to be delayed compared to a calculation where the binding of signal molecules was quasistatic. The buffering of signal molecules is found to have little effect on the ignition process. Contrary to expectation, we find that the ignition does not start when the threshold is reached at the center-instead it allows for the threshold to be approached in the whole colony followed by an almost
simultaneous ignition of the whole biofilm aggregate.
Hyperbaric oxygen sensitizes anoxic Pseudomonas aeruginosa biofilm to ciprofloxacin

Chronic Pseudomonas aeruginosa lung infection is characterized by the presence of endobronchial antibiotic-tolerant biofilm subject to strong oxygen (O2) depletion due to the activity of surrounding polymorphonuclear leukocytes. The exact mechanisms affecting the antibiotic susceptibility of biofilms remain unclear, but accumulating evidence suggests that the efficacy of several bactericidal antibiotics is enhanced by stimulation of aerobic respiration of pathogens, while lack of O2 increases their tolerance. In fact, the bactericidal effect of several antibiotics depends on active aerobic metabolism activity and the endogenous formation of reactive O2 radicals (ROS). In this study we aimed to apply hyperbaric oxygen treatment (HBOT) in order to sensitize anoxic P. aeruginosa agarose-biofilms established to mimic situations with intense O2 consumption by the host response in the cystic fibrosis (CF) lung. Application of HBOT resulted in enhanced bactericidal activity of ciprofloxacin at clinically relevant durations and was accompanied by indications of restored aerobic respiration, involvement of endogenous lethal oxidative stress and increased bacterial growth. The findings highlight that oxygenation by HBOT improves the bactericidal activity of ciprofloxacin on P. aeruginosa biofilm and suggest that bacterial biofilms is sensitized to antibiotics by supplying hyperbaric O2.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen, Technical University of Denmark
Authors: Kolpen, M. (Ekstern), Lerche, C. J. (Ekstern), Kragh, K. N. (Ekstern), Sams, T. (Intern), Koren, K. (Ekstern), Jensen, A. S. (Ekstern), Line, L. (Ekstern), Bjarnsholt, T. (Ekstern), Ciofu, O. (Ekstern), Moser, C. (Ekstern), Kühl, M. (Ekstern), Helby, N. (Ekstern), Jensen, P. Ø. (Ekstern)
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Scopus rating (2017): SNIP 1.263 SJR 2.291 CiteScore 4.15
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.21 SJR 2.275 SNIP 1.328
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.343 SNIP 1.361 CiteScore 4.28
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.361 SNIP 1.428 CiteScore 4.45
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.423 SNIP 1.411 CiteScore 4.67
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Improved Focusing Method for 3-D Imaging using Row–Column-Addressed 2-D Arrays

A row–column-addressed (RCA) 2-D array can be interpreted as two orthogonal 1-D arrays. By transmitting with row elements and receiving the echoes through column elements or vice versa, a rectilinear volume in front of the array can be beamformed. Since the transmit and receive 1-D arrays are orthogonal to each other, only one-way focusing is possible in each transmit or receive plane. For applications, where the scatterers are sparse, e.g., in micro-bubble tracking, this study suggests to multiply the envelope data received by the row elements when transmitting with columns as well as the data received by the column elements when transmitting with rows, to improve the focusing. In this way, at each point a two-way focused profile in both transmit and receive directions can be produced. This paper investigates the performance of the new focusing scheme based on simulations and phantom measurements with a PZT λ/2-pitch 3 MHz 62+62 RCA 2-D transducer probe. A synthetic aperture imaging sequence with single element transmissions at a time, is designed for imaging down to 14 cm at a volume rate of 44 Hz.
Investigation of echogenic surface enhancements for improved needle visualization in ultrasonography: A PRISMA systematic review.

Background: Visualization of standard needles at steep angles in clinical Ultrasound (US) images is a problematic and important concern. This systematic review evaluates published studies that investigate echogenic needles and how surface enhancements can improve needle visualization.

Method: A systematic search was performed in five databases: Cochrane Library, Embase (through Ovid), MEDLINE (through PubMed), Scopus, and Web of Science from inception to April 12th, 2017. Each search was based on the search terms: ultrasound, needle, visualization, and comparison, with related synonyms and spelling matters. Results: 29 studies were identified and included in the qualitative synthesis.

Conclusion: Overall, studies agree, that echogenic surface enhancements improve needle visualization in US images at steep angles regardless of target, applied US device and probe, operators, assessors, and methods of assessment.

Myoendothelial coupling through Cx40 contributes to EDH-induced vasodilation in murine renal arteries: evidence from experiments and modelling

Regulation of renal vascular resistance plays a major role in controlling arterial blood pressure. The endothelium participates in this regulation as endothelial derived hyperpolarization plays a significant role in smaller renal arteries and arterioles, but the exact mechanisms are still unknown. To investigate the role of vascular gap junctions and potassium channels in the renal endothelial derived hyperpolarization. In interlobar arteries from wild-type and connexin40 knockout mice, we assessed the role of calcium-activated small (SK) and intermediate (IK) conductance potassium channels. The role of inward rectifier potassium channels (Kir) and Na+ /K+ -ATPases was evaluated as was the contribution from gap junctions. Mathematical models estimating diffusion of ions and electrical coupling in myoendothelial gap junctions were used to interpret the results. Lack of connexin40 significantly reduces renal endothelial hyperpolarization. Inhibition of SK and IK channels significantly attenuated renal EDH to a similar degree in wild-type and knockout mice. Inhibition of Kir and Na+ /K+ -ATPases affected the response in wild-type and knockout mice but at different levels of stimulation. The model confirms that activation of endothelial SK and IK channels generates a hyperpolarizing current that enters the vascular
smooth muscle cells. Also, extracellular potassium increases sufficiently to activate Kir and Na+ /K+ -ATPases. Renal endothelial hyperpolarization is mainly initiated by activation of IK and SK channels. The model shows that hyperpolarization can spread through myoendothelial gap junctions but enough potassium is released to activate Kir and Na+ /K+ -ATPases. Reduced coupling seems to shift the signalling pathway towards release of potassium. However, an alternative pathway also exists and needs to be investigated.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Universität zu Lübeck, University of Copenhagen
Authors: Brasen, J. C. (Intern), de Wit, C. A. (Ekstern), Sorensen, C. M. (Ekstern)
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Web of Science (2018): Indexed yes
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.99 SJR 1.654 SNIP 1.081
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.654 SNIP 1.075 CiteScore 2.78
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.855 SNIP 1.251 CiteScore 3.5
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.66 SNIP 1.083 CiteScore 3.66
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.531 SNIP 1.191 CiteScore 4.05
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.451 SNIP 1.053 CiteScore 2.64
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.268 SNIP 1.119
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.277 SNIP 1.056
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.149 SNIP 1.038
Scopus rating (2007): SJR 1.056 SNIP 0.912
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.219 SNIP 1.12
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.076 SNIP 0.932
Scopus rating (2004): SJR 1.024 SNIP 0.943
Scopus rating (2003): SJR 0.823 SNIP 0.865
Scopus rating (2002): SJR 0.686 SNIP 0.791
Scopus rating (2001): SJR 0.886 SNIP 0.975
Scopus rating (2000): SJR 0.754 SNIP 0.859
Scopus rating (1999): SJR 0.708 SNIP 0.772
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Novel Approach for Automatic Detection of Atrial Fibrillation Based on Inter Beat Intervals and Support Vector Machine

Atrial fibrillation (AF) is the most common cardiac arrhythmia associated with a major economic burden for the society. Automatic detection of AF in long term recordings can efficiently assist in early diagnosis and management of comorbidities associated with AF. This study presents a novel approach for AF detection based on Inter Beat Intervals (IBI) extracted from long term electrocardiogram (ECG) recordings. Five time-domain features are extracted from the IBIs and a Support Vector Machine (SVM) is used for classification. The results are compared to a state of the art algorithm based on raw ECG. Both algorithms are evaluated on the MIT-BIH Atrial Fibrillation database resulting in equally high classification performance (Sensitivity≥ 95%). The proposed approach requires detection of R-peaks in the ECG signal but allows for significantly reduced computation time without loss of performance.

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Output Pressure and Pulse-Echo Characteristics of CMUTs as Function of Plate Dimensions

This paper presents an experimental study of the acoustic performance of Capacitive Micromachined Ultrasonic Transducers (CMUTs) as function of plate dimensions. The objective is to increase the output pressure without decreasing the pulse-echo signal. The CMUTs are fabricated with a LOCOS process, followed by direct wafer fusion bonding to a Silicon-On-Insulator (SOI) wafer. In this way, the plate thickness is determined by the SOI wafer device layer thickness, resulting in CMUTs with plate thicknesses of 2, 9.3 and 15 μm. The corresponding radii and gap heights resulting in an immersion frequency of 5MHz and a pull-in voltage of 200V are obtained using finite element analysis. Hydrophone and plane reflector measurements are used to assess the acoustic performance. Increasing the plate thickness from 2μm to 15μm decreases the pulse-echo bandwidth from >100% to 30%. A maximum in both peak-to-peak output pressure and pulse-echo signal is obtained for the 9.3μm plate, which still has a moderate pulseecho bandwidth of 60%. The 9.3μm plate results in a 1.9 times higher peak-to-peak output pressure and a 3.6 times higher pulse-echo signal compared to the 2μm plate. By adjusting the plate dimensions of a CMUT it is possible to optimize its acoustic performance for medical imaging applications, including visualization of deeper structures in the body, as well as nonlinear imaging such as tissue harmonic imaging.

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Portable Ultrasound Imaging

This PhD project investigates hardware strategies and imaging methods for hand-held ultrasound systems. The overall idea is to use a wireless ultrasound probe linked to general-purpose mobile devices for the processing and visualization. The approach has the potential to reduce the upfront costs of the ultrasound system and, consequently, to allow for a wide-scale utilization of diagnostic ultrasound in any medical specialties and out of the radiology department. The first part of the contribution deals with the study of hardware solutions for the reduction of the system complexity. Analog and digital beamforming strategies are simulated from a system-level perspective. The quality of the B-mode image is evaluated and the minimum specifications are derived for the design of a portable probe with integrated electronics in-handle. The system is based on a synthetic aperture sequential beamforming approach that allows to significantly reduce the data rate between the probe and processing unit. The second part investigates the feasibility of vector flow imaging in a hand-held ultrasound system. Vector flow imaging overcomes the limitations of conventional imaging methods in terms of flow angle compensation. Furthermore, high frame rate can be obtained by using synthetic aperture focusing techniques. A method is developed combining synthetic aperture sequential beamforming and directional transverse oscillation to achieve the wireless transmission of the data along with a relatively inexpensive 2-D velocity estimation. The performance of the method is thoroughly assessed through simulations and measurements, and in vivo investigations are carried out to show its potential in presence of complex flow dynamics. A sufficient frame rate is achieved to allow for the visualization of vortices in the carotid bifurcation. Furthermore, the method is implemented on a commercially available tablet to evaluate the real-time processing performance in the built-in GPU with concurrent wireless transmission of the data. Based on the demonstrations in this thesis, a flexible framework can be implemented with performance that can be scaled to the needs of the user and according to the computing resources available. The integration of high-frame-rate vector flow imaging in a hand-held ultrasound scanner, in addition, has the potential to improve the operator’s workflow and opens the way to new possibilities in the clinical practice.
**Prediction of Motion Induced Image Degradation Using a Markerless Motion Tracker**

In this work a markerless motion tracker, TCL2, is used to predict image quality in 3D T1 weighted MPRAGE MRI brain scans. An experienced radiologist scored the image quality for 172 scans as being usable or not usable, i.e. if a repeated scan was required. Based on five motion parameters, a classification algorithm was trained and an accuracy for identifying not usable images of 95.9% was obtained with a sensitivity of 91.7% and specificity of 96.3%. This work shows the feasibility of the markerless motion tracker for predicting image quality with a high accuracy.

**Queue-based modelling and detection of parameters involved in stroke outcome**

We designed a queue-based model, and investigated which parameters are of importance when predicting stroke outcome. Medical record forms have been collected for 57 ischemic stroke patients, including medical history and vital sign measurement along with neurological scores for the first twenty-four hours of admission. The importance of each parameter is identified using multiple regression combined with a circular queue to iteratively fit outcome. Out of 39 parameters, the model isolated 14 which combined could estimate outcome with a root mean square error of 1.69 on the Scandinavian Stroke Scale, where outcome for patients were 36.75 ± 10.99. The queue-based model integrating multiple linear regression shows promising results for automatic selection of significant medically relevant parameters.

**Real-time Implementation of Synthetic Aperture Vector Flow Imaging on a Consumer-level Tablet**

In this work, a 2-D vector flow imaging (VFI) method based on synthetic aperture sequential beamforming (SASB) and directional transverse oscillation is implemented on a commercially available tablet. The SASB technique divides the beamforming process in two parts, whereby the required data rate between the probe and back-end can be reduced by a factor of 64 compared to conventional delay-and-sum focusing. The lowered data rate enables real-time wireless transfer for both B-mode and VFI data. In the present setup, element data were acquired from a straight vessel with the SARUS research scanner and processed by a first-stage beamformer in a fixed focus. The data were subsequently transferred to an HTC Nexus 9 tablet through an ASUS RT-AC68U Wi-Fi router to simulate a wireless probe. The second-stage beamforming of the B-mode and flow data and the velocity estimation were implemented on the tablet's built-in GPU (Nvidia Tegra K1) through the OpenGL ES 3.1 API. Real-time performance was achieved with rates up to 26 VFI frames per second (38 ms/frame) for concurrent processing and Wi-Fi transmission.
Revision of the qualification framework at the Technical University of Denmark Part 1: Concepts

When the Technical University of Denmark (DTU) adopted the National Qualification Framework (NQF), it was implemented as an add-on to the existing concept in place for describing educational outcomes, rather than by redesigning the educational outcomes themselves. The system in place does not emphasize the type and extent of knowledge, skills, and competencies adequately to facilitate programme development and evaluations. In this work, an expansion and reorganization of the qualification elements in the NQF at DTU is proposed as a means to facilitate a more detailed design and evaluation of the educational programmes. The top level categories of knowledge, skills, and competencies are reorganized into four categories: -to know, - to be, -to interact, and -to do. Knowledge of praxis is a new element in the category -to know. The new category, -to be, includes mind-set development and self-instruction. The category, -to interact, includes competencies in communication and teamwork. The category, -to do, includes operative skills and competencies in problem solving. Each of the four main categories contain a number of qualification elements. Suitable taxonomies are suggested for each of the main categories.

Revision of the qualification framework at the Technical University of Denmark Part 2: Applications

Using a revised Qualification Framework (QF) with four main categories: -to know, - to be, -to interact, and -to do, this paper demonstrates how to use the elements of the QF to construct Programme-Qualification Matrices. A general Programme- Qualification Matrix defines the qualifications and their respective conceptual understanding common to all engineering programmes. This is complemented by programme-specific qualification matrices with added emphasis on content and context. Redesigned educational outcomes for three bachelor programmes are presented to demonstrate the versatility of the concept.

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Simulating CMUT Arrays Using Time Domain FEA

PZFlex is a commercial FEA software that has been optimized for the ultrasound industry and is commonly used to design piezoelectric ultrasound transducers. However, PZFlex is not commonly used within the CMUT research field. Nevertheless, it has an explicit modeling approach allowing large structures like CMUT arrays to be modeled and its transient analysis intrinsically supplies non-linear and broadband results from a single run. A 3-D model of a CMUT array is developed with multiple cells in each element and one active element surrounded by N passive elements. It is demonstrated that the electro-mechanics can precisely be predicted, within 3%, including the pull-in voltage and the spring softening effect. The transmit impulse response is simulated by deconvolving the extrapolated pressure with the excitation pulse, and it is in excellent agreement with the measured. It is shown that the impulse response can directly be used in Field II to assess the image quality of the transducer using the lateral, axial and cystic resolution for two different CMUT designs.

Spatial Filter Feature Extraction Methods for P300 BCI Speller: A Comparison

Brain Computer Interface (BCI) systems enable subjects affected by neuromuscular disorders to interact with the outside world. A P300 speller uses Event Related Potential (ERP) components, generated in the brain in the presence of a target stimulus, to extract information about the user’s intent. Several methods have been proposed for spatial filtering and classification of the P300 components. In this study, xDAWN algorithm, Independent Component Analysis (ICA) and Principal Component Analysis (PCA) methods are used and evaluated based on the classification performance of two different classifiers, namely the Support Vector Machine (SVM) and Fisher’s Linear Discriminant Analysis (FLDA). In addition, it is shown that the incorporation of some prior knowledge regarding the location of P300 elicitation on the scalp can reduce the computational load while maintaining or even improving the classification performance.
Stenosis of the superficial femoral artery evaluated in-vivo with vector concentration - a novel ultrasound vector velocity derived flow parameter for measurement of flow complexity

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ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
This paper aims to develop a method for achieving micrometre axial scatterer localization for medical ultrasound, surpassing the inherent, pulse length dependence limiting ultrasound imaging. Methods: The method, directly translated from cellular microscopy, is based on multi-focal imaging and the simple, aberration dependent, image sharpness metric of a single point scatterer. The localization of a point scatterer relies on the generation of multiple overlapping sharpness curves, created by deploying three foci during receive processing, and by assessing the sharpness values after each acquisition as a function of depth. Each derived curve peaks around the receive focus and the unique position of the scatterer is identified by combining the data from all curves using a maximum likelihood algorithm with a calibration standard. Results: Simulated and experimental ultrasound point scatter data show that the sharpness method can provide scatterer axial localization with an average accuracy down to 10.21 µm (≈ λ/21) and with up to 11.4 times increased precision compared to conventional localization. The improvements depend on the rate of change of sharpness using each focus, and the signal to noise ratio in each image. Conclusion: Super-resolution axial imaging from optical microscopy has been successfully translated into ultrasound imaging by using raw ultrasound data and standard beamforming. Significance: The normalized sharpness method has the potential to be used in scatterer localization applications and contribute in current super-resolution ultrasound imaging techniques.
Synthetic Aperture Sequential Beamforming using Spatial Matched Filtering

Synthetic Aperture Sequential Beamforming (SASB) has shown to achieve a good resolution and high penetration depth. The low complexity at the transducer level of the beamformer makes it ideal for use with a handheld device. SASB with a low F# (≤ 0.5) can achieve even better resolution at the cost of high grating lobes, which causes loss of contrast in the final image. In this paper, Spatial Matched Filtering (SMF) was used instead the second stage of beamformer, in an attempt to suppress the grating lobes. The advantage of SMF over SASB was investigated by pushing the limits of F#, from 1.5 to 0.5. The effect of the number of emissions used in first stage was also investigated. A 3.3 MHz BK Ultrasound 9040 convex array was simulated in Field II on a point scatter phantom and a cyst phantom. The resolution was quantified with the full-width-half-max (FWHM), and the contrast was measured with the 20 dB cystic resolution. The contrast-to-noise ratio (CNR) was calculated for the cyst mimicking phantom. The results showed that SMF achieved similar resolution as SASB and improved grating lobe suppression leading to an increase in contrast. The grating lobes caused by an F# of 0.5 are dominant in the SASB images, but not as much in SMF images. The CNR for a cyst mimicking phantom was improved 7 dB and 6 dB for SMF over SASB at depth 20 mm and 30 mm, with an F# of 0.5 and 256 emissions. The FWHM for SMF was slightly higher than SASB across all depth and parameter settings, with a maximum difference of 0.3 mm. It was demonstrated that SMF can achieve similar resolution to SASB and for certain parameter settings improve the contrast by suppressing the grating lobe artifacts.

Technological aided assessment of the acutely ill patient - The case of postoperative complications

Surgical interventions come with complications and highly reported mortality after major surgery. The mortality may be a result of delayed detection of severe complications due to lower monitoring frequency in the general wards. Several studies have shown that continuous monitoring is superior to the manually intermittent recorded monitoring in terms of detecting abnormal physiological signs. Hopefully improved observations may result in earlier detection and clinical intervention. This narrative review will describe current monitoring possibilities for postoperative patients and how it may prevent complications. Several wireless systems are being developed for monitoring vital parameters, but many of these are not yet validated for critically ill patients. The ultimate goal with patient monitoring and detect of events is to prevent postoperative complications, death and costs in the health care system. A few studies indicate that monitoring systems detect deteriorating patients earlier than the nurses, and this was associated with less clinical instability. An important caveat of future devices is to assess their effect in relevant patient populations and not only in healthy test-subjects. Implementation of novel technologies is expensive although expected to be cost-effective if just few adverse events can be prevented. The future is here with promising devices and the possibility to give an unprecedented precise risk estimation of adverse post-surgical events. Next step is to integrate existing evidence based treatment algorithms to demonstrate the clinical efficacy of implementing the new technology.
Transmitting Performance Evaluation of ASICs for CMUT-Based Portable Ultrasound Scanners

Portable ultrasound scanners (PUS) have, in recent years, raised a lot of attention, as they can potentially overcome some of the limitations of static scanners. However, PUS have a lot of design limitations including size and power consumption. These restrictions can compromise the image quality of the scanner. In order to overcome these restrictions, application specific integrated circuits (ASICs) are needed to implement the electronics. In this work, a comparative study of the transmitting performance of a capacitive micromachined ultrasonic transducer (CMUT) driven by a commercial generic ultrasound transmitter and an ASIC optimized for CMUT-based PUS is presented. A single CMUT element is pulsed with a 1% dutycycle at a frequency of 5 MHz. The DC bias voltage is 80 V and the pulsing voltage is 20 V. The acoustic performance is assessed by comparing the ultrasonic signals measured with a hydrophone both in the time and frequency domains. The difference in normalized signal amplitude evaluated at the center frequency of the CMUT is −1.9 dB and the measured bandwidth is equivalent. The ASIC consumes only 1.3% of the total power consumption used by the commercial transmitter.
Ultrasonic 3-D Vector Flow Method for Quantitative In Vivo Peak Velocity and Flow Rate Estimation
Current clinical ultrasound (US) systems are limited to show blood flow movement in either 1-D or 2-D. In this paper, a method for estimating 3-D vector velocities in a plane using the transverse oscillation method, a 32×32 element matrix array, and the experimental US scanner SARUS is presented. The aim of this paper is to estimate precise flow rates and peak velocities derived from 3-D vector flow estimates. The emission sequence provides 3-D vector flow estimates at up to 1.145 frames/s in a plane, and was used to estimate 3-D vector flow in a cross-sectional image plane. The method is validated in two phantom studies, where flow rates are measured in a flow-rig, providing a constant parabolic flow, and in a straight-vessel phantom (Ø=8 mm) connected to a flow pump capable of generating time varying waveforms. Flow rates are estimated to be 82.1 ± 2.8 L/min in the flow-rig compared with the expected 79.8 L/min, and to 2.68 ± 0.04 mL/stroke in the pulsating environment compared with the expected 2.57 ± 0.08 mL/stroke. Flow rates estimated in the common carotid artery of a healthy volunteer are compared with magnetic resonance imaging (MRI) measured flow rates using a 1-D through-plane velocity sequence. Mean flow rates were 333 ± 31 mL/min for the presented method and 346 ± 2 mL/min for the MRI measurements.

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BFI (2016): BFI-level 2
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.814 SNIP 1.494 CiteScore 2.43
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.088 SNIP 1.627 CiteScore 2.18
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.872 SNIP 1.496 CiteScore 2.18
ISI indexed (2013): ISI indexed yes
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Vector and Doppler Ultrasound Velocities Evaluated in a Flow Phantom and the Femoropopliteal Vein

Ultrasound is used for evaluating the veins of the lower extremities. Operator and angle dependency limit spectral Doppler ultrasound (SDUS). The aim of the study was to compare peak velocity measurements in a flow phantom and the femoropopliteal vein of 20 volunteers with the angle-independent vector velocity technique vector flow imaging (VFI) and SDUS. In the flow phantom, VFI underestimated velocity (p = 0.01), with a lower accuracy of 5.5% (p = 0.01) and with no difference in precision, that is, error factor, compared with SDUS (VFI: 1.02 vs. SDUS: 1.02, p = 0.58). In vivo, VFI estimated lower velocities (femoral: p = 0.001; popliteal: p = 0.001) with no difference in precision compared with SDUS (femoral: VFI 1.09 vs. SDUS 1.14, p = 0.37; popliteal: VFI 1.13 vs. SDUS 1.06, p = 0.09). In conclusion, the precise VFI technique can be used to characterize venous hemodynamics of the lower extremities despite its underestimation of velocities.
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ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.957 SNIP 1.458 CiteScore 2.66
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.952 SNIP 1.437 CiteScore 2.68
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.306 SNIP 1.572
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.11 SNIP 1.464
BFI (2008): BFI-level 2
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Scopus rating (2007): SJR 1.091 SNIP 1.503
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.292 SNIP 1.68
Scopus rating (2005): SJR 1.378 SNIP 1.66
Scopus rating (2004): SJR 1.214 SNIP 1.677
Web of Science (2004): Indexed yes
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Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.52 SNIP 1.244
Web of Science (2002): Indexed yes
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Vector Flow Imaging Compared with Conventional Doppler Ultrasound and Thermodilution for Estimation of Blood Flow in the Ascending Aorta

Transverse oscillation (TO) is a real-time ultrasound vector flow method implemented on a commercial scanner. The TO setup was examined on a flowrig with constant and pulsatile flow. Subsequently, 25 patients undergoing cardiac bypass surgery were scanned intraoperatively with TO on the ascending aorta and compared to transesophageal echocardiography (TEE) and pulmonary artery catheter thermodilution (PACTD). On the flowrig, TO had a precision of 5.5%, 9.4% and 14.7%, a percentage error of 18.2%, 14.6% and 40.7%, and a mean bias of 0.4 cm/s, 36.8 ml/min and 32.4 ml/min for velocity and flow rate (constant and pulsatile) estimation. The correlation coefficients for all flowrig evaluations were 0.99 indicating systematic bias. After bias correction, the percentage error was reduced to 11.5%, 12.6% and 15.9% for velocity and flow rate (constant and pulsatile) estimation. In the in vivo setup, TO, TEE, and PACTD had a precision of 21.9%, 13.7%, and 12.0%. TO compared with TEE and PACTD had a mean bias of 12.6 cm/s and -0.08 l/min, and a percentage error of 23.4%, and 36.7%, respectively. The percentage error was reduced to 22.9% for the TEE comparison, but increased to 43.8% for the PACTD comparison, after correction for the systematic bias found in the flowrig. TO is a reliable and precise method for velocity and flow rate estimation on a flowrig. However, TO with the present setup, is not interchangeable with PACTD for cardiac volume flow estimation, but is a reliable and precise angle-independent ultrasound alternative for velocity estimation of cardiac flow.

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Scopus rating (2011): SJR 0.768 SNIP 0.716 CiteScore 1.63
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Vector velocity estimation of blood flow – A new application in medical ultrasound

Vector flow techniques in the field of ultrasound encompass different pulse emission and estimation strategies. Numerous techniques have been introduced over the years, and recently commercial implementations usable in the clinic have been made. A number of clinical papers using different vector velocity approaches have been published. This review will give an overview of the most significant in vivo results achieved with ultrasound vector flow techniques, and will outline some of the possible clinical applications for vector velocity estimation in the future.

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Scopus rating (2009): SJR 0.111 SNIP 0.097
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Velocity Estimation in Medical Ultrasound

This article describes the application of signal processing in medical ultrasound velocity estimation. Special emphasis is on the relation among acquisition methods, signal processing, and estimators employed. The description spans from current clinical systems for one-and two-dimensional (1-D and 2-D) velocity estimation to the experimental systems for three-dimensional (3-D) estimation and advanced imaging sequences, which can yield thousands of images or volumes per second with fully quantitative flow estimates. Here, spherical and plane wave emissions are employed to insonify the whole region of interest, and full images are reconstructed after each pulse emission for use in velocity estimation.

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Scopus rating (2016): SJR 2.158 SNIP 5.304 CiteScore 8.96
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Scopus rating (2015): SJR 2.39 SNIP 5.878 CiteScore 8.15
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.71 SNIP 5.067 CiteScore 5.86
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Vital Signs Monitoring and Interpretation for Critically Ill Patients

In current clinical practice, vital signs such as heart rate, blood pressure, oxygen saturation level, respiratory rate and temperature are continuously measured for critically ill patients. Monitored by medical devices, each vital sign provides information about basic body functions and allows medical staff to intervene if health deteriorates. It has been documented that most of the alarms provided by the devices do not require actions, and that this occurs mainly because the signals are treated individually without context. The overload in alarms forces medical staff to make priority decisions, and can cause critical scenarios leading to a patient’s death be overseen. The focus of this project was investigating clinical applicability of combining vital signs for critically ill patients. Several approaches were developed and tested with increasingly homogeneous patient groups. The first study presents a data-driven approach to representation of a patient’s physiological condition by combining vital signs into Early Warning Scores (EWS). Data were collected for 57 critically ill patients who had each been admitted to the intensive care unit at Bispebjerg Hospital for several days. To evaluate the estimation of physiological condition, text-based electronic health records (EHR) were collected, and time-labeled entries were extracted through algorithms from Natural Language Processing (NLP). The combination of EWS and NLP enabled the development of a system which could present and quantify a physiological condition timeline for patients. Promising results were obtained with EWS as measure, in which patients with EWS ≥ 8.5 passed away while all patients who were admitted for over 53 hours with EWS < 6.5 survived. The second study focused on ischemic stroke patients at Zealand University Hospital. Since all patients had same cause of admission and similar comorbidities, they were a more homogeneous critical patient group than in the first study. To predict the degree of disability after one day of admission, features based on vital signs and medical history were used in two prediction models. An introduced queue-based multiple linear regression (qMLR) model achieved best results with a root mean square error (RMSE) of RMSE = 3.11 on a Scandinavian Stroke Scale (SSS) where degree of disability ranged from 0 - 46. Worse outcomes were observed in patients who had pulse > 80 and a negative correlation between systolic and diastolic blood pressures during the first two hours of admission. The final study dealt with classification of diabetes mellitus (DM) in ischemic stroke patients, where current findings indicate that one third of patients have unrecognized DM. A support vector machine was trained using vital signs and medical history, and correctly classified whether patients had DM with an accuracy of 87.5%. The overall conclusion is that vital signs have high potential in applications for critically ill patients. Context-awareness through grouping with existing admission data is a prerequisite, unless vital signs are used to detect a specifically defined pathological events.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Bispebjerg University Hospital, Copenhagen University Hospital
Volumetric 3-D Vector Flow Measurements using a 62×62 Row-Column Addressed Array

Experimental results from volumetric 3-D vector flow measurements using a 62×62 row-column addressed (RCA) array are presented. A plane-by-plane steered transmit sequence and its post processing steps are described for obtaining 3-D vector flow in a volume. A modified version of the transverse oscillation (TO) velocity estimator is used, which exploits the focal lines generated with the tall elements of a RCA array. Validation of the method is made in a flow rig system where circulating blood mimicking fluid produced a steady parabolic flow profile with a flow rate of 13.7 mL/s, translating to a peak velocity of 24.1 cm/s. A volume rate of 16.4 volumes per second is obtained, and estimated flow rates based on nine steered planes within the volume are investigated. A positive bias is found for all investigated planes lying in the range from 6.5% to 21.2% with the standard deviation being less than 4% for all cases. It is concluded that volumetric 3-D vector flow estimation is feasible with an RCA array with only 124 elements.

3-D Imaging using Row–Column-Addressed 2-D Arrays with a Diverging Lens

It has been shown that row–column-addressed (RCA) 2-D arrays can be an inexpensive alternative to fully addressed 2-D arrays. Generally imaging with an RCA 2-D array is limited to its forward-looking volume region. Constructing a double-curved RCA 2-D array or applying a diverging lens over the flat RCA 2-D array, can extend the imaging field-of-view (FOV) to a curvilinear volume without increasing the aperture size, which is necessary for applications such as abdominal and cardiac imaging. Extended FOV and low channel count of double-curved RCA 2-D arrays make it possible to have 3-D imaging with equipment in the price range of conventional 2-D imaging. This study proposes a delay-and-sum (DAS) beamformation scheme specific to double-curved RCA 2-D arrays and validates its focusing ability based on simulations. A synthetic aperture imaging (SAI) sequence with single element transmissions at a time, is designed for imaging down to 14 cm at a volume rate of 88 Hz. The curvilinear imaging performance of a λ/2-pitch 3 MHz 62×62 RCA 2-D array is investigated as a function of depth, using a diverging lens with f-number of -1. The results of this study demonstrate that the proposed beamforming approach is accurate for achieving correct time-of-flight calculations, and hence avoids geometrical distortions.
3-D Vector Flow Estimation With Row–Column-Addressed Arrays

Simulation and experimental results from 3-D vector flow estimations for a 62 × 62 2-D row–column (RC) array with integrated apodization are presented. A method for implementing a 3-D transverse oscillation (TO) velocity estimator on a 3-MHz RC array is developed and validated. First, a parametric simulation study is conducted, where flow direction, ensemble length, number of pulse cycles, steering angles, transmit/receive apodization, and TO apodization profiles and spacing are varied, to find the optimal parameter configuration. The performance of the estimator is evaluated with respect to relative mean bias $\bar{B}$ and mean standard deviation $\bar{\sigma}$. Second, the optimal parameter configuration is implemented on the prototype RC probe connected to the experimental ultrasound scanner SARUS. Results from measurements conducted in a flow-rig system containing a constant laminar flow and a straight-vessel phantom with a pulsating flow are presented. Both an M-mode and a steered transmit sequence are applied. The 3-D vector flow is estimated in the flow rig for four representative flow directions. In the setup with 90° beam-to-flow angle, the relative mean bias across the entire velocity profile is $(-4.7, -0.9, 0.4)\%$ with a relative standard deviation of $(8.7, 5.1, 0.8)\%$ for $(v_x, v_y, v_z)$. The estimated peak velocity is $48.5 \pm 3$ cm/s giving a $-3\%$ bias. The out-of-plane velocity component perpendicular to the cross section is used to estimate volumetric flow rates in the flow rig at a 90° beam-to-flow angle. The estimated mean flow rate in this setup is $91.2 \pm 3.1$ L/h corresponding to a bias of $-11.1\%$. In a pulsating flow setup, flow rate measured during five cycles is $2.3 \pm 0.1$ mL/stroke giving a negative $9.7\%$ bias. It is concluded that accurate 3-D vector flow estimation can be obtained using a 2-D RC-addressed array.
3-D vector flow imaging, Blood flow, Medical ultrasound, Row-column addressed arrays, Transverse oscillation

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3-D Vector Flow Imaging
For the last decade, the field of ultrasonic vector flow imaging has gotten an increasingly attention, as the technique offers a variety of new applications for screening and diagnostics of cardiovascular pathologies. The main purpose of this PhD project was therefore to advance the field of 3-D ultrasonic vector flow estimation and bring it a step closer to a clinical application. A method for high frame rate 3-D vector flow estimation in a plane using the transverse oscillation method combined with a 1024 channel 2-D matrix array is presented. The proposed method is validated both through phantom studies and in vivo. Phantom measurements are compared with their corresponding reference value, whereas the in vivo measurement is validated against the current golden standard for non-invasive blood velocity estimates, based on magnetic resonance imaging (MRI). The study concludes, that a high precision was achieved and that estimates were comparable with MRI derived results. However, the large channel count of the applied transducer hinders a commercial implementation of the 3-D method for two main reasons: The large and heavy connection cable is impractical for clinical use, and the high channel count hampers the task of real-time processing. In a second study, some of the issue with the 2-D matrix array are solved by introducing a 2-D row-column (RC) addressing array with only 62 + 62 elements. It is investigated both through simulations and via experimental setups in various flow conditions, if this significant reduction in the element count can still provide precise and robust 3-D vector flow estimates in a plane. The study concludes that the RC array is capable of estimating precise 3-D vector flow both in a plane and in a volume, despite the low channel count. However, some inherent new challenges are introduced with the array. The major disadvantage with an RC transducer, is the limited field-of-view, which is restricted to the forward looking array. It is discussed, that this drawback may be solved with a diverging lens, providing a larger field-of-view, due the the dispersion of the energy. Based on the presented results it is concluded that 3-D vector flow using TO is a feasible method for obtaining angle-independent estimates of e.g. peak velocities and flow rates at a high frame rate for clinical applications. Moreover, the RC array offers a setup allowing for real-time processing.

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3-D Vector Flow Using a Row-Column Addressed CMUT Array
This paper presents an in-house developed 2-D capacitive micromachined ultrasonic transducer (CMUT) applied for 3-D blood flow estimation. The probe breaks with conventional transducers in two ways; first, the ultrasonic pressure field is generated from thousands of small vibrating micromachined cells, and second, elements are accessed by row and/or column indices. The 62+62 2-D row-column addressed prototype CMUT probe was used for vector flow estimation by transmitting focused ultrasound into a flow-rig with a fully developed parabolic flow. The beam-to-flow angle was 90°. The received data was beamformed and processed offline. A transverse oscillation (TO) velocity estimator was used to estimate the 3-D vector flow along a line originating from the center of the transducer. The estimated velocities in the lateral and axial direction were close to zero as expected. In the transverse direction a characteristic parabolic velocity profile was estimated with a peak velocity of 0.48 m/s ± 0.02 m/s in reference to the expected 0.54 m/s. The results presented are the first 3-D vector flow estimates obtained with a row-column CMUT probe, which demonstrates that the CMUT technology is feasible for 3-D flow estimation.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Center for Fast Ultrasound Imaging, Sound Technology, Inc., BK Ultrasound
Authors: Holbek, S. (Intern), Christiansen, T. L. (Intern), Engholm, M. (Intern), Lei, A. (Intern), Stuart, M. B. (Intern), Beers, C. (Ekstern), Moesner, L. N. (Ekstern), Bagge, J. P. (Ekstern), Thomsen, E. V. (Intern), Jensen, J. A. (Intern)
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Accurate Angle Estimator for High-Frame-rate 2-D Vector Flow Imaging

This paper presents a novel approach for estimating 2-D flow angles using a high-frame-rate ultrasound method. The angle estimator features high accuracy and low standard deviation (SD) over the full 360° range. The method is validated on Field II simulations and phantom measurements using the experimental ultrasound scanner SARUS and a flow rig before being tested in vivo. An 8-MHz linear array transducer is used with defocused beam emissions. In the simulations of a spinning disk phantom, a 360° uniform behavior on the angle estimation is observed with a median angle bias of 1.01° and a median angle SD of 1.8°. Similar results are obtained on a straight vessel for both simulations and measurements, where the obtained angle biases are below 1.5° with SDs around 1°. Estimated velocity magnitudes are also kept under 10% bias and 5% relative SD in both simulations and measurements. An in vivo measurement is performed on a carotid bifurcation of a healthy individual. A 3-s acquisition during three heart cycles is captured. A consistent and repetitive vortex is observed in the carotid bulb during systoles.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Villagómez Hoyos, C. A. (Intern), Stuart, M. B. (Intern), Lindskov Hansen, K. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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A comparative study of pseudorandom sequences used in a c-VEP based BCI for online wheelchair control

In this study, a c-VEP based BCI system was developed to run on three distinctive pseudorandom sequences, namely the m-code, the Gold-code, and the Barker-code. The Visual Evoked Potentials (VEPs) were provoked using these codes. In the online session, subjects controlled a LEGO® Mindstorms® robot around a fixed track. Choosing the optimal code proved a significant increase in accuracy (p...
A comprehensive performance analysis of EEMD-BLMS and DWT-NN hybrid algorithms for ECG denoising

Electrocardiogram (ECG) is a widely used non-invasive method to study the rhythmic activity of the heart. These signals, however, are often obscured by artifacts/noises from various sources and minimization of these artifacts is of paramount importance for detecting anomalies. This paper presents a thorough analysis of the performance of two hybrid signal processing schemes ((i) Ensemble Empirical Mode Decomposition (EEMD) based method in conjunction with the Block Least Mean Square (BLMS) adaptive algorithm (EEMD-BLMS), and (ii) Discrete Wavelet Transform (DWT) combined with the Neural Network (NN), named the Wavelet NN (WNN)) for denoising the ECG signals. These methods are compared to the conventional EMD (C-EMD), C-EEMD, EEMD-LMS as well as the DWT thresholding (DWT-Th) based methods through extensive simulation studies on real as well as noise corrupted ECG signals. Results clearly show the superiority of the proposed methods.
A framework for simulating ultrasound imaging based on first order nonlinear pressure–velocity relations.

An ultrasound imaging framework modeled with the first order nonlinear pressure–velocity relations (NPVR) based simulation and implemented by a half-time staggered solution and pseudospectral method is presented in this paper. The framework is capable of simulating linear and nonlinear ultrasound propagation and reflections in a heterogeneous medium with different sound speeds and densities. It can be initialized with arbitrary focus, excitation and apodization for multiple individual channels in both 2D and 3D spatial fields. The simulated channel data can be generated using this framework, and ultrasound image can be obtained by beamforming the simulated channel data. Various results simulated by different algorithms are illustrated for comparisons. The root mean square (RMS) errors for each compared pulses are calculated. The linear propagation is validated by an angular spectrum approach (ASA) with a RMS error of 3% at the focal point for a 2D field, and Field II with RMS errors of 0.8% and 1.5% at the electronic and the elevation focuses for 3D fields, respectively. The accuracy for the NPVR based nonlinear propagation is investigated by comparing with the Abersim simulation for pulsed fields and with the nonlinear ASA for monochromatic fields. The RMS errors of the nonlinear pulses calculated by the NPVR and Abersim are respectively 2.4%, 7.4%, 17.6% and 36.6% corresponding to initial pressure amplitudes of 50 kPa, 200 kPa, 500 kPa and 1 MPa at the transducer. By increasing the sampling frequency for the strong nonlinearity, the RMS error for 1 MPa initial pressure amplitude is reduced from 36.6% to 27.3%.
Analog Gradient Beamformer for a Wireless Ultrasound Scanner.
This paper presents a novel beamformer architecture for a low-cost receiver front-end, and investigates if the image quality can be maintained. The system is oriented to the development of a hand-held wireless ultrasound probe based on Synthetic Aperture Sequential Beamforming, and has the advantage of effectively reducing circuit complexity and power dissipation. The array of transducers is divided into sub-apertures, in which the signals from the single channels are aligned through a network of cascaded gradient delays, and summed in the analog domain before A/D conversion. The delay values are quantized to simplify the shifting unit, and a single A/D converter is needed for each sub-aperture yielding a compact, low-power architecture that can be integrated in a single chip. A simulation study was performed using a 3.75 MHz convex array, and the point spread function (PSF) for different configurations was evaluated in terms of lateral full-width-at-half-maximum (FWHM) and −20 dB cystic resolution (CR). Several setups were simulated varying the sub-aperture size N and the quantization step, and design constraints were obtained comparing the PSF to that of an ideal non-quantized system. The PSF is shown for $N = 32$ with a quantization step of 12 ns. For this configuration, the FWHM is degraded by 0.25% and the CR is 8.70% lower compared to the ideal situation. The results demonstrate that the gradient beamformer provides an adequate image quality, and open the way to a fully-integrated chip for a compact, low-cost, wireless ultrasound probe.
Analysis of Systolic Backflow and Secondary Helical Blood Flow in the Ascending Aorta Using Vector Flow Imaging

Secondary rotational flow and systolic backflow are seen in the ascending aorta and, in this study, were analyzed with the vector velocity method transverse oscillation. Twenty-five patients were scanned intra-operatively, and the vector velocities were related to estimates of transesophageal echocardiography and pulmonary artery catheter thermodilution, and associated with gender, age, aortic diameter, atherosclerotic plaques, left ventricular ejection fraction and previous myocardial infarctions. Secondary flow was present for all patients. The duration and rotational frequency (p <0.001) and the duration and flow direction of the secondary flow (p <0.002) were associated. Systolic backflow was present in 40% of the patients and associated with systolic velocities (p <0.002) and the presence of atherosclerotic plaques (p <0.001). No other significant associations were observed. The study indicates that backflow is injurious and that secondary flow is a normal flow phenomenon. The study also shows that transverse oscillation can provide new information on blood flow in the ascending aorta.
An improved minimum variance beamforming applied to plane-wave imaging in medical ultrasound

Minimum variance beamformer (MVB) is an adaptive beamformer which provides images with higher resolution and contrast in comparison with non-adaptive beamformers like delay and sum (DAS). It finds weight vector of beamformer by minimizing output power while keeping the desired signal unchanged. We used the eigen-based MVB and generalized coherence factor (GCF) to further improve the quality of MVB beamformed images. The eigen-based MVB projects the weight vector with a transformation matrix constructed from eigen-decomposing of the array covariance matrix that increases resolution and contrast. GCF is used to emphasis on coherence part of images that improves the resolution. Four different datasets provided by IUS 2016 beamforming challenge are used to evaluate the proposed method. In comparison with DAS with rectangular weight vector, our method improved contrast about 8.52 dB and 6.20 dB for simulation and experimental contrast phantoms, respectively. It also enhanced lateral (axial) resolution about 87% (40%) and 73% (21%) for simulated and experimental resolution phantoms, respectively.
A Noise-Assisted Data Analysis Method for Automatic EOG-Based Sleep Stage Classification Using Ensemble Learning

Reducing the number of recording modalities for sleep staging research can benefit both researchers and patients, under the condition that they provide as accurate results as conventional systems. This paper investigates the possibility of exploiting the multisource nature of the electrooculography (EOG) signals by presenting a method for automatic sleep staging using the complete ensemble empirical mode decomposition with adaptive noise algorithm, and a random forest classifier. It achieves a high overall accuracy of 82% and a Cohen’s kappa of 0.74 indicating substantial agreement between automatic and manual scoring.

A novel array processing method for precise depth detection of ultrasound point scatter

A signal based algorithm resulting in increased depth resolution is presented for medical ultrasound. It relies on multiple foci beamforming that is enabled by current ultrasound imaging systems. The concept stems from optical microscopy and is translated here into ultrasound using the Field II simulation software. A 7 MHz linear transducer is used to scan a single point scatterer phantom that can move in the axial direction. Individual beamformer outputs from 3 different foci are post-processed using the highly-dependent on focusing errors, metric of sharpness to estimate the position of the point scatter. A 37.8 μm uncertainty in depth estimation is achieved, which attains an almost 3-fold improvement compared to conventional ultrasound imaging axial resolution. Future work on the development of this algorithm requires experimental validation in tissue-like materials that provide strong aberrations.
Application of a New Robust ECG T-Wave Delineation Algorithm for the Evaluation of the Autonomic Innervation of the Myocardium

T-wave amplitude (TWA) is a well-known index of the autonomic innervation of the myocardium. However, until now it has been evaluated only manually or with simple and inefficient algorithms. In this paper, we developed a new robust single-lead electrocardiogram (ECG) T-wave delineation algorithm that is able to detect the T-wave with a wavelet-based method and automatically calculate the TWA. We evaluated the algorithm on the QT database, achieving a sensitivity of 99.92% for the T wave peak and 99.38% for the T wave end. In addition, the percentage of records automatically delineated with high precision was higher than previous published works. Finally, the algorithm was applied to study the influence of anticholinergic and antidiurenergic drugs (i.e. atropine and metoprolol) on the TWA. It was observed that atropine significantly decreased the TWA when compared to baseline level, that head-up tilt caused a decrease of TWA and that metoprolol blunted this decrease. Through the development of a robust algorithm, this study opens the way for further research on the T-wave analysis for the assessment of the autonomic innervation of the ventricular myocardium.
ultrasound are addressed in this PhD project. They touch upon gain adjustments in ultrasound, automatic synthetic aperture image quality optimization, automated vessel segmentation in ultrasound, and lack of CAD in point-of-care lung ultrasound. The goals of this PhD are achieved for each of the subjects. First, a new automated time gain compensation technique is proposed that compensates for gains of the scans in 2-D. The proposed model outperforms the current 1-D curve compensation in commercial scanners, as the 2-D topology of the scans are not fully integrated in those techniques. Second, an automated generic technique is proposed for optimization of synthetic aperture image quality. This generic model can be used for any imaging regime using any transducer geometry. Third, a hybrid vessel segmentation technique is proposed that combines both vector velocity estimates (VFI) and B-mode images. The technique enables the wall-to-wall visualization of VFI, as well as provides a firm ground for quantitative quantification of VFI in state-of-the-art US scanners. Finally, a new technique is introduced to detect disease-related reverberation artifacts in lung ultrasound, thereby exploiting the full potential of this imaging modality.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Technical University of Denmark
Authors: Moshavegh, R. (Intern), Jensen, J. A. (Intern), Hemmsen, M. C. (Intern), Martins, B. (Ekstern)
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Blood flow velocity in the Popliteal Vein using Transverse Oscillation Ultrasound.
Chronic venous disease is a common condition leading to varicose veins, leg edema, post-thrombotic syndrome and venous ulcerations. Ultrasound (US) is the main modality for examination of venous disease. Color Doppler and occasionally spectral Doppler US (SDUS) are used for evaluation of the venous flow. Peak velocities measured by SDUS are rarely used in a clinical setting for evaluating chronic venous disease due to inadequate reproducibility mainly caused by the angle dependency of the estimate. However, estimations of blood velocities are of importance in characterizing venous disease. Transverse Oscillation US (TOUS), a non-invasive angle independent method, has been implemented on a commercial scanner. TOUS’s advantage compared to SDUS is a more elaborate visualization of complex flow. The aim of this study was to evaluate, whether TOUS perform equal to SDUS for recording velocities in the veins of the lower limbs. Four volunteers were recruited for the study. A standardized flow was provoked with a cuff compression-decompression system placed around the lower leg. The average peak velocity in the popliteal vein of the four volunteers was 151.5 cm/s for SDUS and 105.9 cm/s for TOUS (p < 0.001). The average of the peak velocity standard deviations (SD) were 17.0 cm/s for SDUS and 13.1 cm/s for TOUS (p < 0.005). The study indicates that TOUS estimates lower peak velocity with improved SD when compared to SDUS. TOUS may be a tool for evaluation of venous disease providing quantitative measures for the evaluation of venous blood flow.

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Authors: Bechsgaard, T. (Ekstern), Lindskov Hansen, K. (Ekstern), Brandt, A. H. (Ekstern), Holbek, S. (Intern), Lönn, L. (Ekstern), Strandberg, C. (Forskerdatabase), Bækgaard, N. (Forskerdatabase), Bachmann Nielsen, M. (Ekstern), Jensen, J. A. (Intern)
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Capacitive Substrate Coupling of Row–Column-Addressed 2-D CMUT Arrays

Row–column-addressed CMUT arrays suffer from low receive sensitivity of the bottom elements due to a capacitive coupling to the substrate. The capacitive coupling increases the parasitic capacitance. A simple approach to reduce the parasitic capacitance is presented, which is based on depleting the semiconductor substrate. To reduce the parasitic capacitance by 80% the bulk doping concentration should be at most $10^{12} \text{ cm}^{-3}$. Experimental results show that the parasitic capacitance can be reduced by 87% by applying a substrate potential of 6V relative to the bottom electrodes. The depletion of the semiconductor substrate can be sustained for at least 10 minutes making it applicable for row–column-addressed CMUT arrays for ultrasonic imaging. Theoretically the reduced parasitic capacitance indicates that the receive sensitivity of the bottom elements can be increased by a factor of 2:1.

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Contribution of K+ channels to endothelium-derived hypolocalization-induced renal vasodilation in rats in vivo and in vitro.

We investigated the mechanisms behind the endothelium-derived hyperpolarization (EDH)-induced renal vasodilation in vivo and in vitro in rats. We assessed the role of Ca2+-activated K+ channels and whether K+ released from the endothelial cells activates inward rectifier K+ (Kir) channels and/or the Na+/K+-ATPase. Also, involvement of renal myoendothelial gap junctions was evaluated in vitro. Isometric tension in rat renal interlobar arteries was measured using a wire myograph. Renal blood flow was measured in isoflurane anesthetized rats. The EDH response was defined as the ACh-induced vasodilation assessed after inhibition of nitric oxide synthase and cyclooxygenase using L-NAME and indomethacin, respectively. After inhibition of small conductance Ca2+-activated K+ channels (SKCa) and intermediate conductance Ca2+-activated K+ channels (IKCa) (by apamin and TRAM-34, respectively), the EDH response in vitro was strongly attenuated whereas the EDH response in vivo was not significantly reduced. Inhibition of Kir channels and Na+/K+-ATPases (by ouabain and Ba2+, respectively) significantly attenuated renal vasorelaxation in vitro but did not affect the response in vivo. Inhibition of gap junctions in vitro using carbamoloxolone or 18a-glycyrrhetinic acid significantly reduced the endothelial-derived hyperpolarization-induced vasorelaxation. We conclude that SKCa and IKCa channels are important for EDH-induced renal vasorelaxation in vitro. Activation of Kir channels and Na+/K+-ATPases plays a significant role in the renal vascular EDH response in vitro but not in vivo. The renal EDH response in vivo is complex and may consist of several overlapping mechanisms some of which remain obscure.
Calcium activated K+ channels, Endothelial-derived hyperpolarization, Renal, Vasodilation
Diffusion Retardation by Binding of Tobramycin in an Alginate Biofilm Model.

Microbial cells embedded in a self-produced extracellular biofilm matrix cause chronic infections, e. g. by Pseudomonas aeruginosa in the lungs of cystic fibrosis patients. The antibiotic killing of bacteria in biofilms is generally known to be reduced by 100–1000 times relative to planktonic bacteria. This makes such infections difficult to treat. We have therefore proposed that biofilms can be regarded as an independent compartment with distinct pharmacokinetics. To elucidate this pharmacokinetics we have measured the penetration of the tobramycin into seaweed alginate beads which serve as a model of the extracellular polysaccharide matrix in P. aeruginosa biofilm. We find that, rather than a normal first order saturation curve, the concentration of tobramycin in the alginate beads follows a power-law as a function of the external concentration. Further, the tobramycin is observed to be uniformly distributed throughout the volume of the alginate bead. The power-law appears to be a consequence of binding to a multitude of different binding sites. In a diffusion model these results are shown to produce pronounced retardation of the penetration of tobramycin into the biofilm. This filtering of the free tobramycin concentration inside biofilm beads is expected to aid in augmenting the survival probability of bacteria residing in the biofilm.
Elimination of Second-Harmonics in CMUTs using Square Pulse Excitation

The harmonic imaging mode is today a fundamental part of ultrasound imaging; it is not only used for suppressing the grating lobe artifact, but also to reduce many other acoustical artifacts in the ultrasound image. A vital performance parameter for accepting CMUT probes as a clinical usable transducer technology is, that it can support harmonic imaging. The large bandwidth of the CMUT is a clear advantage for harmonic imaging, but the inherent nonlinear behavior of the CMUT poses an issue as it is difficult to dissociate the harmonics generated in the tissue from the harmonic content of the transmitted signal. This work presents how proper pulse coding of a bipolar pulser, which is present in most commercial ultrasound scanners, can reduce the intrinsic generated harmonic to fundamental pressure amplitude ratio to below −35 dB, making CMUT probes usable for clinical applications.
Evaluation of healthy muscle tissue by strain and shear wave elastography – Dependency on depth and ROI position in relation to underlying bone

Purpose: The aim of this study was to evaluate the influence of depth and underlying bone on strain ratios and shear wave speeds for three different muscles in healthy volunteers. For strain ratios the influence from different reference region-of-interest positions was also evaluated. Material and methods: Ten healthy volunteers (five males and five females) had their biceps brachii, gastrocnemius, and quadriceps muscle examined with strain- and shear wave elastography at three different depths and in regions located above bone and beside bone. Strain ratios were averaged from cine-loops of 10 s length, and shear wave speeds were measured 10 times at each target point. The distance from the skin surface to the centre of each region-of-interest was measured. Measurements were evaluated with descriptive statistics and linear regression. Results: Linear regression showed a significant influence on strain ratio measurements from the reference region-of-interest position, i.e. being above the same structures as the target region-of-interest or not (means: 1.65 and 0.78; \( P < 0.001 \)). For shear wave speeds, there was a significant influence from depth and location above or beside bone (\( P = 0.011 \) and \( P = 0.031 \)). Conclusion: Strain ratio values depend significantly on reference and target region-of-interest being above the same tissue, for instance bone. Strain ratios were not influenced by depth in this study. Shear wave speeds decreased with increasing scanning depth and if there was bone below the region-of-interest.
Experimental 3-D Vector Velocity Estimation with Row-Column Addressed Arrays

Experimental 3-D vector flow estimates obtained with a 62+62 2-D row-column (RC) array with integrated apodization are presented. A transverse oscillation (TO) velocity estimator is implemented on a 3.0 MHz RC array, to yield realtime 3-D vector flow in a cross-sectional scan plane at 750 frames per second. The method is validated in a straight-vessel phantom (Ø = 8 mm) connected to a flow pump capable of generating time-varying carotid waveforms. The out-of-plane velocity component perpendicular to the cross section of the vessel and the cross-sectional area is used to estimate volumetric flow rates. The flow rate measured from five cycles is 2.3 mL/stroke ± 0.1 mL/stroke giving a negative 9.7% bias compared to the pump settings. It is concluded that 124 elements are sufficient to estimate 3-D vector flow, if they are positioned in a row-column wise manner.

General information

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Authors: Holbek, S. (Intern), Stuart, M. B. (Intern), Jensen, J. A. (Intern)
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Fabrication of Capacitive Micromachined Ultrasonic Transducers Using a Boron Etch-Stop Method

Capacitive Micromachined Ultrasonic Transducers (CMUTs) fabricated using Silicon-On-Insulator (SOI) wafers often have large thickness variation of the flexible plate, which causes variation in both pull-in voltage and resonant frequency across the CMUT array. This work presents a bond and boron etch-stop scheme for fabricating the flexible plate of a CMUT. The proposed fabrication method enables precise control of the plate thickness variation and is a low cost alternative to the SOI-based process. N-type silicon wafers are doped with boron to a surface concentration of \(> 10^{20} \text{cm}^{-3}\) using solid planar diffusion predeposition at 1125 °C for 30, 60, and 90 min. Process simulations are used to predict the boron doping profiles and validated with secondary ion mass spectrometry measurements. The doped wafers are fusion-bonded to a silicon dioxide surface and thinned down using an 80 °C, 20 wt% potassium hydroxide solution with isopropyl alcohol added to increase the etch selectivity to the highly doped boron layer. The resulting plate thickness uniformity is estimated from scanning electron micrographs to a mean value of 2.00μm±2.5%. The resonant frequency in air for a 1-D linear CMUT array is measured to 12MHz±2.5%. Furthermore, hydrophone measurements show that the fabricated devices can be used to emit sound pressure in the ultrasonic frequency domain.

General information
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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Technical University of Denmark
Authors: Diederichsen, S. E. (Intern), Sandborg-Olsen, F. (Ekstern), Engholm, M. (Intern), Lei, A. (Intern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)
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Publication: Research - peer-review › Article in proceedings – Annual report year: 2016

High Frame Rate Synthetic Aperture 3D Vector Flow Imaging
3-D blood flow quantification with high spatial and temporal resolution would strongly benefit clinical research on cardiovascular pathologies. Ultrasonic velocity techniques are known for their ability to measure blood flow with high precision at high spatial and temporal resolution. However, current volumetric ultrasonic flow methods are limited to one velocity component or restricted to a reduced field of view (FOV), e.g. fixed imaging planes, in exchange for higher temporal resolutions. To solve these problems, a previously proposed accurate 2-D high frame rate vector flow imaging (VFI) technique is extended to estimate the 3-D velocity components inside a volume at high temporal resolutions (< 1 ms). The full 3-D vector velocities are obtained from beamformed volumetric data using synthetic aperture (SA) techniques combined with a 2-D matrix array. The method is validated using Field II simulations of flow along a straight vessel phantom and with complex flow from a 3-D computational fluid dynamics (CFD) model of a carotid bifurcation. Results from the simulations show that the 3-D velocity components are estimated with a mean relative bias of -12.8%, -10% and 1.42% for the Vx, Vy and Vz respectively; each presented a mean relative standard deviation of 11.8%, 12.3% and 1.11%.

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Authors: Villagómez Hoyos, C. A. (Intern), Holbek, S. (Intern), Stuart, M. B. (Intern), Jensen, J. A. (Intern)
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Main Research Area: Technical/natural sciences
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High frame rate synthetic aperture vector flow imaging for transthoracic echocardiography.

This work presents the first in vivo results of 2-D high frame rate vector velocity imaging for transthoracic cardiac imaging. Measurements are made on a healthy volunteer using the SARUS experimental ultrasound scanner connected to an intercostal phased-array probe. Two parasternal long-axis view (PLAX) are obtained, one centred at the aortic valve and another centred at the left ventricle. The acquisition sequence was composed of 3 diverging waves for high frame rate synthetic aperture flow imaging. For verification a phantom measurement is performed on a transverse straight 5 mm diameter vessel at a depth of 100 mm in a tissue-mimicking phantom. A flow pump produced a 2 ml/s constant flow with a peak velocity of 0.2 m/s. The average estimated flow angle in the ROI was $86.22 \pm 6.66$° with a true flow angle of 90°. A relative velocity bias of $-39\%$ with a standard deviation of $13\%$ was found. In-vivo acquisitions show complex flow patterns in the heart. In the aortic valve view, blood is seen exiting the left ventricle cavity through the aortic valve into the aorta during the systolic phase of the cardiac cycle. In the left ventricle view, blood flow is seen entering the left ventricle cavity through the mitral valve and splitting in two ways when approximating the left ventricle wall. The work presents 2-D velocity estimates on the heart from a non-invasive transthoracic scan. The ability of the method detecting flow regardless of the beam angle could potentially reveal a more complete view of the flow patterns presented on the heart.

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Medical Ultrasound, Vector Flow Imaging, Cardiac Imaging, Blood Flow, Synthetic Aperture
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High-resolution kinetics and modeling of hydrogen peroxide degradation in live cells

Although the role of oxidative stress factors and their regulation is well studied, the temporal dynamics of stress recovery is still poorly understood. In particular, measuring the kinetics of stress recovery in the first minutes after acute exposure provides a powerful technique for assessing the role of regulatory proteins or enzymes through the use of mutant backgrounds. This project endeavors to screen the temporal dynamics of intracellular oxidant levels in live cells as a function of gene deletion in the budding yeast, Saccharomyces cerevisiae. Using the detailed time dynamics of extra- and intra-cellular peroxide we have developed a mathematical model that describes two distinct kinetic processes, an initial rapid degradation in the first 10–20 min followed by a slower process. Using this model, a qualitative comparison allowed us to assign the dependence of temporal events to genetic factors. Surprisingly, we found that the deletion of transcription factors Yap1p or Skn7p was sufficient to disrupt the establishment of the second degradation phase but not the initial phase. A better fundamental understanding of the role protective factors play in the recovery from oxidative stress may lead to strategies for protecting or sensitizing cell to this stress.

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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Regulatory Genomics, Eucaryotic Molecular Cell Biology, Department of Electrical Engineering, Copenhagen Center for Health Technology, Biomedical Engineering
**Hybrid Segmentation of Vessels and Automated Flow Measures in In-Vivo Ultrasound Imaging**

Vector Flow Imaging (VFI) has received an increasing attention in the scientific field of ultrasound, as it enables angle independent visualization of blood flow. VFI can be used in volume flow estimation, but a vessel segmentation is needed to make it fully automatic. A novel vessel segmentation procedure is crucial for wall-to-wall visualization, automation of adjustments, and quantification of flow in state-of-the-art ultrasound scanners. We propose and discuss a method for accurate vessel segmentation that fuses VFI data and B-mode for robustly detecting and delineating vessels. The proposed method implements automated VFI flow measures such as peak systolic velocity (PSV) and volume flow. An evaluation of the performance of the segmentation algorithm relative to expert manual segmentation of 60 frames randomly chosen from 6 ultrasound sequences (10 frame randomly chosen from each sequence) is also presented. Dice coefficient denoting the similarity between segmentations is used for the evaluation. The coefficient ranges between 0 and 1, where 1 indicates perfect agreement and 0 indicates no agreement. The Dice coefficient was 0.91 indicating to a very agreement between automated and manual expert segmentations. The flowrig results also demonstrated that the PSVs measured from VFI had a mean relative error of 14.5% in comparison with the actual PSVs. The error for the PSVs measured from spectral Doppler was 29.5%, indicating that VFI is 15% more precise than spectral Doppler in PSV measurement.

**Hyperpolarized 13C MR angiography**

Magnetic resonance angiography (MRA) is a non-invasive technology that can be used for diagnosis and monitoring of cardiovascular disease; the number one cause of mortality worldwide. Hyperpolarized imaging agents provide signal enhancement of more than 10,000 times, which implies large reduction in acquisition time and improved spatial resolution. We review the role of hyperpolarized 13C agents for MR angiography and present the literature in the field. Furthermore, we present a study of the benefit of intra-arterial injection over intravenous injection of hyperpolarized agent for cerebral angiography in the rat, and compare the performance of two standard angiographic pulse sequences, the gradient echo (GRE) sequence and the balanced steady-state free precession (bSSFP). 2D coronal cerebral angiographies using intra-arterial injections were acquired with a GRE sequence with in-plane resolution of 0.27 mm and matrix size 256x128, and 2D coronal cerebral angiographies were acquired with a bSSFP sequence with in-plane resolution of 0.55 mm and matrix size 128x64. The bSSFP sequence provides higher SNR in phantoms than the GRE sequence. Similarly, intravenous injections are imaged with higher SNR with the bSSFP sequence, where the signal destruction of the GRE sequence is avoided. However, for intra-arterial injections, the bSSFP sequence results in strong artefacts, and the GRE sequence is preferred. Hyperpolarized MRA presents many challenges and cannot currently compete with conventional contrast enhanced MRA. Further research may change this since hyperpolarization is still an immature methodology.
Hyperpolarized 13C Urea Relaxation Mechanism Reveals Renal Changes in Diabetic Nephropathy

Purpose: Our aim was to assess a novel 13C radial fast spin echo golden ratio single shot method for interrogating early renal changes in the diabetic kidney, using hyperpolarized (HP) [13C,15N2]urea as a T2 relaxation based contrast bioprobe. Methods: A novel HP 13C MR contrast experiment was conducted in a group of streptozotocin type-1 diabetic rat
model and age matched controls. Results: A significantly different relaxation time (P=0.004) was found in the diabetic kidney (0.49±0.03 s) compared with the controls (0.64±0.02 s) and secondly, a strong correlation between the blood oxygen saturation level and the relaxation times were observed in the healthy controls. Conclusion: HP [13C,15N2]urea apparent T2 mapping may be a useful for interrogating local renal pO2 status and renal tissue alterations.

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Web of Science (2017): Indexed Yes
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Scopus rating (2016): CiteScore 3.52 SJR 1.945 SNIP 1.451
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.329 SNIP 1.481 CiteScore 3.54
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.015 SNIP 1.382 CiteScore 3.32
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.039 SNIP 1.433 CiteScore 3.46
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
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Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.16 SNIP 1.461 CiteScore 3.45
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.356 SNIP 1.606
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.331 SNIP 1.553
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.468 SNIP 1.5
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 2.397 SNIP 1.536
Scopus rating (2006): SJR 2.319 SNIP 1.756
The main purpose of this PhD project was to develop an ultrasonic method capable of determining intravascular pressure changes non-invasively. Measuring pressure variations is used clinically as a diagnostic marker for the physiological state of a cardiovascular region. Current clinical procedures for assessing pressure changes are by means of invasive devices such as pressure sensing catheters. Such devices suffer severe limitations as they are invasive and require the use of ionizing radiation for guidance and positioning. To overcome the concerns related to the use of invasive pressure catheters this project introduces a method that derives pressure changes from 2-D vector velocity flow data acquired non-invasively. The method is based on the Navier-Stokes equations and is tested on fabricated flow models. Results from the flow models are compared with simulations from finite element modeling. The developed technique showed a standard deviation and bias across constricted flow domains of 9 % and 8 %, respectively. Finally, the first in-vivo examples of deriving pressure changes from 2-D vector velocity ultrasound data is presented. Based on the presented results it is concluded that non-invasive determination of pressure changes from 2-D flow data is feasible. However, when transferring the method into clinical practice, where blood vessels follow more complex flow geometries, the influence of out-of-plane flow movement becomes increasingly more important. Therefore, for scans using a 1-D transducer it is crucial that the out-of-plane flow component is negligible.

**General information**

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Projects:
Imaging of In-Vivo Pressure using Ultrasound
Publication: Research › Ph.D. thesis – Annual report year: 2016

**Intra-operative Vector Flow Imaging Using Ultrasound of the Ascending Aorta among 40 Patients with Normal, Stenotic and Replaced Aortic Valves**

Stenosis of the aortic valve gives rise to more complex blood flows with increased velocities. The angle-independent vector flow ultrasound technique transverse oscillation was employed intra-operatively on the ascending aorta of (I) 20 patients with a healthy aortic valve and 20 patients with aortic stenosis before (IIa) and after (IIb) valve replacement. The results
indicate that aortic stenosis increased flow complexity (p < 0.0001), induced systolic backflow (p < 0.003) and reduced systolic jet width (p < 0.0001). After valve replacement, the systolic backflow and jet width were normalized (p > 0.52 and p > 0.22), but flow complexity was not (p < 0.0001). Flow complexity (p < 0.0001), systolic jet width (p < 0.0001) and systolic backflow (p < 0.001) were associated with peak systolic velocity. The study found that aortic stenosis changes blood flow in the ascending aorta and valve replacement corrects some of these changes. Transverse oscillation may be useful for assessment of aortic stenosis and optimization of valve surgery. (E-mail: lindskov@gmail.com) 2016 World Federation for Ultrasound in Medicine & Biology
Scopus rating (2005): SJR 1.378 SNIP 1.66
Scopus rating (2004): SJR 1.214 SNIP 1.677
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.6 SNIP 1.354
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.52 SNIP 1.244
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.482 SNIP 1.04
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Scopus rating (2000): SJR 0.546 SNIP 1.276
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.555 SNIP 1.312
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In Vivo High Frame Rate Vector Flow Imaging Using Plane Waves and Directional Beamforming
Directional beamforming (DB) estimates blood flow velocities accurately when the flow angle is known. However, for automatically finding the flow angle a computationally expensive approach is used. This work presents a method for estimating the flow angle using a combination of inexpensive transverse oscillation (TO) estimators and only 3 directional beamformed lines. The suggested DB vector flow estimator is employed with steered plane wave transmissions for high frame rate imaging. Two distinct plane wave sequences are used: a short sequence (3 angles) for fast flow and an interleaved long sequence (21 angles) for both slow flow and B-mode. Parabolic flow with a peak velocity of 0.5 m/s is measured at beam-to-flow angles of 60° and 90°. The DB method estimates the angle with a bias and standard deviation (STD) less than 2°, and the STD of the velocity magnitude is 2.5%. This is 7-8.5% when using TO. The long sequence has a higher sensitivity, and when used for estimation of slow flow with a peak velocity of 0.04 m/s, the STD is 2.5% and bias is 0.1%. This is a factor of 4 better than the short sequence is used. The carotid bifurcation was scanned on a healthy volunteer, and the short sequence was used with TO and DB to estimate velocity vectors. The STD of the velocity profile over a cardiac cycle was 6.1% for TO and 4.9% for DB.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital, University of Copenhagen
Authors: Jensen, J. (Intern), Villagómez Hoyos, C. A. (Intern), Stuart, M. B. (Intern), Ewertsen, C. (Ekstern), Nielsen, M. B. (Forskerdatabase), Jensen, J. A. (Intern)
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Neurofeedback Therapy for Enhancing Visual Attention: State-of-the-Art and Challenges
We have witnessed a rapid development of brain-computer interfaces (BCIs) linking the brain to external devices. BCIs can be utilized to treat neurological conditions and even to augment brain functions. BCIs offer a promising treatment for mental disorders, including disorders of attention. Here we review the current state of the art and challenges of attention-
based BCIs, with a focus on visual attention. Attention-based BCIs utilize electroencephalograms (EEGs) or other recording techniques to generate neurofeedback, which patients use to improve their attention, a complex cognitive function. Although progress has been made in the studies of neural mechanisms of attention, extraction of attention-related neural signals needed for BCI operations is a difficult problem. To attain good BCI performance, it is important to select the features of neural activity that represent attentional signals. BCI decoding of attention-related activity may be hindered by the presence of different neural signals. Therefore, BCI accuracy can be improved by signal processing algorithms that dissociate signals of interest from irrelevant activities. Notwithstanding recent progress, optimal processing of attentional neural signals remains a fundamental challenge for the development of efficient therapies for disorders of attention.

**General information**

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Applied Electronics, Copenhagen Center for Health Technology, Duke University
Authors: Ordikhani-Seyedlar, M. (Intern), Lebedev, M. A. (Ekstern), Sørensen, H. B. D. (Intern), Puthusserypady, S. (Intern)
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Web of Science (2017): Indexed Yes
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.964 SNIP 1.033 CiteScore 3.47
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.648 SNIP 0.957 CiteScore 3.23
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.124 SNIP 0.963 CiteScore 3.41
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Web of Science (2013): Indexed yes
Scopus rating (2012): SJR 2.686 SNIP 1.171 CiteScore 4.05
ISI indexed (2012): ISI indexed yes
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Scopus rating (2011): SJR 2.055 SNIP 0.857 CiteScore 2.35
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Novel Automatic Detection of Pleura and B-lines (Comet-Tail Artifacts) on In-Vivo Lung Ultrasound Scans.

This paper presents a novel automatic method for detection of B-lines (comet-tail artifacts) in lung ultrasound scans. B-lines are the most commonly used artifacts for analyzing the pulmonary edema. They appear as laser-like vertical beams, which arise from the pleural line and spread down without fading to the edge of the screen. An increase in their number is associated with presence of edema. All the scans used in this study were acquired using a BK3000 ultrasound scanner (BK Ultrasound, Denmark) driving a 102-element 5.5 MHz wide linear transducer (10L2W, BK Ultrasound). The dynamic received focus technique was employed to generate the sequences. Six subjects, among those three patients after major surgery and three normal subjects, were scanned once and Six ultrasound sequences each containing 50 frames were acquired. The proposed algorithm was applied to all 300 in-vivo lung ultrasound images. The pleural line is first segmented on each image and then the B-line artifacts spreading down from the pleural line are detected and overlayed on the image. The resulting 300 images showed that the mean lateral distance between B-lines detected on images acquired from patients decreased by 20% in compare with that of normal subjects. Therefore, the method can be used as the basis of a method of automatically and qualitatively characterizing the distribution of B-lines.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen Center for Health Technology, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Moshavegh, R. (Intern), Hansen, K. L. (Ekstern), Møller-Sørensen, H. (Ekstern), Hemmsen, M. C. (Intern), Ewertsen, C. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Optimization of Synthetic Aperture Image Quality
Synthetic Aperture (SA) imaging produces high-quality images and velocity estimates of both slow and fast flow at high frame rates. However, grating lobe artifacts can appear both in transmission and reception. These affect the image quality and the frame rate. Therefore optimization of parameters effecting the image quality of SA is of great importance, and this paper proposes an advanced procedure for optimizing the parameters essential for acquiring an optimal image quality, while generating high resolution SA images. Optimization of the image quality is mainly performed based on measures such as F-number, number of emissions and the aperture size. They are considered to be the most contributing acquisition factors in the quality of the high resolution images in SA. Therefore, the performance of image quality is quantified in terms of full-width at half maximum (FWHM) and the cystic resolution (CTR). The results of the study showed that SA imaging with only 32 emissions and maximum sweep angle of 22 degrees yields a very good image quality compared with using 256 emissions and the full aperture size. Therefore the number of emissions and the maximum sweep angle in the SA can be optimized to reach a reasonably good performance, and to increase the frame rate by lowering the required number of emissions. All the measurements are performed using the experimental SARUS scanner connected to a λ/2-pitch transducer. A wire phantom and a tissue mimicking phantom containing anechoic cysts are scanned using the optimized parameters for the transducer. Measurements coincide with simulations.

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Optimized Plane Wave Imaging for Fast and High-Quality Ultrasound Imaging

This paper presents a method for optimizing parameters affecting the image quality in plane wave imaging. More specifically, the number of emissions and steering angles is optimized to attain the best images with the highest frame rate possible. The method is applied to a specific problem, where image quality for a λ-pitch transducer is compared with a λ/2-pitch transducer. Grating lobe artifacts for λ-pitch transducers degrade the contrast in plane wave images, and the impact on frame rate is studied. Field II simulations of plane wave images are made for all combinations of the parameters, and the optimal setup is selected based on Pareto optimality. The optimal setup for a simulated 4.1-MHz λ-pitch transducer uses 61 emissions and a maximum steering angle of 20° for depths from 0 to 60 mm. The achieved lateral full-width at half-maximum (FWHM) is 1.5λ and the contrast is −29 dB for a scatterer at 9 mm (24λ). Using a λ/2-pitch transducer and only 21 emissions within the same angle range, the image quality is improved in terms of contrast, which is −37 dB. For imaging in regions deeper than 25 mm (66λ), only 21 emissions are optimal for both the transducers, resulting in a −36 dB contrast at 34 mm (90λ). Measurements are performed using the experimental SARUS scanner connected to a λ-pitch and λ/2-pitch transducer. A wire phantom and a tissue mimicking phantom containing anechoic cysts are scanned and show the performance using the optimized sequences for the transducers. FWHM is 1.6λ and contrast is −25 dB for a wire at 9 mm using the λ-pitch transducer. For the λ/2-pitch transducer, contrast is −29 dB. In vivo scans of the carotid artery of a healthy volunteer show improved contrast and present fewer artifacts, when using the λ/2-pitch transducer compared with the λ-pitch. It is demonstrated with a frame rate, which is three times higher for the λ/2-pitch transducer.
Plane-Wave Imaging Challenge in Medical Ultrasound

Plane-Wave imaging enables very high frame rates, up to several thousand frames per second. Unfortunately the lack of transmit focusing leads to reduced image quality, both in terms of resolution and contrast. Recently, numerous beamforming techniques have been proposed to compensate for this effect, but comparing the different methods is difficult due to the lack of appropriate tools. PICMUS, the Plane-Wave Imaging Challenge in Medical Ultrasound aims to provide these tools. This paper describes the PICMUS challenge, its motivation, implementation, and metrics.
Portable Prescreening System for Sleep Apnea

Obstructive sleep apnea (OSA) occurs in more than 4% of the adult population. Diagnoses for OSA in sleep clinics are costly and more than half of those submitted to a sleep clinic do not have OSA. A simple, easy, and portable home-based monitoring system to evaluate who are in high- or low-risk of suffering from OSA would be beneficial. The system must be able to identify individuals with a high pre-test reliability regarding OSA with the aim of referral and further investigation. We aimed to develop a portable, smartphone, and home-based monitoring system to classify whether a patient screened for sleep apnea is at high risk or low risk of having OSA. A new test setup was developed containing an Android based smartphone, the built-in accelerometer, and a microphone. To ease the clinical analysis of the data a MATLAB based graphical user interface has been developed visualizing the data allowing the user to navigate through the data and the detected apnea events. The events are classified using both features from the audio and the signal from the accelerometer placed on sternum. Furthermore, using the accelerometer data the sleep position is estimated and the morphology from the respiratory pattern is available describing the events and making it possible to distinguish between OSA and central sleep apnea (CSA).

Preliminary investigation of an ultrasound method for estimating pressure changes in deep-positioned vessels.

This paper presents a method for measuring pressure changes in deep-tissue vessels using vector velocity ultrasound data. The large penetration depth is ensured by acquiring data using a low frequency phased array transducer. Vascular pressure changes are then calculated from 2-D angle-independent vector velocity fields using a model based on the Navier-Stokes equations. Experimental scans are performed on a fabricated flow phantom having a constriction of 36% at a depth of 100 mm. Scans are carried out using a phased array transducer connected to the experimental scanner, SARUS. 2-D fields of angle-independent vector velocities are acquired using directional synthetic aperture vector flow imaging. The obtained results are evaluated by comparison to a
3-D numerical simulation model with equivalent geometry as the designed phantom. The study showed pressure drops across the constricted phantom varying from -40 Pa to 15 Pa with a standard deviation of 32%, and a bias of 25% found relative to the peak simulated pressure drop. This preliminary study shows that pressure can be estimated non-invasively to a depth that enables cardiac scans, and thereby, the possibility of detecting the pressure drops across the mitral valve.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Waterloo, University of Hong Kong
Authors: Olesen, J. B. (Intern), Villagómez Hoyos, C. A. (Intern), Traberg, M. S. (Intern), Chee, A. J. Y. (Ekstern), Yiu, B. Y. S. (Ekstern), Ho, C. K. (Ekstern), Yu, A. C. H. (Ekstern), Jensen, J. A. (Intern)
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Quantitative Measurements using Ultrasound Vector Flow Imaging
Duplex Vector Flow Imaging (VFI) imaging is introduced as a replacement for spectral Doppler, as it automatically can yield fully quantitative flow estimates without angle correction. Continuous VFI data over 9 s for 10 pulse cycles were acquired by a 3 MHz convex probe connected to the SARUS scanner for pulsating flow mimicking the femoral artery from a CompuFlow 1000 pump (Shelley Medical). Data were used in four estimators based on directional transverse oscillation for velocity, flow angle, volume flow, and turbulence estimation and their respective precisions. An adaptive lag scheme gave the ability to estimate a large velocity range, or alternatively measure at two sites to find e.g. stenosis degree in a vessel. The mean angle at the vessel center was estimated to 90.9°±8.2° indicating a laminar flow from a turbulence index being close to zero (0.1 ±0.1). Volume flow was 1.29 ±0.26 mL/stroke (true: 1.15 mL/stroke, bias: 12.2%). Measurements down to 160 mm were obtained with a relative standard deviation and bias of less than 10% for the lateral component for stationary, parabolic flow. The method can, thus, find quantitative velocities, angles, and volume flows at sites currently inaccessible to spectral systems, and at much larger velocities and ranges than conventional systems without any angle correction making measurements less time-consuming and more correct.

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Authors: Jensen, J. A. (Intern)
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Reinforcement of the bactericidal effect of ciprofloxacin on Pseudomonas aeruginosa biofilm by hyperbaric oxygen treatment

Chronic Pseudomonas aeruginosa lung infection is the most severe complication in cystic fibrosis patients. It is characterised by antibiotic-tolerant biofilms in the endobronchial mucus with zones of oxygen (O2) depletion mainly due to polymorphonuclear leucocyte activity. Whilst the exact mechanisms affecting antibiotic effectiveness on biofilms remain unclear, accumulating evidence suggests that the efficacy of several bactericidal antibiotics such as ciprofloxacin is enhanced by stimulation of the aerobic respiration of pathogens, and that lack of O2 increases their tolerance. Reoxygenation of O2-depleted biofilms may thus improve susceptibility to ciprofloxacin possibly by restoring aerobic respiration. We tested such a strategy using reoxygenation of O2-depleted P. aeruginosa strain PAO1 agarose-embedded biofilms by hyperbaric oxygen treatment (HBOT) (100% O2, 2.8bar), enhancing the diffusive supply for aerobic respiration during ciprofloxacin treatment. This proof-of-principle study demonstrates that biofilm reoxygenation by HBOT can significantly enhance the bactericidal activity of ciprofloxacin on P. aeruginosa. Combining ciprofloxacin treatment with HBOT thus clearly has potential to improve the treatment of P. aeruginosa biofilm infections.
Robust microbubble tracking for super resolution imaging in ultrasound

Currently ultrasound resolution is limited by diffraction to approximately half the wavelength of the sound wave employed. In recent years, super resolution imaging techniques have overcome the diffraction limit through the localization and tracking of a sparse set of microbubbles through the vasculature. However, this has only been performed on fixated tissue, limiting its clinical application. This paper proposes a technique for making super resolution images on non-fixated tissue by first compensating for tissue movement and then tracking the individual microbubbles. The experiment is performed on the kidney of an anesthetized Sprage-Dawley rat by infusing SonoVue at 0.1× original concentration. The algorithm demonstrated in vivo that the motion compensation was capable of removing the movement caused by the mechanical ventilator. The results show that microbubbles were localized with a higher precision, reducing the standard deviation of the super localizations from 22μm to 8 μm. The paper proves that the restriction of completely fixated tissue can be eliminated, when making super resolution imaging with microbubbles.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Information Technology, Technical University of Denmark, Heriot-Watt University, University of Copenhagen
Authors: Hansen, K. B. (Ekstern), Villagómez Hoyos, C. A. (Intern), Brasen, J. C. (Intern), Diamantis, K. (Ekstern), Sboros, V. (Ekstern), Sorensen, C. M. (Ekstern), Jensen, J. A. (Intern)
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An automatic approach for simulating the emitted pressure, intensity, and MI of advanced ultrasound imaging sequences is presented. It is based on a linear simulation of pressure fields using Field II, and it is hypothesized that linear simulation can attain the needed accuracy for predicting Mechanical Index (MI) and Ispta.3 as required by FDA. The method is performed on four different imaging schemes and compared to measurements conducted using the SARUS experimental scanner. The sequences include focused emissions with an F-number of 2 with 64 elements that generate highly non-linear fields. The simulation time is between 0.67 ms to 2.8 ms per emission and imaging point, making it possible to simulate even complex emission sequences in less than 1 s for a single spatial position. The linear simulations yield a relative accuracy on MI between -12.1% to 52.3% and for Ispta.3 between -38.6% to 62.6%, when using the impulse response of the probe estimated from an independent measurement. The accuracy is increased to between -22% to 24.5% for MI and between -33.2% to 27.0% for Ispta.3, when using the pressure response measured at a single point to scale the simulation. The spatial distribution of MI and Ita.3 closely matches that for the measurement, and simulations can therefore be used to select the region for measuring the intensities, resulting in a significant reduction in measurement time. It can validate emission sequences by showing symmetry of emitted pressure fields, focal position, and intensity distribution.
Safety Assessment of Advanced Imaging Sequences I: Measurements

A method for rapid measurement of intensities (Ispta), mechanical index (MI), and probe surface temperature for any ultrasound scanning sequence is presented. It uses the scanner's sampling capability to give an accurate measurement of the whole imaging sequence for all emissions to yield the true distributions. The method is several orders of magnitude faster than approaches using an oscilloscope, and it also facilitates validating the emitted pressure field and the scanner's emission sequence software. It has been implemented using the experimental SARUS scanner and the Onda AIMS III intensity measurement system (Onda Corporation, Sunnyvale, CA, USA). Four different sequences have been measured: a fixed focus emission, a duplex sequence containing B-mode and flow emissions, a vector flow sequence with B-mode and flow emissions in 17 directions, and finally a synthetic aperture (SA) duplex flow sequence. A BK8820e (BK Medical, Herlev, Denmark) convex array probe is used for the first three sequences and a BK8670 linear array probe for the SA sequence. The method is shown to give the same intensity values within 0.24% of the AIMS III Soniq 5.0 (Onda Corporation, Sunnyvale, CA, USA) commercial intensity measurement program. The approach can measure and store data for a full imaging sequence in 3.8 to 8.2 s per spatial position. Based on Ispta, MI, and probe surface temperature, the method gives the ability to determine whether a sequence is within US FDA limits, or alternatively indicate how to scale it to be within limits.
Sleep stability and transitions in patients with idiopathic REM sleep behavior disorder and patients with Parkinson's disease

Objective: Patients with idiopathic rapid eye movement (REM) sleep behavior disorder (iRBD) are at high risk of developing Parkinson's disease (PD). As wake/sleep-regulation is thought to involve neurons located in the brainstem and hypothalamic areas, we hypothesize that the neurodegeneration in iRBD/PD is likely to affect wake/sleep and REM/non-REM (NREM) sleep transitions. Methods: We determined the frequency of wake/sleep and REM/NREM sleep transitions and the stability of wake (W), REM and NREM sleep as measured by polysomnography (PSG) in 27 patients with PD, 23 patients with iRBD, 25 patients with periodic leg movement disorder (PLMD) and 23 controls. Measures were computed based on manual scorings and data-driven labeled sleep staging. Results: Patients with PD showed significantly lower REM stability than controls and patients with PLMD. Patients with iRBD had significantly lower REM stability compared with controls. Patients with PD and RBD showed significantly lower NREM stability and significantly more REM/NREM transitions than controls. Conclusions: We conclude that W, NREM and REM stability and transitions are progressively affected in iRBD and PD, probably reflecting the successive involvement of brain stem areas from early on in the disease. Significance: Sleep stability and transitions determined by a data-driven approach could support the evaluation of iRBD and PD patients.
Steady State Visual Evoked Potential Based Brain-Computer Interface for Cognitive Assessment

Cognitive assessment is of growing importance, with the general population getting older and a rapidly growing incidence of dementia, which is a major public health issue. Treatment of dementia must, to be most effective, start early in the disease process. Thus, early detection of cognitive decline is important. Cognitive decline may be detected using fully automated computerized assessment. Such systems will provide inexpensive and widely available screenings of cognitive ability. The aim of this pilot study is to develop a real time steady state visual evoked potential (SSVEP) based brain-computer interface (BCI) for neurological cognitive assessment. It is intended for use by patients who suffer from diseases impairing their motor skills, but are still able to control their gaze. Results are based on 11 healthy test subjects. The system
performance have an average accuracy of 100% ± 0%. The test subjects achieved an information transfer rate (ITR) of 14.64 bits/min ± 7.63 bits/min and a subject test performance of 47.22% ± 34.10%. This study suggests that BCI may be applicable in practice as a computerized cognitive assessment tool. However, many improvements are required for the system to be fully valid and of clinical use.

**General information**

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Organisations: Copenhagen Center for Health Technology, Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, University of Copenhagen, Zealand University Hospital
Authors: Westergren, N. (Ekstern), Bendtsen, R. L. (Ekstern), Kjaer, T. W. (Ekstern), Thomsen, C. E. (Ekstern), Puthusserypady, S. (Intern), Sørensen, H. B. D. (Intern)
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**Surveillance for hemodialysis access stenosis: usefulness of ultrasound vector volume flow**

**Purpose:**
To investigate if ultrasound vector-flow imaging (VFI) is equal to the reference method ultrasound dilution technique (UDT) in estimating volume flow and changes over time in arteriovenous fistulas (AVFs) for hemodialysis.

**Materials and methods:**
From January 2014 to January 2015, patients with end-stage renal disease and matured functional AVFs were consecutively solicited to participate in this prospective study. All patients were included after written informed consent and approval by the National Committee on Biomedical Research Ethics and the local Ethics Committee (journal no. H-4-2014-FSP). VFI and UDT measurements were performed monthly over a six-month period. Nineteen patients were included in the study. VFI measurements were performed before dialysis, and UDT measurements after. Statistical analyses were performed with Bland-Altman plot, Student’s t-test, four-quadrant plot, and regression analysis. Repeated measurements and precision analysis were used for reproducibility determination.

**Results:**
Precision measurements for UDT and VFI were 32% and 20%, respectively (p = 0.33). Average volume flow measured with UDT and VFI were 1161 mL/min (±778 mL/min) and 1213 mL/min (±980 mL/min), respectively (p = 0.3). The mean difference was -51 mL/min (CI: -150 mL/min to 46 mL/min) with limits of agreement from -35% to 54%, with a strong correlation (r² = 0.87). A large change in volume flow between dialysis sessions detected by UDT was confirmed by VFI (p = 0.0001), but the concordance rate was poor (0.72).

**Conclusions:**
VFI is an acceptable method for volume flow estimation and volume flow changes over time in AVFs.
Synthetic aperture ultrasound Fourier beamformation using virtual sources

An efficient Fourier beamformation algorithm is presented for multistatic synthetic aperture ultrasound imaging using virtual sources (FBV). The concept is based on the frequency domain wavenumber algorithm from radar and sonar and is extended to a multi-element transmit/receive configuration using virtual sources. Window functions are used to extract the azimuth processing bandwidths and weight the data to reduce sidelobes in the final image. Field II simulated data and SARUS measured data are used to evaluate the results in terms of point spread function, resolution, contrast, SNR, and
processing time. Lateral resolutions of 0.53 mm and 0.66 mm are obtained for FBV and DAS on point target simulated data. Corresponding axial resolutions are 0.21 mm for FBV and 0.20 mm for DAS. The results are also consistent over different depths evaluated using a simulated phantom containing several point targets at different depths. FBV shows a better lateral resolution at all depths, and the axial and cystic resolutions of -6 dB, -12 dB and -20 dB are almost the same for FBV and DAS. To evaluate the cyst phantom metrics, three different criteria of Power Ratio (PR), Contrast Ratio (CR), and contrast to noise ratio (CNR) have been used. Results show that the algorithms have a different performance in the cyst center and near the boundary. FBV has a better performance near the boundary, however, DAS is better in the more central area of the cyst. Measured data from phantoms are also used for evaluation. The results confirm the applicability of FBV in ultrasound and 20 times less processing time in comparison with DAS is attained. Evaluating the results over a wide variety of parameters and having almost the same results for simulated and measured data demonstrates the ability of FBV in preserving the quality of image as DAS, while providing a more efficient algorithm with 20 times less computations.
The main objective of this project was to continue the development of a synthetic aperture vector flow estimator. This type of estimator is capable of overcoming two of the major limitations in conventional ultrasound systems: 1) the inability to scan large region of interest with high temporal resolutions; 2) the lack of capability in detecting flow other than the one along the direction of the beam. Addressing these technical limitations would translate in the clinic as a gain in valuable clinical information and a removal of operator-dependant sources of error, which would improve the diagnosis. The main contribution of this work was the development of an angle estimator which features high accuracy and low standard deviation over the full $360^\circ$ range. The estimator demonstrated its capability of operating at high frame rates ($> 1000$ Hz), and simultaneously detecting a large range of flow velocities ($0.05 - 3$ m s$^{-1}$). The estimator was also extended to a variety of geometries without major modifications, including a 2-D matrix array for full 3-D velocity estimation. Furthermore, a developed novel energy based tissue echo-canceler provided a new effective perspective for removing the tissue signal, specially when the tissue and flow spectra overlaps. The approach was investigated with a series of flow simulations that included vessel wall movement, and demonstrated its capability of diminish the effects of a moving vessel wall in both simulations and in vivo measurements. Finally, this thesis showed that novel information can be obtained with vector velocity methods providing quantitative estimates of blood flow and insight into the complexity of the hemodynamics dynamics. This could give the clinician a new tool in assessment and treatment of a broad range of diseases.
System-Level Design of an Integrated Receiver Front End for a Wireless Ultrasound Probe

In this paper, a system-level design is presented for an integrated receive circuit for a wireless ultrasound probe, which includes analog front ends and beam formation modules. This paper focuses on the investigation of the effects of architectural design choices on the image quality. The point spread function is simulated in Field II from 10 to 160 mm using a convex array transducer. A noise analysis is performed, and the minimum signal-to-noise ratio (SNR) requirements are derived for the low-noise amplifiers (LNAs) and A/D converters (ADCs) to fulfill the design specifications of a dynamic range of 60 dB and a penetration depth of 160 mm in the B-mode image. Six front-end implementations are compared using Nyquist-rate and modulator ADCs. The image quality is evaluated as a function of the depth in terms of lateral full-width at halfmaximum (FWHM) and −12-dB cystic resolution (CR). The designs that minimally satisfy the specifications are based on an 8-b 30-MSPS Nyquist converter and a single-bit third-order 240-MSPS modulator, with an SNR for the LNA in both cases equal to 64 dB. The mean lateral FWHM and CR are 2.4% and 7.1% lower for the architecture compared with the Nyquist-rate one. However, the results generally show minimal differences between equivalent architectures. Advantages and drawbacks are finally discussed for the two families of converters.
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BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.928 SNIP 1.562
Web of Science (2010): Indexed yes
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Ultralydskanning er førstevalg ved mistanke om kronisk venesygdom i underekstremiteterne

General information
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Ultrasound Vector Flow Imaging: Part II: Parallel Systems
The paper gives a review of the current state-of-the-art in ultrasound parallel acquisition systems for flow imaging using spherical and plane waves emissions. The imaging methods are explained along with the advantages of using these very fast and sensitive velocity estimators. These experimental systems are capable of acquiring thousands of images per second for fast moving flow as well as yielding estimates of low velocity flow. These emerging techniques allow vector flow systems to assess highly complex flow with transitory vortices and moving tissue, and they can also be used in functional ultrasound imaging for studying brain function in animals. The paper explains the underlying acquisition and estimation methods for fast 2-D and 3-D velocity imaging and gives a number of examples. Future challenges and the potentials of parallel acquisition systems for flow imaging are also discussed.
Ultrasound Vector Flow Imaging: Part I: Sequential Systems

The paper gives a review of the most important methods for blood velocity vector flow imaging (VFI) for conventional, sequential data acquisition. This includes multibeam methods, speckle tracking, transverse oscillation, color flow mapping derived vector flow imaging, directional beamforming, and variants of these. The review covers both 2-D and 3-D velocity estimation and gives a historical perspective on the development along with a summary of various vector flow visualization algorithms. The current state-of-the-art is explained along with an overview of clinical studies conducted and methods for presenting and using VFI. A number of examples of VFI images are presented, and the current limitations and potential solutions are discussed.
Doppler ultrasound, Vector Flow Imaging, Velocity estimation
Vector Velocity Estimation for Portable Ultrasound using Directional Transverse Oscillation and Synthetic Aperture Sequential Beamforming

In this paper, a vector flow imaging method is presented, which combines the directional transverse oscillation approach with synthetic aperture sequential beamforming to achieve an efficient estimation of the velocities. A double oscillating field is synthesized using two sets of focused emissions separated by a distance in the lateral direction. A low resolution line (LRL) is created for each emission in the first stage beamformer, and a second beamformer provides the high resolution data used for the velocity estimation. The method makes it possible to have continuously available data in the whole image. Therefore, high and low velocities can be estimated with a high frame rate and a low standard deviation. The first stage is a fixed-focus beamformer that can be integrated in the transducer handle, enabling the wireless transmission of the LRLs. The approach does not require any angle compensation or prior knowledge on the beam-to-flow angle. The feasibility of the method is demonstrated through simulations and flow rig measurements of a parabolic flow in a vessel at 90-degree beam-to-flow angle. The mean bias obtained from 50 independent measurements is equal to -0.67% for the lateral profile and -0.43% for the axial profile. The relative standard deviation is 3.19% and 0.47% for the lateral and axial profiles. It is, therefore, demonstrated that vector velocity estimation can be efficiently integrated in a portable ultrasound scanner with state-of-the-art performance.

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Vector velocity volume flow estimation: Sources of error and corrections applied for arteriovenous fistulas

A method for vector velocity volume flow estimation is presented, along with an investigation of its sources of error and correction of actual volume flow measurements. Volume flow errors are quantified theoretically by numerical modeling, through flow phantom measurements, and studied in vivo. This paper investigates errors from estimating volumetric flow using a commercial ultrasound scanner and the common assumptions made in the literature. The theoretical model shows, e.g. that volume flow is underestimated by 15%, when the scan plane is off-axis with the vessel center by 28% of the vessel radius. The error sources were also studied in vivo under realistic clinical conditions, and the theoretical results were applied for correcting the volume flow errors. Twenty dialysis patients with arteriovenous fistulas were scanned to obtain vector flow maps of fistulas. When fitting an ellipse to cross-sectional scans of the fistulas, the major axis was on average 10.2 mm, which is 6.6% larger than the minor axis. The ultrasound beam was on average 1.5 mm from the vessel center, corresponding to 28% of the semi-major axis in an average fistula. Estimating volume flow with an elliptical, rather than circular, vessel area and correcting the ultrasound beam for being off-axis, gave a significant (p = 0.008) reduction in error from 31.2% to 24.3%. The error is relative to the Ultrasound Dilution Technique, which is considered the gold standard for volume flow estimation for dialysis patients. The study shows the importance of correcting for volume flow errors, which are often made in clinical practice.
Visualizing Patient Journals by Combining Vital Signs Monitoring and Natural Language Processing

This paper presents a data-driven approach to graphically presenting text-based patient journals while still maintaining all textual information. The system first creates a timeline representation of a patients’ physiological condition during an admission, which is assessed by electronically monitoring vital signs and then combining these into Early Warning Scores (EWS). Hereafter, techniques from Natural Language Processing (NLP) are applied on the existing patient journal to extract all entries. Finally, the two methods are combined into an interactive timeline featuring the ability to see drastic changes in the patients’ health, and thereby enabling staff to see where in the journal critical events have taken place.

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Sleep Spindles as Biomarker for Early Detection of Neurodegenerative Disorders

The present invention relates to the use of sleep spindles as a novel biomarker for early diagnosis of synucleinopathies, in particular Parkinson’s disease (PD). The method is based on automatic detection of sleep spindles. The method may be combined with measurements of one or more further biomarkers derived from polysomnographic recordings.

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3-D Imaging Using Row-Column-Addressed Arrays With Integrated Apodization: Part II: Transducer Fabrication and Experimental Results

This paper demonstrates the fabrication, characterization, and experimental imaging results of a 62×62 element λ/2-pitch row-column-addressed capacitive micromachined ultrasonic transducer (CMUT) array with integrated apodization. A new fabrication process was used to manufacture a 26.3 mm by 26.3 mm array using five lithography steps. The array includes an integrated apodization, presented in detail in Part I of this paper, which is designed to reduce the amplitude of the ghost echoes that are otherwise prominent for row-column-addressed arrays. Custom front-end electronics were produced with the capability of transmitting and receiving on all elements, and the option of disabling the integrated apodization. The center frequency and -6-dB fractional bandwidth of the array elements were 2.77 ± 0.26 MHz and 102 ± 10%, respectively. The surface transmit pressure at 2.5 MHz was 590 ± 73 kPa, and the sensitivity was 0.299 ± 0.090 V/Pa. The nearest neighbor crosstalk level was -23.9 ± 3.7 dB, while the transmit-to-receive-elements crosstalk level was -40.2 ± 3.5 dB. Imaging of a 0.3-mm-diameter steel wire using synthetic transmit focusing with 62 single-element emissions demonstrated axial and lateral FWHMs of 0.71 mm and 1.79 mm (f-number: 1.4), respectively, compared with simulated axial and lateral FWHMs of 0.69 mm and 1.76 mm. The dominant ghost echo was reduced by 15.8 dB in measurements using the integrated apodization compared with the disabled configuration. The effect was reproduced in simulations, showing a ghost echo reduction of 18.9 dB.

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Authors: Christiansen, T. L. (Intern), Rasmussen, M. F. (Intern), Bagge, J. P. (Ekstern), Moesner, L. N. (Ekstern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)

This paper investigates the effect of transducer-integrated apodization in row–column-addressed arrays and presents a beamforming approach specific for such arrays. Row–column addressing 2-D arrays greatly reduces the number of active channels needed to acquire a 3-D volume. A disadvantage of row–column-addressed arrays is an apparent ghost effect in the point spread function caused by edge waves. This paper investigates the origin of the edge waves and the effect of introducing an integrated apodization to reduce the ghost echoes. The performance of a λ/2-pitch 5-MHz 128 × 128 row–column-addressed array with different apodizations is simulated. A Hann apodization is shown to decrease imaging performance away from the center axis of the array because of a decrease in main lobe amplitude. Instead, a static roll-off apodization region located at the ends of the line elements is proposed. In simulations, the peak ghost echo intensity of a scatterer at (x,y, z) = (8, 3, 30) mm was decreased by 43 dB by integrating roll-off apodization into the array. The main lobe was unaffected by the apodization. Simulations of a 3-mm-diameter anechoic blood vessel at 30 mm depth showed that applying the transducer-integrated apodization increased the apparent diameter of the vessel from 2.0 mm to 2.4 mm, corresponding to an increase from 67% to 80% of the true vessel diameter. The line element beamforming approach is shown to be essential for achieving correct time-of-flight calculations, and hence avoid geometrical distortions. In Part II of this work, experimental results from a capacitive micromachined ultrasonic transducer with integrated roll-off apodization are given to validate the effect of integrating apodization into the line elements.

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Authors: Rasmussen, M. F. (Intern), Christiansen, T. L. (Intern), Thomsen, E. V. (Intern), Jensen, J. A. (Intern)
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3-D Vector Velocity Estimation with Row-Column Addressed Arrays
The concept of 2-D row-column (RC) addressed arrays for 3-D imaging have shown to be an interesting alternative to 2-D matrix array, due to the reduced channel count. However, the properties for RC arrays to estimate blood velocities have never been reported, which is of great importance for a clinical implementation of this type of array. The aim of this study is, thus, to develop a technique for estimating 3-D vector flow with a RC array using the transverse oscillation (TO) method. The properties are explored both in a simulation study and with a prototype probe for experimental use. In both setups, a 124 channel 2-D RC array with integrated apodization, pitch = 270 µm and a center frequency of 3.0 MHz was used. The performance of the estimator was tested on a simulated vessel (Ø = 12 mm) with a parabolic flow profile and a peak velocity of 1 m/s. Measurements were made in a flowrig (Ø = 12 mm) containing a laminar parabolic flow and a peak velocity of 0.54 m/s. Data was sampled and stored on the experimental ultrasound scanner SARUS. Simulations yields
relative mean biases at (-1.1%, -1.5%, -1.0%) with mean standard deviations of \( \sigma^* \) were (8.5%, 9.0%, 1.4%) % for \((v_x, v_y, v_z)\) from a 3-D velocity vector in a 15\(^\circ\) rotated vessel with a 75\(^\circ\) beam-to-flow angle. In the experimental setup with a 90\(^\circ\) beam-to-flow angle, the relative mean biases were (-2.6%, -1.3%, 1.4%) with a relative standard deviation of (5.0%, 5.2%, 1.0%) for the respective transverse, lateral and axial velocity component.

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**A 3D Learning Playground for Potential Attention Training in ADHD**

This paper presents a novel brain-computer interface (BCI) system that could potentially be used for enhancing the attention ability of subjects with attention deficit hyperactivity disorder (ADHD). It employs the steady state visual evoked potential (SSVEP) paradigm. The developed system consists of a 3D classroom environment with active 3D distractions and 2D games executed on the blackboard. The system is concealed as a game (with stages of varying difficulty) with an underlying story to motivate the subjects. It was tested on eleven healthy subjects and the results undeniably establish that by moving to a higher stage in the game where the 2D environment is changed to 3D along with the added 3D distractions, the difficulty level in keeping attention on the main task increases for the subjects. Results also show a mean accuracy of 92.26 ± 7.97% and a mean average selection time of 3.07 ± 1.09 seconds.

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Authors: Ali, A. (Ekstern), Puthusserypady, S. (Intern)
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**A Brain Computer Interface for Robust Wheelchair Control Application Based on Pseudorandom Code Modulated Visual Evoked Potential.**

In this pilot study, a novel and minimalistic Brain Computer Interface (BCI) based wheelchair control application was developed. The system was based on pseudorandom code modulated Visual Evoked Potentials (c-VEPs). The visual stimuli in the scheme were generated based on the Gold code, and the VEPs were recognized and classified using subject-specific algorithms. The system provided the ability of controlling a wheelchair model (LEGO R MINDSTORM R EV3 robot) in 4 different directions based on the elicited c-VEPs. Ten healthy subjects were evaluated in testing the system where an average accuracy of 97% was achieved. The promising results illustrate the potential of this approach when considering a real wheelchair application.

**General information**
The acoustical cross-talk in row–column addressed 2-D transducer arrays for volumetric ultrasound imaging is investigated. Experimental results from a 2.7 MHz, λ/2-pitch capacitive micromachined ultrasonic transducer (CMUT) array with 62 rows and 62 columns are presented and analyzed in the frequency-wavenumber domain. The sources of cross-talk are identified and predicted theoretically. The nearest neighbor cross-talk is 23.9±3.7 dB when the array is used as a 1-D array with the rows functioning as both transmitters and receivers. In the row–column configuration, with the columns transmitting and the rows receiving, the cross-talk is reduced to 40.2±3.5 dB.
Advanced automated gain adjustments for in-vivo ultrasound imaging

Automatic gain adjustments are necessary on the state-of-the-art ultrasound scanners to obtain optimal scan quality, while reducing the unnecessary user interactions with the scanner. However, when large anechoic regions exist in the scan plane, the sudden and drastic variation of attenuations in the scanned media complicates the gain compensation. This paper presents an advanced and automated gain adjustment method that precisely compensate for the gains on scans and dynamically adapts to the drastic attenuation variations between different media. The proposed algorithm makes use of several ultrasonic physical estimates such as scattering strength, focus gain, acoustic attenuation, and noise level to gain a more quantitative understanding of the scanned media and to provide an intuitive adjustment of gains on the scan. The proposed algorithm was applied to a set of 45 in-vivo movie sequences each containing 50 frames. The scans are acquired using a recently commercialized BK3000 ultrasound scanner (BK Ultrasound, Denmark). Matching pairs of in-vivo sequences, unprocessed and processed with the proposed method were visualized side by side and evaluated by 4 radiologists for image quality. Wilcoxon signed-rank test was then applied to the ratings provided by radiologists. The average VAS score was highly positive 12.16 (p-value: 2.09 x 10^-23) favoring the gain-adjusted scans with the proposed algorithm.

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Authors: Moshavegh, R. (Intern), Hemmsen, M. C. (Intern), Martins, B. (Ekstern), Hansen, K. L. (Ekstern), Ewertsen, C. (Ekstern), Brandt, A. H. (Ekstern), Bechsgaard, T. (Ekstern), Bachmann Nielsen, M. (Ekstern), Jensen, J. A. (Intern)
A hand-held row-column addressed CMUT probe with integrated electronics for volumetric imaging

A 3 MHz, λ/2-pitch 62+62 channel row-column addressed 2-D CMUT array designed to be mounted in a probe handle and connected to a commercial BK Medical scanner for real-time volumetric imaging is presented. It is mounted and wire-bonded on a flexible PCB, which is connected to two rigid PCBs with pre-amplifiers for driving the cable to the scanner. The array and PCBs are encapsulated in a 3-D printed handle, and a grounded shielding layer and silicone coating is applied to the front-side of the array for physical and electrical isolation. The handle is assembled together with a 192-channel coaxial cable that connects it to the ultrasound scanner, which supplies the probe with a 190 V DC bias voltage and up to ±75V AC excitation voltage. The probe was successfully connected to a BK3000 scanner and used as two decoupled 1-D phased arrays. Volumetric imaging was demonstrated using the experimental SARUS scanner with 132 volumes/sec.

Assessment of flatness of assumed planar surfaces for ultrasound investigation of elastic surfaces

Assessment of flatness of assumed planar surfaces for ultrasound investigation of elastic surfaces

Assessment of flatness of assumed planar surfaces for ultrasound investigation of elastic surfaces
Automated Hierarchical Time Gain Compensation for In Vivo Ultrasound Imaging

Time gain compensation (TGC) is essential to ensure the optimal image quality of the clinical ultrasound scans. When large fluid collections are present within the scan plane, the attenuation distribution is changed drastically and TGC compensation becomes challenging. This paper presents an automated hierarchical TGC (AHTGC) algorithm that accurately adapts to the large attenuation variation between different types of tissues and structures. The algorithm relies on estimates of tissue attenuation, scattering strength, and noise level to gain a more quantitative understanding of the underlying tissue and the ultrasound signal strength. The proposed algorithm was applied to a set of 44 in vivo abdominal movie sequences each containing 15 frames. Matching pairs of in vivo sequences, unprocessed and processed with the proposed AHTGC were visualized side by side and evaluated by two radiologists in terms of image quality. Wilcoxon signed-rank test was used to evaluate whether radiologists preferred the processed sequences or the unprocessed data. The results indicate that the average visual analogue scale (VAS) is positive (p-value: $2.34 \times 10^{-13}$) and estimated to be $1.01$ (95% CI: $0.85$; $1.16$) favoring the processed data with the proposed AHTGC algorithm.
Cardiovascular diseases are projected to remain the single leading cause of death globally. Timely diagnosis and treatment of these diseases are crucial to prevent death and dangerous complications. One of the important tools in early diagnosis of arrhythmias is analysis of electrocardiograms (ECGs) obtained from ambulatory long-term recordings. The design of novel patch-type ECG recorders has increased the accessibility of these long-term recordings. In many applications, it is furthermore an advantage for these devices that the recorded ECGs can be analyzed automatically in real time. The purpose of this study was therefore to design a novel algorithm for automatic heart beat detection, and embed the algorithm in the CE marked ePatch heart monitor. The algorithm is based on a novel cascade of computationally efficient filters, optimized adaptive thresholding, and a refined search back mechanism. The design and optimization of the algorithm was performed on two different databases: The MIT-BIH arrhythmia database (Se=99.90%, P+=99.87%) and a private ePatch training database (Se=99.88%, P+=99.37%). The offline validation was conducted on the European ST-T database (Se=99.84%, P+=99.71%). Finally, a double-blinded validation of the embedded algorithm was conducted on a private ePatch validation database (Se=99.91%, P+=99.79%). The algorithm was thus validated with high clinical performance on more than 300 ECG records from 189 different subjects with a high number of different abnormal beat morphologies. This demonstrates the strengths of the algorithm, and the potential for this embedded algorithm to improve the possibilities of early diagnosis and treatment of cardiovascular diseases.
B.C.I inside a virtual reality classroom: a potential training tool for attention

**Background:** A growing population is diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and are currently being treated with psychostimulants. Brain Computer Interface (BCI) is a method of communicating with an external program or device based on measured electrical signals from the brain. A particular brain signal, the P300 potential, can be measured about 300 ms after a voluntary cognitive involvement to external stimuli. By utilizing the P300 potential, we have designed a BCI- assisted exercising tool targeting attention enhancement within an immersive 3D virtual reality (VR) classroom.

**Methods:** Combining a low-cost infrared camera with an “off-axis perspective projection” algorithm to achieve the illusion of 3D, an engaging training environment has been created. The setup also includes a single measurement electrode placed on the scalp above the parietal lobe (P2). Two sets of experiments have been performed to elicit the P300 potential. One used a system which is a variant of Farwell and Donchin’s famous P300 speller and the other used a system where the user is required to search for a specific letter in a series of changing images. A non-linear optimized support vector machine (SVM) classifier has been used to automatically detect the P300 potential.

**Results:** Six subjects have participated in the preliminary experiment to test the prototype system, and an average error rate below 0.30 have been achieved, which is noteworthy considering the simplicity of the scheme.

**Conclusions:** This work has successfully demonstrated a non-intrusive, low-cost, and portable system targeting attention in a motivating and engaging environment.

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Bringing transcranial mapping into shape: Sulcus-aligned mapping captures motor somatotopy in human primary motor hand area

Motor representations express some degree of somatotopy in human primary motor hand area (M1HAND), but within-M1HAND corticomotor somatotopy has been difficult to study with transcranial magnetic stimulation (TMS). Here we introduce a “linear” TMS mapping approach based on the individual shape of the central sulcus to obtain mediolateral corticomotor excitability profiles of the abductor digiti minimi (ADM) and first dorsal interosseus (FDI) muscles. In thirteen young volunteers, we used stereotactic neuronavigation to stimulate the right M1HAND with a small eight-shaped coil at 120% of FDI resting motor threshold. We pseudorandomly stimulated six targets located on a straight mediolateral line corresponding to the overall orientation of the central sulcus with a fixed coil orientation of 45° to the mid-sagittal line (STRAIGHT-450 FIX) or seven targets in the posterior part of the crown of the central sulcus following the bending of the
central sulcus (CURVED). CURVED mapping employed a fixed (CURVED-450 FIX) or flexible coil orientation producing always a current perpendicular to the sulcal wall (CURVED-900 FLEX). During relaxation, CURVED but not STRAIGHT mapping revealed distinct corticomotor excitability peaks in M1HAND with the excitability maximum of ADM located medially to the FDI maximum. This mediolateral somatotopy was still present during tonic contraction of the ADM or FDI. During ADM contraction, cross-correlation between the spatial excitability profiles of ADM and FDI was lowest for CURVED-900 FLEX. Together, the results show that within-M1HAND somatotopy can be readily probed with linear TMS mapping aligned to the sulcal shape. Sulcus-aligned linear mapping will benefit non-invasive studies of representational plasticity in human M1HAND.

**General information**

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Authors: Raffin, E. (Ekstern), Pellegrino, G. (Ekstern), Di Lazzaro, V. (Ekstern), Thielscher, A. (Intern), Siebner, H. R. (Ekstern)
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Characterization of early and mature electrophysiological biomarkers of patients with Parkinson's disease

Neurodegenerative diseases (NDD) are highly disabling and severe diseases, and become more common with increasing age. As no cure exist and as the aging population increases, NDDs are considered to be one of the most serious health problems facing modern society. The most elusive goal in the field of NDD is to find a neuroprotective agent, and if such treatment becomes available, it is essential that the patients can be identified as early as possible. Parkinson's disease (PD) is the second most common NDD, and early disease identification is an active field of research as no reliable markers yet exist [83]. Sleep disturbances are common non-motor symptoms of PD, and strong findings associating a specific sleep disorder ("iRBD") to Parkinsonism suggest that sleep disturbances might precede the clinical diagnosis of PD. Analysis of sleep thus hold potential to serve as early disease identification, but as the current standard for sleep analysis relies on manual scorings guided by standards designed to fit healthy and normal sleep, manual sleep analysis of pathological sleep lacks substance. This dissertation hypothesizes that automated sleep analysis can identify altered patterns of EEG and EOG in pathological sleep and may serve to reveal PD biomarkers. The aims of this dissertation was to: 1) Develop full data-driven sleep models based on EEG, EOG or both, that can describe sleep in detail and can be used in the analysis of normal as well as pathological sleep. 2) Extract appropriate features from the automated sleep models describing alterations in the sleep patterns of patients with PD or iRBD. 3) Identify changes of sleep spindles in the EEG of patients with PD by extracting features describing spindle morphology. The results showed that patients with PD or iRBD reflect 1) altered eye movements during sleep, 2) altered amount and stability of data-determined stages linked to N3 and REM sleep, 3) more REM-NREM sleep transitions determined by a data-driven model, 4) decreased spindle density and 5) altered spindle morphology compared to non-NDD subjects. In conclusion, this dissertation illustrates how appropriate biomedical signal processing can be used to reveal indicative alterations in the sleep EEG and EOG of patients with iRBD and PD. The automated methods developed analyze sleep in a robust and standardized way and can be supportive for sleep evaluation. Conclusively, this dissertation contributes to the field of early PD identification, but substantiates the claim that no known PD biomarker is reliable enough to stand alone.

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Authors: Christensen, J. A. E. (Intern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern), Rahn Christensen, S. (Ekstern), Arvastson, L. (Ekstern)
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Clinical evaluation of synthetic aperture harmonic imaging for scanning focal malignant liver lesions
The purpose of the study was to perform a clinical comparison of synthetic aperture sequential beamforming tissue harmonic imaging (SASB-THI) sequences with a conventional imaging technique, dynamic receive focusing with THI (DRF-THI). Both techniques used pulse inversion and were recorded interleaved using a commercial ultrasound system (UltraView 800, BK Medical, Herlev, Denmark). Thirty-one patients with malignant focal liver lesions (confirmed by biopsy or computed tomography/magnetic resonance) were scanned. Detection of malignant focal liver lesions and preference of image quality were evaluated blinded off-line by eight radiologists. In total, 2,032 evaluations of 127 image sequences were completed. The sensitivity (77% SASB-THI, 76% DRF-THI, p = 0.54) and specificity (71% SASB-THI, 72% DRF-THI, p = 0.67) of detection of liver lesions and the evaluation of image quality (p = 0.63) did not differ between SASB-THI and DRF-THI. This study indicates the ability of SASB-THI in a true clinical setting.
Comparing twelve-lead electrocardiography with close-to-heart patch based electrocardiography

Electrocardiographic (ECG) recording using adhesive patch-type ECG monitors (PEMs) has several advantages over conventional ECG recorders. However, due to the unconventional electrode locations used in PEM systems, the morphology of the acquired ECG signals may differ from conventional ECG leads used in the clinic impeding clinical interpretation. In this study, recordings from an ePatch® lead system involving three torso sites are compared with concurrently recorded standard 12-lead ECG. Pearson's correlation coefficients (CC) of ~0.90 and 0.91 is found between two of the PEM signals and the standard 12-lead ECG signals aVR and V2, respectively. Deriving the 12-lead ECG from the PEM leads through linear transforms on a subject-specific basis yield CC values ranging from 0.78 to 0.96 between measured and derived leads. The corresponding CC values for the PEM ECG leads range from 0.88 to 0.95. It is found that the PEM lead system captures 'residual' information not contained in the standard 12-lead ECG and i.a. a negative deflection after the T-wave is discovered in the PEM signals.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, DELTA Microelectronics, University of Copenhagen
Authors: Hansen, I. H. (Intern), Hoppe, K. (Ekstern), Gjerde, A. (Ekstern), Kanters, J. K. (Ekstern), Sørensen, H. B. D. (Intern)
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Compressive sensing of full wave field data for structural health monitoring applications
Numerous nondestructive evaluations and structural health monitoring approaches based on guide waves rely on analysis of wave fields recorded through scanning laser Doppler vibrometers (SLDVs) or ultrasonic scanners. The informative content which can be extracted from these inspections is relevant; however, the acquisition process is generally time-consuming, posing a limit in the applicability of such approaches. To reduce the acquisition time, we use a random sampling scheme based on compressive sensing (CS) to minimize the number of points at which the field is measured. The CS reconstruction performance is mostly influenced by the choice of a proper decomposition basis to exploit the sparsity of the acquired signal. Here, different bases have been tested to recover the guided waves wave field acquired on both an aluminum and a composite plate. Experimental results show that the proposed approach allows a reduction of the measurement locations required for accurate signal recovery to less than 34% of the original sampling grid.

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Authors: di Ianni, T. (Intern), De Marchi, L. (Ekstern), Perelli, A. (Ekstern), Marzani, A. (Ekstern)
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Adaptive behavior relies on combining bottom-up sensory inputs with top-down control signals to guide responses in line with current goals and task demands. Over the past decade, accumulating evidence has suggested that the dorsal and ventral frontoparietal attentional systems are recruited interactively in this process. This fMRI study used concurrent transcranial magnetic stimulation (TMS) as a causal perturbation approach to investigate the interactions between dorsal and ventral attentional systems and sensory processing areas. In a sustained spatial attention paradigm, human participants detected weak visual targets that were presented in the lower-left visual field on 50% of the trials. Further, we manipulated the presence/absence of task-irrelevant auditory signals. Critically, on each trial we applied 10 Hz bursts of four TMS (or Sham) pulses to the intraparietal sulcus (IPS). IPS-TMS relative to Sham-TMS increased activation in the parietal cortex regardless of sensory stimulation, confirming the neural effectiveness of TMS stimulation. Visual targets increased activations in the anterior insula, a component of the ventral attentional system responsible for salience detection. Conversely, they decreased activations in the ventral visual areas. Importantly, IPS-TMS abolished target-evoked activation increases in the right temporoparietal junction (TPJ) of the ventral attentional system, whereas it eliminated target-evoked activation decreases in the right fusiform. Our results demonstrate that IPS-TMS exerts profound directional causal influences not only on visual areas but also on the TPJ as a critical component of the ventral attentional system. They reveal a complex interplay between dorsal and ventral attentional systems during target detection under sustained spatial attention.
Convex Array Vector Velocity Imaging Using Transverse Oscillation and Its Optimization
A method for obtaining vector flow images using the transverse oscillation (TO) approach on a convex array is presented. The paper presents optimization schemes for TO fields and evaluates their performance using simulations and measurements with an experimental scanner. A 3-MHz 192-element convex array probe (pitch 0.33 mm) is used in both simulations and measurements. A parabolic velocity profile is simulated at a beam-to-flow angle of 90°. The optimization routine changes the lateral oscillation period \( \lambda_x \) as a function of depth to yield the best possible estimates based on the energy ratio between positive and negative spatial frequencies in the ultrasound field. The energy ratio is reduced from −17.1 dB to −22.1 dB. Parabolic profiles are estimated on simulated data using 16 emissions. The optimization gives a reduction in standard deviation from 8.81% to 7.4% for 16 emissions, with a reduction in lateral velocity bias from −15.93% to 0.78% at 90° (transverse flow) at a depth of 40 mm. Measurements have been performed using the experimental ultrasound scanner and a convex array transducer. A bias of −0.93% was obtained at 87° for a parabolic velocity profile along with a standard deviation of 6.37%. The livers of two healthy volunteers were scanned using the experimental setup. The in vivo images demonstrate that the method yields realistic estimates with a consistent angle and mean velocity across three heart cycles.
Design of Low Power Algorithms for Automatic Embedded Analysis of Patch ECG Signals

The diagnosis of cardiac arrhythmias often depends on information from long-term ambulatory electrocardiographic (ECG) monitoring. For several decades, these recordings have been obtained by wired Holter recorders. However, to overcome some of the known disadvantages of the old technologies, several different cable-free wireless patch-type ECG recorders have recently reached the market. One of these recorders is the ePatch designed by the Danish company DELTA. The extended monitoring period available with the patch recorders has demonstrated to increase the diagnostic yield of outpatient ECG monitoring. Furthermore, the patch recorders facilitate the possibility of outpatient ECG monitoring in new clinically relevant areas, e.g. telemedicine monitoring of cardiac patients in their homes. Some of these new applications could benefit from real-time embedded interpretation of the recorded ECGs. Such algorithms could allow the real-time transmission of clinically relevant information to a central monitoring station. The first step in embedded ECG interpretation is the automatic detection of each individual heartbeat. An important part of this project was therefore to design a novel algorithm that was optimized for heartbeat detection in ePatch ECGs and embed the algorithm in the ePatch sensor for realtime analysis. We designed the algorithm based on a novel cascade of computational efficient filters and adaptive thresholds. We evaluated the algorithm on both standard databases and three different manually annotated ePatch databases. We found a very high detection performance with respect to both normal and abnormal beats as well as different types of artifacts arising from different daily life activities (average detection performance on 952,632 manually annotated beats obtained from 198 different patients: Se = 99.86% and P+ = 99.74%). This shows the possibilities for the embedded analysis of the ePatch ECGs, and the designed algorithm thus provides a platform for further research in this area. The expected advantages of the patch recorders are, however, unconditionally limited by their ability to record high-quality diagnostic ECGs throughout the recording period. Another main focus of this thesis was therefore to investigate different important clinical aspects of the novel ePatch recorder. To achieve this, we designed two pilot studies that were intended to provide information about the clinical usability of the ePatch ECGs for heart rhythm analysis. In the first pilot study, two medical doctors were asked to provide an individual assessment of the usefulness of 200 ePatch ECG segments for heart rhythm analysis. They found that more than 98% of the segments were useful. The second pilot study was designed as a high level comparison between the diagnostic information that could be extracted from simultaneous recordings obtained with the ePatch recorder and the traditional telemetry equipment. This comparison was conducted by
a cardiologist on 11 admitted patients. He found no clinically relevant differences between the information extracted from the two systems. Both pilot studies thus indicate a high potential for the clinical application of ECGs recorded with the ePatch system. To further investigate the general signal quality obtained by the ePatch, we designed a novel algorithm for the automatic estimation of the overall percentage of analyzable time (PAT) in ECGs. The algorithm obtained very high classification performance and is therefore expected to provide a reliable estimation of the overall PAT. We then applied the algorithm to investigate the PAT in 250 different ePatch recordings. We found that 10% of the recordings obtained less than 10% analyzable time, and they were considered as incorrect measurements. For the remaining 90% of the recordings, we found a very high PAT (median: 100% (interquartile range: 97.9% to 100%); mean: (92.4 ± 18.8)%). We therefore didn’t find indications of problems related to the general signal quality obtained by the ePatch recorder. Overall, we thus find a high potential for the application of the ePatch recorder in many different clinical settings in the future.

**General information**

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen Center for Health Technology, Odense University Hospital
Authors: Saadi, D. B. (Intern), Sørensen, H. B. D. (Intern), Egstrup, K. (Ekstern)
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**ECG De-noising: A Comparison Between EEMD-BLMS and DWT-NN Algorithms.**

Electrocardiogram (ECG) is a widely used noninvasive method to study the rhythmic activity of the heart and thereby to detect the abnormalities. However, these signals are often obscured by artifacts from various sources and minimization of these artifacts are of paramount important. This paper proposes two adaptive techniques, namely the EEMD-BLMS (Ensemble Empirical Mode Decomposition in conjunction with the Block Least Mean Square algorithm) and DWT-NN (Discrete Wavelet Transform followed by Neural Network) methods in minimizing the artifacts from recorded ECG signals, and compares their performance. These methods were first compared on two types of simulated noise corrupted ECG signals: Type-I (desired ECG+noise frequencies outside the ECG frequency band) and Type-II (ECG+noise frequencies both inside and outside the ECG frequency band). Subsequently, they were tested on real ECG recordings. Results clearly show that both the methods works equally well when used on Type-I signals. However, on Type-II signals the DWT-NN performed better. In the case of real ECG data, though both methods performed similar, the DWT-NN method was a slightly better in terms of minimizing the high frequency artifacts.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark
Authors: Kærgaard, K. (Ekstern), Jensen, S. H. (Ekstern), Puthusserypady, S. (Intern)
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EEG recordings as a source for the detection of IRBD
The purpose of this pilot study was to develop a supportive algorithm for the detection of idiopathic Rapid Eye-Movement (REM) sleep Behaviour Disorder (iRBD) from EEG recordings. iRBD is defined as REM sleep without atonia with no current sign of neurodegenerative disease, and is one of the earliest known biomarkers of Parkinson's Disease (PD). It is currently diagnosed by polysomnography (PSG), primarily based on EMG recordings during REM sleep. The algorithm was developed using data collected from 42 control subjects and 34 iRBD subjects. A feature was developed to represent high amplitude contents of the EEG and a semi-automatic signal reduction method was introduced. The reduced feature set was used for a subject-based classification. With a subject specific re-scaling of the feature set and the use of an outlier detection classifier the algorithm reached an accuracy of 0.78. The result shows that EEG recordings contain valid information for a supportive algorithm for the detection of iRBD. Further investigation could lead to promising application of EEG recordings as a supportive source for the detection of iRBD.
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Web of Science (2018): Indexed yes
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BFI (2014): BFI-level 2
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Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.872 SNIP 1.496 CiteScore 2.18
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
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Web of Science (2012): Indexed yes
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Scopus rating (2010): SJR 0.928 SNIP 1.562
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
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Scopus rating (2008): SJR 1.324 SNIP 1.567
Web of Science (2008): Indexed yes
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Web of Science (2005): Indexed yes
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Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 1.437 SNIP 1.742
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 1.525 SNIP 1.916
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 1.703 SNIP 1.6
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Endothelial derived hyperpolarization in renal interlobar arteries.
In small arteries, vascular smooth muscle cells (VSMCs) and endothelial cells (ECs) are connected by myoendothelial junctions (MEJ), usually extending from the EC. Ca2+ activated K+ channels (IKCa and SKCa) located in the MEJ are suggested to play a role in NO-independent endothelium derived hyperpolarization (EDH) of VSMCs. The IKCa and SKCa channels could affect the VSMC through direct electrical coupling via myoendothelial gap junctions (MEGJ). Alternatively, K+ released from the EC into the intercellular space between EC and VSMC could activate VSMC Kir and Na/K-ATPases.
A spatiotemporal model was constructed to simulate possible effect of IKCa and SKCa activation in MEJ. The model suggested that a significant part of the K+ current entered the VSMC via MEGJ. The simulation also showed that activation of IKCa and SKCa elevated extracellular K+ slightly, which could affect VSMC Kir and Na/K-ATPases.
Experiments were conducted in the wire-myograph using renal interlobar arteries from wild-type and Cx40 knock-out mice. NO synthase and the cyclooxygenase were inhibited using L-NAME and indomethacin. The EDH elicited in renal vessels from wild-type and Cx40 knock-out mice were not significantly different. Inhibition of IKCa and SKCa using TRAM-34 and Apamin significantly reduced EDH in renal vessels from both wild-type and Cx40 KO mice. Inhibition of Kir and Na/K-ATPases reduced EDH in Cx40 KO mice but not in wild-type mice. We suggest that EDH consists of at least two independent pathways, K+ current through MEGJs and increased extracellular K+, which can relay the signal from the IKCa and SKCa channels.

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Authors: Brasen, J. C. (Intern), Sørensen, C. M. (Ekstern)
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Scopus rating (2015): SJR 1.654 SNIP 1.075 CiteScore 2.78
Web of Science (2015): Indexed yes
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Facing and Overcoming Sensitivity Challenges in Biomolecular NMR Spectroscopy

In the Spring of 2013, NMR spectroscopists convened at the Weizmann Institute in Israel to brainstorm on approaches to improve the sensitivity of NMR experiments, particularly when applied in biomolecular settings. This multi-author interdisciplinary Review presents a state-of-the-art description of the primary approaches that were considered. Topics discussed included the future of ultrahigh-field NMR systems, emerging NMR detection technologies, new approaches to nuclear hyperpolarization, and progress in sample preparation. All of these are orthogonal efforts, whose gains could multiply and thereby enhance the sensitivity of solid- and liquid-state experiments. While substantial advances have been made in all these areas, numerous challenges remain in the quest of endowing NMR spectroscopy with the sensitivity that has characterized forms of spectroscopies based on electrical or optical measurements. These challenges, and the ways by which scientists and engineers are striving to solve them, are also addressed.

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Scopus rating (2014): SJR 5.811 SNIP 2.307 CiteScore 10.84
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Scopus rating (2010): SJR 5.921 SNIP 2.303
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Scopus rating (2009): SJR 5.571 SNIP 2.246
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Scopus rating (2007): SJR 4.528 SNIP 1.888
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Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 4.797 SNIP 2.279
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 4.247 SNIP 2.198
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 3.559 SNIP 2.117
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 4.012 SNIP 2.142
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First Clinical Investigations of New Ultrasound Techniques in Three Patient Groups: Patients with Liver Tumors, Arteriovenous Fistulas, and Arteriosclerotic Femoral Arteries

In this PhD project two newer ultrasound techniques are for the first time used for clinical scans of patients with malignant liver tumors (Study I), arteriovenous fistulas for hemodialysis (Study II) and arteriosclerotic femoral arteries (Study III). The same commercial ultrasound scanner was used in all three studies. Study I was a comparative study of B-mode ultrasound images obtained with conventional technique and the experimental technique Synthetic Aperture Sequential Beamforming (SASB). SASB is a data reducing version of the technique synthetic aperture, which has the potential to produce ultrasound images of very high quality with high frame rate. Synthetic aperture is unfortunately very demanding computationally, and is therefore used only in experimental scanners. SASB reduces the data volume by a factor of 64, thereby making it possible to implement the technology on a commercial ultrasound scanner, to perform wireless data transfer and in the future to develop e.g. a wireless ultrasonic transducer. Nineteen patients with either primary liver cancer or liver metastases from colon cancer were ultrasound scanned the day before planned liver resection. Patients were scanned simultaneously with the conventional technique and SASB, and the image quality was subsequently evaluated from a clinical perspective by five radiologists with ultrasound experience. The evaluations showed a slight (statistically insignificant) advantage to SASB, and the study thereby showed that SASB, in spite of the significant data reduction, is suitable for clinical use. In Study II, 20 patients with arteriovenous fistulas for hemodialysis were ultrasound scanned directly on the most superficial and accessible part of the fistula. The vector ultrasound technique Vector Flow Imaging (VFI) was used. VFI can quantitatively estimate the direction and velocity of the blood flow in a vessel, independently of the angle of insonation. Conventional Doppler technique is dependent on an angle of insonation < 60-70° when a quantitative estimation of flow is needed. It is therefore challenging to use on the very superficial arteriovenous fistulas. The fistulas were scanned perpendicular to the vessel, the cross-sectional area was calculated and blood flow velocity measured. The average flow velocity was calculated and multiplied by the cross sectional area, thereby calculating volume flow in the fistula. This was compared with the gold standard for volume flow measurements (ultrasound dilution technique), and was 31 – 35 % lower than the gold standard, but showed a 4 significantly improved standard deviation. The study thus demonstrated a new, direct and intuitive way to measure blood flow in arteriovenous fistulas. Study III was also a flow study using VFI. Eleven patients with arteriosclerotic disease in the superficial femoral artery had an ultrasound scan of the vessel performed just before a planned angiography of the arteries. If turbulent/disturbed flow was identified with VFI, and suspicion of a flow disturbing arteriosclerotic lesion was raised, recordings of the flow were made. The recordings were subsequently analyzed, and for each recording blood flow velocity at the lesion was compared with the flow velocity in a healthy adjacent arterial segment. If the velocity at the lesion was higher than in the healthy segment, it was considered a stenosis. By comparison with the subsequent angiography a strong correlation was found between the calculated velocity ratios and the measured angiographic stenosis degrees. Thus, it was possible to assess stenosis degree quantitatively from the VFI ultrasound scan. Furthermore, it was calculated that a doubling of the flow velocity indicates a stenosis degree of 50 %, and thus a clinically significant stenosis requiring treatment. The study is the first of its kind where a vector ultrasound technique is used to calculate velocity ratios related to arteriosclerotic stenoses, and the obtained results are consistent with previous studies performed with conventional Doppler technique. Use of VFI is more intuitive, and may be used to perform faster and more accurate screening of these patients before they are referred to angiography. The three studies demonstrate the first application of the new ultrasound techniques in selected groups of patients. For all three studies the results are promising, and hopefully the techniques will find their way into everyday clinical practice for the benefit of both patients and healthcare practitioners.
Fourier beamformation of multistatic synthetic aperture ultrasound imaging

A new Fourier beamformation (FB) algorithm is presented for multistatic synthetic aperture ultrasound imaging. It can reduce the number of computations by a factor of 20 compared to conventional Delay-and-Sum (DAS) beamformers. The concept is based on the wavenumber algorithm from radar and sonar in the frequency domain, which is extended to a multistatic configuration. Window functions are used to reduce the sidelobe levels. Field II simulated data have been used to evaluate the results in terms of point spread function, resolution, contrast, and processing time. Lateral resolutions of 0.75 mm and 0.82 mm are obtained for FB and DAS on simulated point target data. Corresponding axial resolutions are 0.33 mm for FB and 0.35 mm for DAS. The cystic resolution of point targets at different depths for −20 dB and −6 dB demonstrates a better resolution for FB at all depths. A cyst phantom was also used to calculate the contrast ratio, which is 94.04% and 94.72% for DAS and FB, respectively. The corresponding processing times are 118 sec and 2186 sec for FB and DAS. Results show that FB can reduces the processing time by the factor of 20.4 while retaining the image quality.

High Frame Rate Vector Velocity Estimation using Plane Waves and Transverse Oscillation

This paper presents a method for estimating 2-D vector velocities using plane waves and transverse oscillation. The approach uses emission of a low number of steered plane waves, which result in a high frame rate and continuous acquisition of data for the whole image. A transverse oscillating field is obtained by filtering the beamformed RF images in the Fourier domain using a Gaussian filter centered at a desired oscillation frequency. Performance of the method is quantified through measurements with the experimental scanner SARUS and the BK 2L8 linear array transducer. Constant parabolic flow in a flow rig phantom is scanned at beam-to-flow angles of 90, 75, and 60°. The relative bias is between -1.4 % and -5.8 % and the relative std. between 5 % and 8.2 % for the lateral velocity component at the measured beam-to-flow angles. The estimated flow angle is 73.4°± 3.6° for the measurement at 75°. Measurement of pulsatile flow through a constricted vessel demonstrate the application of the method in a realistic flow environment with large spatial and temporal flow gradients.
High Resolution Depth-Resolved Imaging From Multi-Focal Images for Medical Ultrasound

An ultrasound imaging technique providing subdiffraction limit axial resolution for point sources is proposed. It is based on simultaneously acquired multi-focal images of the same object, and on the image metric of sharpness. The sharpness is extracted by image data and presents higher values for in-focus images. The technique is derived from biological microscopy and is validated here with simulated ultrasound data. A linear array probe is used to scan a point scatterer phantom that moves in depth with a controlled step. From the beamformed responses of each scatterer position the image sharpness is assessed. Values from all positions plotted together form a curve that peaks at the receive focus, which is set during the beamforming. Selection of three different receive foci for each acquired dataset will result in the generation of three overlapping sharpness curves. A set of three calibration curves combined with the use of a maximum-likelihood algorithm is then able to estimate, with high precision, the depth location of any emitter from each single image. Estimated values are compared with the ground truth demonstrating that an accuracy of 28.6 µm (0.13λ) is achieved for a 4 mm depth range.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Heriot-Watt University, University of Edinburgh
Authors: Diamantis, K. (Ekstern), Dalgarno, P. A. (Ekstern), Greenaway, A. H. (Ekstern), Anderson, T. (Ekstern), Jensen, J. A. (Intern), Sboros, V. (Ekstern)
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Image Quality Degradation from Transmit Delay Profile Quantization

The investigated hypothesis is that quantization of the transmit delay profiles degrades the image quality in plane wave ultrasound imaging. Simulated point spread functions show that transmit delay profile quantization gives rise to artefacts behind the point target. The axial and lateral 6 dB resolution is unaffected, but contrast is reduced. This is quantified by a 20 dB cystic resolution of 1.23 mm compared to 0.53 mm for the ideal (non-quantized) case at 10 mm depth. It is also shown that providing individually phase-shifted excitation waveforms to each element restores the image quality, as seen by the 20 dB cystic resolution being restored to 0.53 mm. The impact on high-quality imaging is discussed.

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Authors: Stuart, M. B. (Intern), Jensen, J. (Intern), di Ianni, T. (Intern), Jensen, J. A. (Intern)
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Implementation of real-time duplex synthetic aperture ultrasonography
This paper presents a real-time duplex synthetic aperture imaging system, implemented on a commercially available tablet. This includes real-time wireless reception of ultrasound signals and GPU processing for B-mode and Color Flow Imaging (CFI). The objective of the work is to investigate the implementation complexity and processing demands. The image processing is performed using the principle of Synthetic Aperture Sequential Beamforming (SASB) and the flow estimator is implemented using the cross-correlation estimator. Results are evaluated using a HTC Nexus 9 tablet and a BK Medical BK3000 ultrasound scanner emulating a wireless probe. The duplex imaging setup consists of interleaved B-mode and CFM frames. The required data throughput for real-time imaging is 36.1 MB/s. The measured data throughput peaked at 39.562 MB/s, covering the requirement for real-time data transfer and overhead in the TCP/IP protocol. Benchmarking of real-time imaging showed a total processing time of 25.7 ms (39 frames/s) which is less than the acquisition time (29.4 ms). In conclusion, the proposed implementation demonstrates that both B-mode and CFM can be executed in-time for real-time ultrasound imaging and that the required bandwidth between the probe and processing unit is within the current Wi-Fi standards.

Improved Vector Velocity Estimation using Directional Transverse Oscillation
A method for estimating vector velocities using transverse oscillation (TO) combined with directional beamforming is presented. Directional Transverse Oscillation (DTO) is self-calibrating, which increases the estimation accuracy and finds the lateral oscillation period automatically. A normal focused field is emitted and the received signals are beamformed in the lateral direction transverse to the ultrasound beam. A lateral oscillation is obtained by having a receive apodization waveform with two separate peaks. The IQ data are obtained by making a Hilbert transform of the directional signal, and a modified TO estimator can be used to find both the lateral and axial velocity. The approach is self-calibrating as the lateral oscillation period directly is estimated from the directional signal through a Fourier transform. The approach was implemented on the SARUS scanner using a BK Medical 8820e transducer with a focal point at 105.6 mm (F#=5) for Vector Flow Imaging (VFI). A 6 mm radius tube in a circulating flow rig was scanned and the parabolic volume flow of 112.7 l/h (peak velocity 0.55 m/s) measured by a Danfoss Magnetic flow meter for reference. Velocity estimates for DTO are found for 32 emissions at a 90 degrees beam-to-flow angle at a vessel depth of 30 mm. The standard deviation (SD) drops from 9.14% for TO to 5.4%, when using DTO. The bias is -5.05% and the angle is found within +/- 3.93 degrees. At 70 mm a relative SD of 7% is obtained, the bias is -1.74%, and the angle is found within +/- 2.6 degrees showing a low bias across depths.
Increased Frame Rate for Plane Wave Imaging Without Loss of Image Quality

Clinical applications of plane wave imaging necessitate the creation of high-quality images with the highest possible frame rate for improved blood flow tracking and anatomical imaging. However, linear array transducers create grating lobe artefacts, which degrade the image quality especially in the near field for λ-pitch transducers. Artefacts can only partly be suppressed by increasing the number of emissions, and this paper demonstrates how the frame rate can be increased without loss of image quality by using λ/2-pitch transducers. The number of emissions and steering angles are optimized in a simulation study to get the best images with as high a frame rate as possible. The optimal setup for a simulated 4.1 MHz λ-pitch transducer is 73 emissions and a maximum steering of 22°. The achieved FWHM is 1.3λ and the cystic resolution is -25 dB for a scatter at 9 mm. Only 37 emissions are necessary within the same angle range when using a λ/2-pitch transducer, and the cystic resolution is reduced to -56 dB. Measurements are performed with the experimental SARUS scanner connected to a λ-pitch and λ/2-pitch transducer. A wire phantom and a tissue mimicking phantom containing anechoic cysts are scanned and show the performance using the optimized sequences for the transducers. Measurements confirm results from simulations, and the λ-pitch transducer show artefacts at undesirable strengths of -25 dB for a low number of emissions.

Influence of K+-channels and gap junctions on endothelium derived hyperpolarization-induced renal vasodilation in rats

We investigated the role of Ca2+-activated K+ -channels in the endothelial derived hyperpolarization-induced renal vasodilation in vitro and in vivo in rats. Also, the possible role of K+- induced activation of inward rectifier K+ (KIR) channels and Na+ /K+ -ATPase was assessed. Furthermore, involvement of renal myoendothelial gap junctions was evaluated in vitro. Because assessment of endothelial derived hyperpolarization-induced renal vasodilation in vivo is hampered by experimental limitations, we have combined in vivo and in vitro experiments. Isometric tension in rat renal interlobar arteries was measured using a wire myograph. Renal blood flow was measured in isoflurane and pentobarbital anesthetized rats. The ACh-induced response was measured before and after inhibition of the nitric oxide synthase with L-NAME and cyclooxygenase using indomethacin. Blockade of small conductance Ca2+-activated K+ -channels (SKCa) by apamin and intermediate conductance Ca2+-activated K+ -channels (IKCa) by TRAM-34 significantly decreased the
endothelial derived hyperpolarization-induced vasorelaxation in vitro but had no effect in vivo. Inhibition of Kir-channels by Ba2+ and Na+/K+-ATPases by ouabain significantly attenuated renal vasorelaxation in vitro but had no effect in vivo. In vitro, inhibition of gap junctions using carbenoxolone or 18a-glycyrrhetinic acid significantly reduced the endothelial derived hyperpolarization-induced vasorelaxation. In conclusion we found that in vitro, renal vascular SKCa and IKCa-channels are essential for the endothelial derived hyperpolarization-induced vasorelaxation. Furthermore, activation of Kir-channels, Na+/K+-ATPases and vascular gap junctions play a significant role in the renal vascular endothelial derived hyperpolarization-response in vitro. In vivo the endothelial derived hyperpolarization response seems unaffected by the present blockade of various K+ channels.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen
Authors: Rasmussen, K. M. (Ekstern), Brasen, J. C. (Intern), Salomonsson, M. (Ekstern), Sørensen, C. M. (Ekstern)
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Inter-expert and intra-expert reliability in sleep spindle scoring

Objectives
To measure the inter-expert and intra-expert agreement in sleep spindle scoring, and to quantify how many experts are needed to build a reliable dataset of sleep spindle scorings.

Methods
The EEG dataset was comprised of 400 randomly selected 115 s segments of stage 2 sleep from 110 sleeping subjects in the general population (57 ± 8, range: 42–72 years). To assess expert agreement, a total of 24 Registered Polysomnographic Technologists (RPSGTs) scored spindles in a subset of the EEG dataset at a single electrode location (C3-M2). Intra-expert and inter-expert agreements were calculated as F1-scores, Cohen’s kappa (κ), and intra-class correlation coefficient (ICC).

Results
We found an average intra-expert F1-score agreement of 72 ± 7% (κ: 0.66 ± 0.07). The average inter-expert agreement was 61 ± 6% (κ: 0.52 ± 0.07). Amplitude and frequency of discrete spindles were calculated with higher reliability than the estimation of spindle duration. Reliability of sleep spindle scoring can be improved by using qualitative confidence scores, rather than a dichotomous yes/no scoring system.

Conclusions
We estimate that 2–3 experts are needed to build a spindle scoring dataset with ‘substantial’ reliability (κ: 0.61–0.8), and 4 or more experts are needed to build a dataset with ‘almost perfect’ reliability (κ: 0.81–1).

Significance
Spindle scoring is a critical part of sleep staging, and spindles are believed to play an important role in development, aging, and diseases of the nervous system.
Sleep spindles, Agreement, Reliability, Inter-rater, Inter-expert, Intra-rater, Intra-expert, Electroencephalography, Polysomnography, Event detection, Sleep staging, Sleep scoring

Investigation of the Minimum Conditions for Reliable Estimation of Clinically Relevant HRV Measures: Introducing a Novel Approach to the Validation of HRV Measurement Systems

The R-peak localization error (jitter) of a heart rate variability (HRV) system has a great impact on the values of the HRV measures. Only a few studies have analyzed this subject and purely done so from the aspect of choice of sampling frequency. In this study we provide an overview of the various factors that comprise the jitter of
any HRV system that records and stores the raw ECG signal. Furthermore, with this method the differences between the HRV measures of the system and HRV measures corresponding to the physiological truth can be quantified. The method is used to obtain the physiologically true R-peak locations of subjects from Physionet’s ‘Normal Sinus Rhythm Database’. The effects of jitter are then analyzed via mathematical modelling for short-term and long-term HRV for various HRV measures. The effects of abnormal beats and missed and false detections are analyzed as well.

General information
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Organisations: Copenhagen Center for Health Technology, Department of Electrical Engineering, Biomedical Engineering , Technical University of Denmark, DELTA, University of Copenhagen
Authors: Ahrens, E. (Ekstern), Sørensen, H. B. D. (Intern), Langberg, H. (Ekstern), Hoppe, K. (Ekstern), Bodholt Saadi, D. (Ekstern)
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In Vivo 3-D Vector Velocity Estimation with Continuous Data
In this study, a method for estimating 3-D vector velocities at very high frame rate using continuous data acquisition is presented. An emission sequence was designed to acquire real-time continuous data in one plane. The transverse oscillation (TO) method was used to estimate 3-D vector flow in a carotid flow phantom and in vivo in the common carotid artery of a healthy 27-year old female. Based on the out-of-plane velocity component during four periodic cycles, estimated flow rates in an experimental setup was 2.96 ml/s ± 0.35 ml/s compared to the expected 3.06 ml/s ± 0.09 ml/s. In the in vivo measurements, three heart cycles acquired at 2.1 kHz showed peak out-of-plane velocities of 83 cm/s, 87 cm/s and 90 cm/s in agreement with the 92 cm/s found with spectral Doppler. Mean flow rate was estimated to 257 ml/min. The results demonstrate that accurate real-time 3-D vector velocities can be obtained using the TO method, which can be used to improve operator-independece when examining blood flow in vivo, thereby increasing accuracy and consistency.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Holbek, S. (Intern), Pihl, M. J. (Intern), Ewertsen, C. (Ekstern), Bachmann Nielsen, M. (Ekstern), Jensen, J. A. (Intern)
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In-Vivo High Dynamic Range Vector Flow Imaging
Current vector flow systems are limited in their detectable range of blood flow velocities. Previous work on phantoms has shown that the velocity range can be extended using synthetic aperture directional beamforming combined with an adaptive multi-lag approach. This paper presents a first invivo example with a high dynamic velocity range. Velocities with
an order of magnitude apart are detected on the femoral artery of a 41 years old healthy individual. Three distinct heart cycles are captured during a 3 secs acquisition. The estimated vector velocities are compared against each other within the heart cycle. The relative standard deviation of the measured velocity magnitude between the three peak systoles was found to be 5.11% with a standard deviation on the detected angle of 1.06° . In the diastole, it was 1.46% and 6.18° , respectively. Results proves that the method is able to estimate flow in-vivo and provide quantitative results in a high dynamic velocity range. Providing velocity measurements during the whole cardiac cycle for both arteries and veins.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Villagómez Hoyos, C. A. (Intern), Stuart, M. B. (Intern), Jensen, J. A. (Intern)
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In Vivo Real Time Volumetric Synthetic Aperture Ultrasound Imaging
Synthetic aperture (SA) imaging can be used to achieve real-time volumetric ultrasound imaging using 2-D array transducers. The sensitivity of SA imaging is improved by maximizing the acoustic output, but one must consider the limitations of an ultrasound system, both technical and biological. This paper investigates the in vivo applicability and sensitivity of volumetric SA imaging. Utilizing the transmit events to generate a set of virtual point sources, a frame rate of 25 Hz for a 90° x 90° field-of-view was achieved. Data were obtained using a 3.5 MHz 32 x 32 elements 2-D phased array transducer connected to the experimental scanner (SARUS). Proper scaling is applied to the excitation signal such that intensity levels are in compliance with the U.S. Food and Drug Administration regulations for in vivo ultrasound imaging. The measured Mechanical Index and spatial-peak- temporal-average intensity for parallel beamforming (PB) are 0.83 and 377.5mW/cm², and for SA are 0.48 and 329.5mW/cm². A human kidney was volumetrically imaged with SA and PB techniques simultaneously. Two radiologists for evaluation of the volumetric SA were consulted by means of a questionnaire on the level of details perceivable in the beamformed images. The comparison was against PB based on the in vivo data. The feedback from the domain experts indicates that volumetric SA images internal body structures with a better contrast resolution compared to PB at all positions in the entire imaged volume. Furthermore, the autocovariance of a homogeneous area in the in vivo SA data, had 23.5% smaller width at the half of its maximum value compared to PB.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital, BK Medical Aps
Authors: Bouzari, H. (Intern), Rasmussen, M. F. (Intern), Brandt, A. H. (Ekstern), Stuart, M. B. (Intern), Nikolov, S. (Ekstern), Jensen, J. A. (Intern)
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KV 7.4 channels participate in the control of rodent renal vascular resting tone.

Aim: We tested the hypothesis that KV7 channels contribute to basal renal vascular tone and that they participate in agonist-induced renal vasoconstriction or vasodilation. Methods: KV7 channel subtypes in renal arterioles were characterized by immunofluorescence. Renal blood flow (RBF) was measured using an ultrasonic flow probe. The isometric tension of rat interlobar arteries was examined in a wire myograph. Mice afferent arteriolar diameter was assessed utilizing the perfused juxtamedullary nephron technique. Results: Immunofluorescence revealed that KV7.4 channels were expressed in rat afferent arterioles. The KV7 blocker XE991 dose-dependently increased the isometric tension of rat interlobar arteries and caused a small (approx. 4.5%) RBF reduction in vivo. Nifedipine abolished these effects. Likewise, XE991 reduced mouse afferent arteriolar diameter by approx. 5%. The KV7.2–5 stimulator flupirtine dose-dependently relaxed isolated rat interlobar arteries and increased (approx. 5%) RBF in vivo. The RBF responses to NE or Ang II administration were not affected by pre-treatment with XE991 or flupirtine. XE991 pre-treatment caused a minor augmentation of the acetylcholine-induced increase in RBF, while flupirtine pre-treatment did not affect this response. Conclusion: It is concluded that KV7 channels, via nifedipine sensitive channels, have a role in the regulation of basal renal vascular tone. There is no indication that KV7 channels have an effect on agonist-induced renal vasoconstriction while there is a small effect on acetylcholine-induced vasodilation.
Microbial Biofilm as a Smart Material

Microbial biofilm colonies will in many cases form a smart material capable of responding to external threats dependent on their size and internal state. The microbial community accordingly switches between passive, protective, or attack modes of action. In order to decide which strategy to employ, it is essential for the biofilm community to be able to sense its own size. The sensor designed to perform this task is termed a quorum sensor, since it only permits collective behaviour once a sufficiently large assembly of microbes have been established. The generic quorum sensor construct involves two genes, one coding for the production of a diffusible signal molecule and one coding for a regulator protein dedicated to sensing the signal molecules. A positive feedback in the signal molecule production sets a well-defined condition for switching into the collective mode. The activation of the regulator involves a slow dimerization, which allows low-pass filtering of the activation of the collective mode. Here, we review and combine the model components that form the basic quorum sensor in a number of Gram-negative bacteria, e.g., *Pseudomonas aeruginosa*.

General information

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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Regulatory Genomics, Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen, University of Cambridge

Authors: Garde, C. (Intern), Welch, M. (Ekstern), Ferkinghoff-Borg, J. (Ekstern), Sams, T. (Intern)

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Micromachined Ultrasonic Transducers for 3-D Imaging

Real-time ultrasound imaging is a widely used technique in medical diagnostics. Recently, ultrasound systems offering real-time imaging in 3-D has emerged. However, the high complexity of the transducer probes and the considerable...
increase in data to be processed compared to conventional 2-D ultrasound imaging results in expensive systems, which limits the more wide-spread use and clinical development of volumetric ultrasound. The main goal of this thesis is to demonstrate new transducer technologies that can achieve real-time volumetric ultrasound imaging without the complexity and cost of state-of-the-art 3-D ultrasound systems. The focus is on row-column addressed transducer arrays. This previously sparsely investigated addressing scheme offers a highly reduced number of transducer elements, resulting in reduced transducer manufacturing costs and data processing. To produce such transducer arrays, capacitive micromachined ultrasonic transducer (CMUT) technology is chosen for this project. Properties such as high bandwidth and high design flexibility makes this an attractive transducer technology, which is under continuous development in the research community.

A theoretical treatment of CMUTs is presented, including investigations of the anisotropic plate behaviour and modal radiation patterns of such devices. Several new CMUT fabrication approaches are developed and investigated in terms of oxide quality and surface protrusions, culminating in a simple four-mask process capable of producing 62+62-element row-column addressed CMUT arrays with negligible charging issues. The arrays include an integrated apodization, which reduces the ghost echoes produced by the edge waves in such arrays by 15.8 dB. The acoustical cross-talk is measured on fabricated arrays, showing a 24 dB reduction in cross-talk compared to 1-D arrays for 2-D imaging. Volumetric imaging is successfully demonstrated using a beamformer specifically developed for row-column addressed arrays. Furthermore, a technique for estimating flow velocities in all three dimensions is presented.

Based on the developed techniques, a complete hand-held 3MHz λ/2-pitch ultrasound probe for volumetric imaging with 62+62 elements and in-handle electronics is produced and used on a commercial bk3000 scanner from BK Medical. The scanner is made for conventional 2-D ultrasound imaging, proving that the developed technology enables realtime volumetric ultrasound imaging with a total system cost and complexity equivalent to that of 2-D ultrasound imaging systems.

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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Christiansen, T. L. (Intern), Thomsen, E. V. (Intern), Jensen, J. A. (Intern)
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Modeling the effects of noninvasive transcranial brain stimulation at the biophysical, network, and cognitive Level
Noninvasive transcranial brain stimulation (NTBS) is widely used to elucidate the contribution of different brain regions to various cognitive functions. Here we present three modeling approaches that are informed by functional or structural brain mapping or behavior profiling and discuss how these approaches advance the scientific potential of NTBS as an interventional tool in cognitive neuroscience. (i) Leveraging the anatomical information provided by structural imaging, the electric field distribution in the brain can be modeled and simulated. Biophysical modeling approaches generate testable predictions regarding the impact of interindividual variations in cortical anatomy on the injected electric fields or the influence of the orientation of current flow on the physiological stimulation effects. (ii) Functional brain mapping of the spatiotemporal neural dynamics during cognitive tasks can be used to construct causal network models. These models can identify spatiotemporal changes in effective connectivity during distinct cognitive states and allow for examining how effective connectivity is shaped by NTBS. (iii) Modeling the NTBS effects based on neuroimaging can be complemented by behavior-based cognitive models that exploit variations in task performance. For instance, NTBS-induced changes in response speed and accuracy can be explicitly modeled in a cognitive framework accounting for the speed-accuracy trade-off. This enables to dissociate between behavioral NTBS effects that emerge in the context of rapid automatic responses or in the context of slow deliberate responses. We argue that these complementary modeling approaches facilitate the use of NTBS as a means of dissecting the causal architecture of cognitive systems of the human brain.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Christian Albrechts University, Copenhagen University Hospital
Monitoring mammary tumor progression and effect of tamoxifen treatment in MMTV-PymT using MRI and magnetic resonance spectroscopy with hyperpolarized [1-13C]pyruvate
Purpose: To use dynamic magnetic resonance spectroscopy (MRS) of hyperpolarized 13C-pyruvate to follow the progress over time in vivo of breast cancer metabolism in the MMTV-PymT model, and to follow the response to the anti-estrogen drug tamoxifen. Methods: Tumor growth was monitored by anatomical MRI by measuring tumor volumes. Dynamic MRS of hyperpolarized 13C was used to measure an "apparent" pyruvate-to-lactate rate constant (kp) of lactate dehydrogenase (LDH) in vivo. Further, ex vivo pathology and in vitro LDH initial reaction velocity were evaluated. Results: Tamoxifen significantly halted the tumor growth measured as tumor volume by MRI. In the untreated animals, kp correlated with tumor growth. The kp was somewhat but not significantly lower in the treated group. Studies in vitro confirmed the effects of tamoxifen on tumor growth, and here the LDH reaction velocity was reduced significantly in the treated group. Conclusion: These hyperpolarized 13C MRS findings indicate that tumor metabolic changes affects kp. The measured kp did not relate to treatment response to the same extent as did tumor growth, histological evaluation, and in vitro determination of LDH activity. © 2014 Wiley Periodicals, Inc.
MR principles, imaging and contrast: Diagnostic Imaging techniques Ph.D. course

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Neue Ansätze zur Empfindlichkeitssteigerung in der biomolekularen NMR-Spektroskopie

General information
A non-invasive method for estimating pressure changes along a streamline using ultrasound is presented. The suggested method estimates pressure gradients from 2-D vector velocity fields. Changes in pressure are derived using a model based on the Navier-Stokes equations. Scans of a carotid bifurcation phantom with a 70% constriction are performed using a linear array transducer connected to the experimental scanner, SARUS. 2-D fields of angle-independent vector velocities are acquired to a depth of 3 cm using directional synthetic aperture vector flow imaging. The performance of the suggested estimator is evaluated by comparing its results to a 3-D numerical simulation model. The study showed pressure drops across the constricted phantom varying from -5 Pa to 7 Pa with a standard deviation of 4%. The proposed method had a normalised rootmean-square error of 10% in reference to the simulation model. Further, an in-vivo scan of the carotid bifurcation is made to show the feasibility of the technique in a less experimental environment.
Output pressure and harmonic characteristics of a CMUT as function of bias and excitation voltage

The large bandwidth makes CMUT based transducers interesting for both conventional and harmonic imaging. The inherent nonlinear behavior of the CMUT, however, poses an issue for harmonic imaging as it is difficult to dissociate the harmonics generated in the tissue from the harmonic content of the transmitted signal. The generation of intrinsic harmonics by the CMUT can be minimized by decreasing the excitation signal. This, however, leads to lower fundamental pressure which limits the desired generation of harmonics in the medium. This work examines the output pressure and harmonic characteristics of a CMUT as function of bias and excitation voltage. The harmonic to fundamental ratio of the surface pressures declines for decreasing excitation voltage and increasing bias voltage. The ratio, however, becomes unchanged for bias levels close to the pull-in voltage. The harmonic limitations of the CMUT is emphasized by a maximum ratio of ~12 dB between harmonics generated in the medium and total harmonics measured at 10 mm.

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Authors: Lei, A. (Intern), Diederichsen, S. E. (Intern), Hansen, S. M. (Intern), Stuart, M. B. (Intern), Bouzari, H. (Intern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)
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Placement of field probes for stabilization of breathing-induced B0-fluctuations in the brain

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Danish Research Centre for Magnetic Resonance, Leiden University Medical Center, University Medical Centre Utrecht, Leiden University
Authors: Andersen, M. (Intern), Madsen, K. H. (Ekstern), Hanson, L. G. (Intern), Boer, V. (Ekstern), van der Velden, T. (Ekstern), Klomp, D. (Ekstern), Wezel, J. (Ekstern), van Osch, M. J. (Ekstern), Webb, A. G. (Ekstern), Versluis, M. J. (Ekstern)
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Bibliographical note
Prostate displacement during transabdominal ultrasound image-guided radiotherapy assessed by real-time four-dimensional transperineal monitoring

Background. Transabdominal ultrasound (TAUS) imaging is currently available for localizing the prostate in daily image-guided radiotherapy (IGRT). The aim of this study was to determine the induced prostate displacement during such TAUS imaging. The prostate displacement was monitored using a novel transperineal four-dimensional (4D) US (TPUS) system.

Material and methods. Ten prostate cancer patients, with a mean age of 68 years (58/76), were US scanned in the computed tomography (CT) room utilizing the Clarity 4D TPUS monitoring system. The patients were asked to comply with a moderate bladder filling protocol. After US-CT fusion, the prostate volume was delineated and used as a reference for weekly US imaging in the treatment room. Immediately after treatment delivery the TPUS monitoring system was set up. During real-time monitoring of the prostate, a conventional 2D probe was applied to simulate a TAUS scan. The time dependent prostate displacements induced by the 2D probe pressure were recorded for the three orthogonal directions. In total 42 monitoring curves with applied 2D probe were recorded. Results. Data analysis of 42 US scans resulted in pressure induced prostate displacements with mean values (± SD) (mm); inferior (I-S): (0.1 0.8); left (L-R): (0.2 0.7); and anterior (A-P): (0.1 1.0). The majority of the displacements were within 1 – 2 mm. Only two scans (5%) (A-P direction) and 16% of Euclidean distances were larger than 2.0 mm. The largest displacement was 2.6 mm in the anterior direction. Conclusion. The novel 4D TPUS system was capable of tracking and recording the prostate positional displacements. The study demonstrated that the prostate induced displacements due to applied TAUS IGRT are small, and in most cases clinically irrelevant to prostate radiotherapy. In ex...
Idiopathic REM sleep behavior disorder (iRBD) is a very strong predictor for later development of Parkinson's disease (PD), and is characterized by REM sleep without atonia (RSWA), resulting in increased muscle activity during REM sleep. Abundant studies have shown the loss of atonia during REM sleep, but our aim was to investigate whether iRBD and PD patients have increased muscle activity in both REM and NREM sleep compared to healthy controls. This was achieved by developing a semi-automatic algorithm for quantification of mean muscle activity per second during all sleep stages for the enrolled patients. The three groups examined included patients suffering from iRBD, PD and healthy control subjects (CO). To determine muscle activity, a baseline and threshold were established after pre-processing of the raw surface electromyography (sEMG) signal. The signal was then segmented according to the different sleep stages and muscle activity beyond the threshold was counted. The results were evaluated statistically using the two-sided Mann-Whitney U-test. The results suggested that iRBD patients also exhibit distinctive muscle activity characteristics in NREM sleep, however not as evident as in REM sleep, leading to the conclusion that RSWA still is the most distinct characteristic of RBD. Furthermore, the muscle activity of PD patients was comparable to that of controls with only slightly elevated amplitudes.

**Quantification of muscle activity during sleep for patients with neurodegenerative diseases**

Idiopathic REM sleep behavior disorder (iRBD) is a very strong predictor for later development of Parkinson's disease (PD), and is characterized by REM sleep without atonia (RSWA), resulting in increased muscle activity during REM sleep. Abundant studies have shown the loss of atonia during REM sleep, but our aim was to investigate whether iRBD and PD patients have increased muscle activity in both REM and NREM sleep compared to healthy controls. This was achieved by developing a semi-automatic algorithm for quantification of mean muscle activity per second during all sleep stages for the enrolled patients. The three groups examined included patients suffering from iRBD, PD and healthy control subjects (CO). To determine muscle activity, a baseline and threshold were established after pre-processing of the raw surface electromyography (sEMG) signal. The signal was then segmented according to the different sleep stages and muscle activity beyond the threshold was counted. The results were evaluated statistically using the two-sided Mann-Whitney U-test. The results suggested that iRBD patients also exhibit distinctive muscle activity characteristics in NREM sleep, however not as evident as in REM sleep, leading to the conclusion that RSWA still is the most distinct characteristic of RBD. Furthermore, the muscle activity of PD patients was comparable to that of controls with only slightly elevated amplitudes.
Quantified pH imaging with hyperpolarized 13C-bicarbonate: Quantified pH Imaging with Hyperpolarized Bicarbonate

Because pH plays a crucial role in several diseases, it is desirable to measure pH in vivo noninvasively and in a spatially localized manner. Spatial maps of pH were quantified in vitro, with a focus on method-based errors, and applied in vivo. In vitro and in vivo 13C mapping were performed for various flip angles for bicarbonate (BiC) and CO2 with spectral-spatial excitation and spiral readout in healthy Lewis rats in five slices. Acute subcutaneous sterile inflammation was induced with Concanavalin A in the right leg of Buffalo rats. pH and proton images were measured 2 h after induction. After optimizing the signal to noise ratio of the hyperpolarized 13C-bicarbonate, error estimation of the spectral-spatial excited spectrum reveals that the method covers the biologically relevant pH range of 6 to 8 with low pH error (<0.2). Quantification of pH maps shows negligible impact of the residual bicarbonate signal. pH maps reflect the induction of acute metabolic alkalosis. Inflamed, infected regions exhibit lower pH. Hyperpolarized 13C-bicarbonate pH mapping was shown to be sensitive in the biologically relevant pH range. The mapping of pH was applied to healthy in vivo organs and interpreted within inflammation and acute metabolic alkalosis models. Magn Reson Med 73:2274–2282, 2015. © 2014 Wiley Periodicals, Inc.

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Authors: Scholz, D. J. (Ekstern), Janich, M. A. (Ekstern), Köllisch, U. (Ekstern), Schulte, R. F. (Ekstern), Ardenkjær-Larsen, J. H. (Intern), Frank, A. (Ekstern), Haase, A. (Ekstern), Schwaiger, M. (Ekstern), Menzel, M. I. (Ekstern)
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Real-time brain computer interface using imaginary movements

Background: Brain Computer Interface (BCI) is the method of transforming mental thoughts and imagination into actions. A real-time BCI system can improve the quality of life of patients with severe neuromuscular disorders by enabling them to communicate with the outside world. In this paper, the implementation of a 2-class real-time BCI system based on the event related desynchronization (ERD) of the sensorimotor rhythms (SMR) is described. Methods: Off-line measurements were conducted on 12 healthy test subjects with 3 different feedback systems (cross, basket and bars). From the collected electroencephalogram (EEG) data, the optimum frequency bands for each of the subjects were determined first through an exhaustive search on 325 bandpass filters. The features were then extracted for the left and right hand imaginary movements using the Common Spatial Pattern (CSP) method. Subsequently, a Bayes linear classifier (BLC) was developed and used for signal classification. These three subject-specific settings were preserved for the on-line experiments with the same feedback systems. Results: Six of the 12 subjects were qualified for the on-line experiments based on their high off-line classification accuracies (CAs > 75 %). The overall mean on-line accuracy was found to be 80%. Conclusions: The subject-specific settings applied on the feedback systems have resulted in the development of a successful real-time BCI system with high accuracies.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, University Hospital Roskilde, Technical University of Denmark
Authors: El-Madani, A. (Ekstern), Sørensen, H. B. D. (Intern), Kjær, T. W. (Ekstern), Thomsen, C. E. (Intern), Puthusserypady, S. (Intern)
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Real-time cardiac metabolism assessed with hyperpolarized [1-13C]acetate in a large-animal model

Dissolution-dynamic nuclear polarization (dissolution-DNP) for magnetic resonance (MR) spectroscopic imaging has recently emerged as a novel technique for noninvasive studies of the metabolic fate of biomolecules in vivo. Since acetate is the most abundant extra- and intracellular short-chain fatty acid, we focused on [1-13C]acetate as a promising candidate for a chemical probe to study the myocardial metabolism of a beating heart. The dissolution-DNP procedure of Na[1-13C]acetate for in vivo cardiac applications with a 3 T MR scanner was optimized in pigs during bolus injection of doses of up to 3 mmol. The Na[1-13C]acetate formulation was characterized by a liquid-state polarization of 14.2% and a T1Eff in vivo of 17.6 ± 1.7 s. In vivo Na[1-13C]acetate kinetics displayed a bimodal shape: [1-13C]acetyl carnitine (AcC) was detected in a slice covering the cardiac volume, and the signal of 13C-acetate and 13C-AcC was modeled using the total area under the curve (AUC) for kinetic analysis. A good correlation was found between the ratio AUC(AcC)/AUC(acetate) and the apparent kinetic constant of metabolic conversion, from [1-13C]acetate to [1-13C]AcC (kAcC), divided by the AcC longitudinal relaxation rate (r1). Our study proved the feasibility and the limitations of administration of large doses of hyperpolarized [1-13C]acetate to study the myocardial conversion of [1-13C]acetate in [1-13C]acetyl-carnitine generated by acetyltransferase in healthy pigs.
Simultaneous Hyperpolarized 13C-Pyruvate MRI and 18F-FDG PET (HyperPET) in 10 Dogs with Cancer

With the introduction of combined PET/MR spectroscopic (MRS) imaging, it is now possible to directly and indirectly image the Warburg effect with hyperpolarized (13)C-pyruvate and (18)F-FDG PET imaging, respectively, via a technique we have named hyperPET. The main purpose of this present study was to establish a practical workflow for performing (18)F-FDG PET and hyperpolarized (13)C-pyruvate MRS imaging simultaneously for tumor tissue characterization and on a larger scale test its feasibility. In addition, we evaluated the correlation between (18)F-FDG uptake and (13)C-lactate production. Ten dogs with biopsy-verified spontaneous malignant tumors were included for imaging. All dogs underwent a protocol of simultaneous (18)F-FDG PET, anatomic MR, and hyperpolarized dynamic nuclear polarization with (13)C-pyruvate imaging. The data were acquired using a combined clinical PET/MR imaging scanner. We found that combined (18)F-FDG PET and (13)C-pyruvate MRS imaging was possible in a single session of approximately 2 h. A continuous workflow was obtained with the injection of (18)F-FDG when the dogs was placed in the PET/MR scanner. (13)C-MRS dynamic acquisition demonstrated an axial slab increased (13)C-lactate production in 9 of 10 dogs. For the 9 dogs, the (13)C-lactate was detected after a mean of 25 s (range, 17-33 s), with a mean to peak of (13)C-lactate at 49 s (range, 40-62 s). (13)C-pyruvate could be detected on average after 13 s (range, 5-26 s) and peaked on average after 25 s (range, 13-42 s). We noticed concordance of (18)F-FDG uptake and production of (13)C-lactate in most, but not all, axial slices. In this study, we have shown in a series of dogs with cancer that hyperPET can easily be performed within 2 h. We showed mostly correspondence between (13)C-lactate production and (18)F-FDG uptake and expect the combined modalities to reveal additional metabolic information to improve prognostic value and improve response monitoring.
The aim of this study was to identify changes of sleep spindles (SS) in the EEG of patients with Parkinson's disease (PD). Five sleep experts manually identified SS at a central scalp location (C3-A2) in 15 PD and 15 age- and sex-matched control subjects. Each SS was given a confidence score, and by using a group consensus rule, 901 SS were identified and characterized by their (1) duration, (2) oscillation frequency, (3) maximum peak-to-peak amplitude, (4) percent-to-peak amplitude, and (5) density. Between-group comparisons were made for all SS characteristics computed, and...
significant changes for PD patients vs. control subjects were found for duration, oscillation frequency, maximum peak-to-peak amplitude and density. Specifically, SS density was lower, duration was longer, oscillation frequency slower and maximum peak-to-peak amplitude higher in patients vs. controls. We also computed inter-expert reliability in SS scoring and found a significantly lower reliability in scoring definite SS in patients when compared to controls. How neurodegeneration in PD could influence SS characteristics is discussed. We also note that the SS morphological changes observed here may affect automatic detection of SS in patients with PD or other neurodegenerative disorders (NDDs).

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Authors: Christensen, J. A. E. (Intern), Nikolic, M. (Ekstern), Warby, S. C. (Ekstern), Koch, H. (Ekstern), Zoetmulder, M. (Ekstern), Frandsen, R. (Ekstern), Moghadam, K. K. (Ekstern), Sørensen, H. B. D. (Intern), Mignot, E. (Ekstern), Jennum, P. J. (Ekstern)
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Sleep spindle alterations in patients with Parkinson's disease
The aim of this study was to identify changes of sleep spindles (SS) in the EEG of patients with Parkinson's disease (PD). Five sleep experts manually identified SS at a central scalp location (C3-A2) in 15 PD and 15 age- and sex-matched control subjects. Each SS was given a confidence score, and by using a group consensus rule, 901 SS were identified and characterized by their (1) duration, (2) oscillation frequency, (3) maximum peak-to-peak amplitude, (4) percent-to-peak amplitude, and (5) density. Between-group comparisons were made for all SS characteristics computed, and significant changes for PD patients vs. control subjects were found for duration, oscillation frequency, maximum peak-to-peak amplitude and density. Specifically, SS density was lower, duration was longer, oscillation frequency slower and maximum peak-to-peak amplitude higher in patients vs. controls. We also computed inter-expert reliability in SS scoring and found a significantly lower reliability in scoring definite SS in patients when compared to controls. How neurodegeneration in PD could influence SS characteristics is discussed. We also note that the SS morphological changes observed here may affect automatic detection of SS in patients with PD or other neurodegenerative disorders (NDDs).

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Authors: Christensen, J. A. E. (Intern), Nikolic, M. (Ekstern), Warby, S. C. (Ekstern), Koch, H. (Ekstern), Zoetmulder, M. (Ekstern), Frandsen, R. (Ekstern), Moghadam, K. K. (Ekstern), Sørensen, H. B. D. (Intern), Mignot, E. (Ekstern), Jennum, P. J. (Ekstern)
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Sleep-stage transitions during polysomnographic recordings as diagnostic features of type 1 narcolepsy
Objective: Type 1 narcolepsy/hypocretin deficiency is characterized by excessive daytime sleepiness, sleep fragmentation, and cataplexy. Short rapid eye movement (REM) latency (≤15 min) during nocturnal polysomnography (PSG) or during naps of the multiple sleep latency test (MSLT) defines a sleep-onset REM sleep period (SOREMP), a diagnostic hallmark. We hypothesized that abnormal sleep transitions other than SOREMPs can be identified in type 1 narcolepsy. Methods: Sleep-stage transitions (one to 10 epochs to one to five epochs of any other stage) and bout length features (one to 10 epochs) were extracted from PSGs. The first 15 min of sleep were excluded when a nocturnal SOREMP was recorded. F0.1 measures and receiver operating characteristic curves were used to identify specific (≥98%) features. A data set of 136 patients and 510 sex- and age-matched controls was used for the training. A data set of 19 cases and 708 sleep-clinic patients was used for the validation. Results: (1) ≥5 transitions from ≥5 epochs of stage N1 or W to ≥2 epochs of REM sleep, (2) ≥22 transitions from ≥3 epochs of stage N2 or N3 to ≥2 epochs of N1 or W, and (3) ≥16 bouts of ≥6 epochs of N1 or W were found to be highly specific (≥98%). Sensitivity ranged from 16% to 30%, and it did not vary substantially with and without medication or a nocturnal SOREMP. In patients taking antidepressants, nocturnal SOREMPs occurred much less frequently (16% vs. 36%, p <0.001). Conclusions: Increased sleep-stage transitions notably from ≥2.5 min of W/N1 into REM are specifically diagnostic for narcolepsy independent of a nocturnal SOREMP.
Surveillance of Hemodialysis Vascular Access with Ultrasound Vector Flow Imaging

The aim of this study was prospectively to monitor the volume flow in patients with arteriovenous fistula (AVF) with the angle independent ultrasound technique Vector Flow Imaging (VFI). Volume flow values were compared with Ultrasound dilution technique (UDT). Hemodialysis patients need a well-functioning vascular access with as few complications as possible and preferred vascular access is an AVF. Dysfunction due to stenosis is a common complication, and regular
monitoring of volume flow is recommended to preserve AVF patency. UDT is considered the gold standard for volume flow surveillance, but VFI has proven to be more precise, when performing single repeated instantaneous measurements. Three patients with AVF were monitored with UDT and VFI monthly for five months. A commercial ultrasound scanner with a 9 MHz linear array transducer with integrated VFI was used to obtain data. UDT values were obtained with Transonic HD03 Flow-QC Hemodialysis Monitor. Three independent measurements at each scan session were obtained with UDT and VFI each month. Average deviation of volume flow between UDT and VFI was 25.7% (CI: 16.7% to 34.7%) (p= 0.73). The standard deviation for all patients, calculated from the mean variance of each individual scan sessions, was 199.8 ml/min for UDT and 47.6 ml/min for VFI (p = 0.002). VFI volume flow values were not significantly different from the corresponding estimates obtained using UDT, and VFI measurements were more precise than UDT. The study indicates that VFI can be used for surveillance of volume flow.

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Authors: Brandt, A. H. (Ekstern), Olesen, J. B. (Intern), Lindskov Hansen, K. (Ekstern), Rix, M. (Ekstern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
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The diagnostic value of power spectra analysis of the sleep electroencephalography in narcoleptic patients
Objective: Manifestations of narcolepsy with cataplexy (NC) include disturbed nocturnal sleep – hereunder sleep–wake instability, decreased latency to rapid eye movement (REM) sleep, and dissociated REM sleep events. In this study, we characterized the electroencephalography (EEG) of various sleep stages in NC versus controls. Methods: EEG power spectral density (PSD) was computed in 136 NC patients and 510 sex- and agematched controls. Features reflecting differences in PSD curves were computed. A Lasso-regularized regression model was used to find an optimal feature subset, which was validated on 19 NC patients and 708 non-NC patients from a sleep clinic. Reproducible features were analyzed using receiver operating characteristic (ROC) curves. Results: Thirteen features were selected based on the training dataset. Three were applicable in the validation dataset, indicating that NC patients show (1) increased alpha power in REM sleep, (2) decreased sigma power in wakefulness, and (3) decreased delta power in stage N1 versus wakefulness. Sensitivity of these features ranged from 4% to 10% with specificity around 96%, and it did not vary substantially with and without treatment. Conclusions: EEG spectral analysis of REM sleep, wake, and differences between N1 and wakefulness contain diagnostic features of NC. These traits may represent sleepiness and dissociated REM sleep in patients with NC. However, the features are not sufficient for differentiating NC from controls, and further analysis is needed to completely evaluate the diagnostic potential of these features.

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Authors: Christensen, J. A. E. (Intern), Munk, E. G. S. (Ekstern), Peppard, P. E. (Ekstern), Young, T. (Ekstern), Mignot, E. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern)
The effects of the CXCR2 antagonist, MK-7123, on bone marrow functions in healthy subjects

The CXCR2 antagonist MK-7123 causes dose-dependent reductions in absolute neutrophil counts (ANC) and decreases neutrophil tissue responses, but its effects on bone marrow functions are not yet known. We conducted a double-blind, randomized study in 18 healthy subjects comparing the effects of either MK-7123 (30 mg, po, daily for 28 days) or placebo on peripheral blood counts and bone marrow myeloid cell populations. MK-7123 caused a reversible decrease (approximately 50%) in the ANC as demonstrated on days 1 and 28, the first and last days of the treatment period. Bone marrow aspirate smears and biopsy imprints did not differ in the proportion of mature neutrophils in pretreatment, day 28, day 56 or placebo samples. There were no treatment effects on biopsy or aspirate clot cellularity, myeloid to erythroid or myeloid post-mitotic to mitotic ratios; flow-cytometric analyses of aspirate cells; or bone marrow fat to cell balance as
assessed by MRI. MK-7123 was generally well tolerated with neutropenia being the most common adverse event; however, there were no clinical symptoms associated with decreased ANCs. These findings indicate that the CXCR2 antagonist MK-7123 causes rapidly reversible decrease in the ANC without measurable myelosuppressive effects. The results support the development of CXCR2 antagonists as potentially useful anti-inflammatory agents, primarily interrupting neutrophil trafficking. © 2015 Published by Elsevier Ltd.
The Pseudomonas Quinolone Signal (PQS)

Pseudomonas aeruginosa is an opportunistic human pathogen that routinely appears near the top of public health threat lists worldwide. P. aeruginosa causes infections by secreting a wealth of exceptionally active exo-products, leading to tissue damage. The synthesis of many of these virulence factors is now known to be under the control of the quorum sensing (QS) system. Over the last 15 years, the Pseudomonas quinolone signal (PQS) has been found to play a crucial role in QS by linking the two segments (las and rhl) of the P. aeruginosa N-acylhomoserine lactone-dependent QS signaling pathways. Herein, we present the discovery and elucidation of PQS signaling from a historical perspective, and also outline some of the outstanding research questions that still need to be addressed. Finally, we show how a better understanding of the biochemistry underpinning this pathway is leading to the development of new antimicrobial interventions with clear therapeutic potential.
The Ups and Downs of Classical and Quantum Formulations of Magnetic Resonance

This chapter describes typical misunderstandings frequently encountered in introductions to nuclear magnetic resonance (NMR), for example, as used for chemical analysis and for magnetic resonance imaging (MRI). It is aimed at those users who are familiar with the basics but have an interest in the connection between the seemingly very different classical and quantum descriptions. Such understanding is needed by students, authors, and lecturers, in particular. With limited complexity, the text introduces probabilistic classical and quantum mechanics with emphasis on similarities and differences. It describes important concepts and the roles of measurement, eigenstates, superpositions, entanglement, and interference, all discussed with reference to spin dynamics for both isolated nuclei and ensembles. The dynamics of basic NMR are shown to be similar to those of coupled oscillators (e.g., pendulums), which gives insight into the resonance phenomenon itself as well as spectral features resulting from intramolecular J-coupling of atomic nuclei. It is discussed how classical and quantum mechanics give rise to similar expectations for basic NMR and why a classical understanding is central.

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The use of dynamic nuclear polarization (13)C-pyruvate MRS in cancer

In recent years there has been an immense development of new targeted anti-cancer drugs. For practicing precision medicine, a sensitive method imaging for non-invasive, assessment of early treatment response and for assisting in developing new drugs is warranted. Magnetic Resonance Spectroscopy (MRS) is a potent technique for non-invasive in
vivo investigation of tissue chemistry and cellular metabolism. Hyperpolarization by Dynamic Nuclear Polarization (DNP) is capable of creating solutions of molecules with polarized nuclear spins in a range of biological molecules and has enabled the real-time investigation of in vivo metabolism. The development of this new method has been demonstrated to enhance the nuclear polarization more than 10,000-fold, thereby significantly increasing the sensitivity of the MRS with a spatial resolution to the millimeters and a temporal resolution at the subsecond range. Furthermore, the method enables measuring kinetics of conversion of substrates into cell metabolites and can be integrated with anatomical proton magnetic resonance imaging (MRI). Many nuclei and substrates have been hyperpolarized using the DNP method. Currently, the most widely used compound is (13)C-pyruvate due to favoring technicalities. Intravenous injection of the hyperpolarized (13)C-pyruvate results in appearance of (13)C-lactate, (13)C-alanine and (13)C-bicarbonate resonance peaks depending on the tissue, disease and the metabolic state probed. In cancer, the lactate level is increased due to increased glycolysis. The use of DNP enhanced (13)C-pyruvate has in preclinical studies shown to be a sensitive method for detecting cancer and for assessment of early treatment response in a variety of cancers. Recently, a first-in-man 31-patient study was conducted with the primary objective to assess the safety of hyperpolarized (13)C-pyruvate in healthy subjects and prostate cancer patients. The study showed an elevated (13)C-lactate/(13)C-pyruvate ratio in regions of biopsy-proven prostate cancer compared to noncancerous tissue. However, more studies are needed in order to establish use of hyperpolarized (13)C MRS imaging of cancer.

Towards Quasi-continuous Heart Rate Variability Estimation using a Patch Type Electrocardiogram Recorder
Changes in different heart rate variability (HRV) measures have been found to possess predictive information in patients with many different diseases, e.g. myocardial infarction, diabetic neuropathy, and patients at risk of developing sepsis. At the same time, the emerging of patch type electrocardiogram recorders facilitates new possibilities for long-term monitoring, real-time data analysis, and wireless transmission of clinically relevant parameters, e.g. short-term HRV measures. This information might in the future assist the healthcare professionals in timely notification of changes in the risk stratification profile obtained from the HRV measures. The purpose of this study is therefore to investigate the possibilities for quasi-continuous estimation of reliable HRV measures using the ePatch heart monitor. We compared the physiologically true values of 11 selected HRV measures with the values obtained using automatically generated RR series from electrocardiograms recorded with the ePatch using four different sampling frequencies (128 Hz, 256 Hz, 512 Hz, and 1024 Hz). We found no significant differences between neither the mean nor the median values of the obtained HRV measures for any of the sampling frequencies. This is very promising for the future application of the ePatch for quasi-continuous monitoring of HRV measures.
Transverse oscillation vector flow imaging for transthoracic echocardiography

This work presents the development and first results of in vivo transthoracic cardiac imaging using an implementation of Vector Flow Imaging (VFI) via the Transverse Oscillation (TO) method on a phased-array transducer. Optimal selection of the lateral wavelength of the transversely-oscillating receive field is described, and results from Field II simulations are presented. Measurements are made using the SARUS experimental ultrasound scanner driving an intercostal phased-array probe. The acquisition sequence was composed of interleaved frames of 68-line B-mode and 17-direction, 32-shot vector velocity flow images. A flow pump was programmed for constant flow for in vitro acquisitions at varying depths in a tissue-mimicking fluid. Additionally, mitral, aortic, and tricuspid valves of two healthy volunteers were scanned from intercostal acoustic windows. The acquired RF data were beamformed via the TO method, and fourth-order estimators were employed for the velocity estimation. The resulting images were compared with those from conventional spectral Doppler and color flow mapping sequences. VFI is shown to be a clinically-feasible tool, which enables new exibility for choosing acoustic windows, visualizing turbulent ow patterns, and measuring velocities.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Bradway, D. (Intern), Lindskov Hansen, K. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Utilizing 3-D and 4-D ultrasound systems to improve radiation treatment of cervix and prostate cancer patients.

Radiotherapy plays an important role in modern treatment for cancer, such as cervical and prostate radiation treatment. One of the major issues in radiotherapy is that the target should be aligned to the planned target volume prior to each treatment fraction, for which different kilovoltage (kV) and megavoltage (MV) image guided radiotherapy (IGRT) methods are developed. However, these ionization systems provide poor visualization of soft tissue, and therefore the bone matching is frequently applied as a daily tumor alignment method in cervical radiotherapy. In this project, the Clarity 3D ultrasound system, non-invasive, non-ionizing, and good in visualization soft tissue, was used to apply uterine matching for determining the uterine shifts relative to the bone structure. The main purpose was to investigate the reliability of the Clarity system as a possible IGRT method. We found that the conventional probe (C-probe) has limitations, while applying transabdominal US (TAUS) scan, when it came to capturing the entire uterus owing to the difficulty in probe handling. Contrarily, the novel autoscan-probe (A-probe) was shown to be capable of capturing the entire uterus in almost all of the scans. The operators found the A-probe to be more user-friendly, and image acquisition was also performed more smoothly. In conclusion the A-probe is a more reliable IGRT tool, and it might replace the kV- and the MV IGRT systems.

In prostate radiotherapy, the movement of the prostate during radiation delivery (intrafractional prostate motion) remains challenging. To determine the intrafractional prostate motion, various imaging techniques have been introduced, such as kV, and MV imaging, CineMRI, implanted markers and transponders. Most of the systems are based on acquiring pre- and posttreatment images, which has limitations in addressing real-time prostate motion, and includes inter-observer variations while matching image to image. In this project, the recently developed transperineal ultrasound 4D autoscan probe is used to investigate the real-time prostate monitoring. The purpose of this study was to investigate the feasibility of the 4D autoscan in tracking the prostate for a duration of 2 to 2.5 minutes. We found that most of the intrafractional prostate motion is less than 2 mm, which was in concordance with previously reported data. Thus, during a RapidArc/VMAT plan delivery with a beam-on time of approximately 2.5 minutes, the intrafractional prostate motion is negligible. But, since the prostate motion increases with monitoring time, the prostate displacement during 3D conformal and IMRT plans must be taken into consideration. Additionally, we conducted a prostate probe pressure study, in which TAUS scan was simulated, using a C-probe, while the prostate was continuously monitored using the TPUS autoscan. We found that the TAUS induced pressure displacement of the prostate, in most cases, was clinically irrelevant. Since this conclusion was in opposition to most of the previously published results, which reported displacements of up to 7 mm, we discovered that 4D real-time monitoring is the most reliable method for determining the pressure displacement compared to US/US or US/CT matching methods, in which the considerable inter-observer variability, due to variations in applied probe pressure and image/image match, limits the accuracy of the readings.
Vector flow imaging of the ascending aorta. Are systolic backflow and atherosclerosis related?

In the ascending aorta, atherosclerotic plaque formation, which is a risk factor for cerebrovascular events, most often occurs along the inner curvature. Atherosclerosis is a multifactorial disease, but the predilection site for the aortic vessel degradation is probably flow dependent. To better understand the aortic flow and especially the complex flow patterns, the ascending aorta was scanned intraoperatively in patients undergoing heart surgery using the angle-independent vector velocity ultrasound method Transverse Oscillation (TO). The primary aim of the study was to analyze systolic backflow in relation to atherosclerosis. Thirteen patients with normal aortic valves were included in the study. TO implemented on a conventional US scanner (ProFocus 2202 UltraView, BK Medical, Herlev, Denmark) with a linear array transducer (8870, BK Medical, Herlev, Denmark) was used intraoperatively on the ascending aorta in long axis view. The presence of systolic backflow, visualized with TO, was correlated to aortic atherosclerosis, to systolic velocities obtained with transesophageal echocardiography and cardiac output obtained with pulmonary artery catheter thermodilution, to gender, age, aortic diameter, left ventricular ejection fraction (LVEF) and previous myocardial infarctions (MI). Systolic backflow in the ascending aorta was present for 38% (n=5) of the patients. The location of the backflow was strongly associated to the location of the plaques (p<0.005), and backflow was associated to high systolic velocities (p<0.05). The other obtained parameters were not associated to systolic backflow. It was shown that systolic backflow is a common flow feature in the ascending aorta, and that backflow is associated to atherosclerotic plaques and systolic velocities. The study indicates that vector flow imaging using TO can provide important blood flow information in the assessment of atherosclerosis.

Velocity Estimation of the Main Portal Vein with Transverse Oscillation.

This study evaluates if Transverse Oscillation (TO) can provide reliable and accurate peak velocity estimates of blood flow the main portal vein. TO was evaluated against the recommended and most widely used technique for portal flow estimation, Spectral Doppler Ultrasound (SDU). The main portal vein delivers blood from the bowls to the liver, and patients with certain liver diseases have decreased flow in the portal vein. Errors in velocity estimation with SDU are well described, when the beam-to-flow angle is >70 degrees. TO estimates the flow angle independently and is not limited by the beam-to-flow angle. It is less operators depended, as no angle correction is necessary. TO measurements were performed with a 3 MHz convex probe (BK medical 8820e, Herlev, Denmark) connected to the experimental ultrasound scanner SARUS (Synthetic Aperture Real-time Ultrasound Scanner). SDU velocity measurements were performed with a commercial ultrasound scanner (BK 3000, BK Ultrasound, Herlev Denmark) and a convex probe (BK ultrasound 6C2, Herlev, Denmark). Ten healthy volunteers were scanned, and recordings of the portal flow during 3-5 heartbeats were conducted with an intercostal and subcostal view. Intercostal TO peak velocities were not significantly different from SDU peak velocities (TO=0.203m/s, SDU=0.202m/s, p=0.94). Subcostal and Intercostal obtained TO values were not significantly different (intercostal mean TO=0.203m/s, subcostal mean TO=0.180m/s, p=0.26). SDU values obtained intercostal and subcostal were significantly different (intercostal mean SDU=0.202m/s, subcostal mean SDU=0.320m/s, p=0.001). Standard deviation for TO beam-to-flow angle was 10.3°- 91.5°, indicating a large beam-to-flow angle variability in the portal vein. This can affect the peak velocity estimation, and is not addressed in SDU. The TO convex array implementation provides the first vector velocity measurements below 60mm (mean 89mm), and is a useful alternative for
flow estimation in abdominal ultrasound. It may provide new information of abdominal fluid dynamics and yield both
velocity and angle estimates for a more realistic flow characterization

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging,
Copenhagen University Hospital
Authors: Brandt, A. H. (Ekstern), Hansen, K. L. (Intern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Volumetric Ultrasound Imaging with Row-Column Addressed 2-D Arrays Using Spatial Matched Filter Beamforming
For 3-D ultrasound imaging with row-column addressed 2-D arrays, the two orthogonal 1-D transmit and receive arrays
are both used for one-way focusing in the lateral and elevation directions separately and since they are not in the same
plane, the two-way focusing is the same as one-way focusing. However, the achievable spatial resolution and contrast
of the B-mode images in Delay and Sum (DAS) beamforming are limited by the aperture size and by the operating
frequency. This paper, investigates Spatial Matched Filter (SMF) beamforming on row-column addressed 2-D arrays to
increase spatial resolution. The performance is investigated on both simulated and experimentally collected 3-D data by
comparing the Point Spread Functions (PSFs) and the phantom images obtained with standard DAS and with SMF.
Results show that the SMF beamformer outperforms DAS in both simulated and experimental trials and that a higher
contrast resolution can be achieved by SMF beamforming (i.e., narrower main lobe and lower side lobes). The 6dB, 20dB
and 40dB cystic resolution for a DAS simulated PSF at (0,0,30)mm are 1.22mm, 3.54mm and 7.46mm, for SMF
beamforming they are 1.11mm, 2.33mm and 5.42mm accordingly. For measured RF-data of an iron needle facing toward
the transducer positioned at (0,0,32.5)mm along the central axis, the 6dB, 20dB and 40dB cystic resolution for DAS
beamforming are 1.99mm, 2.19mm and 4.26mm, and they are 0.8mm, 2.06mm and 4.18mm for SMF beamforming
accordingly. SMF beamforming increases the contrast resolution which turns into a better quality of the B-mode images.

General information
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Organisations: Department of Systems Biology, Department of Electrical Engineering, Biomedical Engineering,
Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Center for Fast Ultrasonography Imaging, BK Medical Aps
Authors: Bouzari, H. (Intern), Engholm, M. (Intern), Christiansen, T. L. (Intern), Stuart, M. B. (Intern), Nikolov, S. I.
(Ekstern), Thomsen, E. V. (Intern), Thomsen, E. V. (Intern), Jensen, J. A. (Intern)
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Angle independent velocity spectrum determination.
An ultrasound imaging system (100) includes a transducer array (102) that emits an ultrasound beam and produces at least one transverse pulse-echo field that oscillates in a direction transverse to the emitted ultrasound beam and that receive echoes produced in response thereto and a spectral velocity estimator (110) that determines a velocity spectrum for flowing structure, which flows at an angle of 90 degrees and flows at angles less than 90 degrees with respect to the emitted ultrasound beam, based on the received echoes.

Ultrasound imaging probe with sigma-delta beamformer and apodization therein
An ultrasound transducer probe (104) includes a transducer array (108) of elements (110) that emit an ultrasound signal and receive analog echo signals produced in response thereto and a beamformer (112), housed by the probe, that converts the analog echo signals to digital signals, applies delays to the digital signals, and sums the delayed digital signals, produces a value of a bit stream, wherein the beamformer apodizes the signals.
2-D Tissue Motion Compensation of Synthetic Transmit Aperture Images

Synthetic transmit aperture (STA) imaging is susceptible to tissue motion because it uses summation of low-resolution images to create the displayed high-resolution image. A method for 2-D tissue motion correction in STA imaging is presented. It utilizes the correlation between high-resolution images recorded using the same emission sequence. The velocity and direction of the motion are found by crosscorrelating short high-resolution lines beamformed along selected angles. The motion acquisition is interleaved with the regular B-mode emissions in STA imaging, and the motion compensation is performed by tracking each pixel in the reconstructed image using the estimated velocity and direction. The method is evaluated using simulations, and phantom and in vivo experiments. In phantoms, a tissue velocity of 15 cm/s at a 45° angle was estimated with relative bias and standard deviation of −6.9% and 5.4%; the direction was estimated with relative bias and standard deviation of −8.4% and 6.6%. The contrast resolution in the corrected image was −0.65% lower than the reference image. Abdominal in vivo experiments with induced transducer motion demonstrate that severe tissue motion can be compensated for, and that doing so yields a significant increase in image quality.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, DAKO Denmark A/S
Authors: Gammelmark, K. L. (Ekstern), Jensen, J. A. (Intern)
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3-D Velocity Estimation for Two Planes in vivo

3-D velocity vectors can provide additional flow information applicable for diagnosing cardiovascular diseases e.g. by estimating the out-of-plane velocity component. A 3-D version of the Transverse Oscillation (TO) method has previously been used to obtain this information in a carotid flow phantom with constant flow. This paper presents the first in vivo measurements of the 3-D velocity vector, which were obtained over 3 cardiac cycles in the common carotid artery of a 32-year-old healthy male volunteer. Data were acquired using a Vermon 3.5 MHz 32x32 element 2-D phased array transducer and stored on the experimental scanner SARUS. The full 3-D velocity profile can be created and examined at peak-systole and end-diastole without ECG gating in two planes. Maximum out-of-plane velocities for the three peak-systoles and end-diastoles were 68.5 ± 5.1 cm/s and 26.3 ± 3.3 cm/s, respectively. In the longitudinal plane, average maximum peak velocity in flow direction was 65.2 ± 14.0 cm/s at peak-systole and 33.6 ± 4.3 cm/s at end-diastole. A commercial BK Medical ProFocus UltraView scanner using a spectral estimator gave 79.3 cm/s and 14.6 cm/s for the same volunteer. This demonstrates that real-time 3-D vector velocity imaging without ECG gating yields quantitative in vivo estimations on flow direction and magnitude.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Holbek, S. (Intern), Pihl, M. J. (Intern), Ewertsen, C. (Ekstern), Bachmann, M. B. (Ekstern), Jensen, J. A. (Intern)
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Accuracy and Sources of Error for an Angle Independent Volume Flow Estimator

This paper investigates sources of error for a vector velocity volume flow estimator. Quantification of the estimator's accuracy is performed theoretically and investigated in vivo. Womersley's model for pulsatile flow is used to simulate velocity profiles and calculate volume flow errors in cases of elliptical vessels and not placing the transducer at the vessel center. Simulations show, i.e., that volume flow is underestimated with 5%, when the transducer is placed 15% from the vessel center. Twenty patients with arteriovenous fistulas for hemodialysis are scanned in a clinical study. A BK Medical UltraView 800 ultrasound scanner with a 9 MHz linear array transducer is used to obtain Vector Flow Imaging sequences of a superficial part of the fistulas. Cross-sectional diameters of each fistula are measured on B-mode images by rotating the scan plane 90 degrees. The major axis of the fistulas was on average 8.6% larger than the minor axis, so elliptic dimensions should be taken into account in volume flow estimation. The ultrasound beam was on average 1.5 ± 0.8 mm off-axis, corresponding to 28.5 ± 11.3% of the major semi-axis of a fistula, and this could result in 15% underestimated volume flow according to the simulation. Volume flow estimates were corrected for the beam being off-axis, but was not able to significantly decrease the error relative to measurements with the reference method.

A comparison between temporal and subband minimum variance adaptive beamforming

This paper compares the performance between temporal and subband Minimum Variance (MV) beamformers for medical ultrasound imaging. Both adaptive methods provide an optimized set of apodization weights but are implemented in the time and frequency domains respectively. Their performance is evaluated with simulated synthetic aperture data obtained from Field II and is quantified by the Full-Width-Half-Maximum (FWHM), the Peak-Side-Lobe level (PSL) and the contrast level. From a point phantom, a full sequence of 128 emissions with one transducer element transmitting and all 128 elements receiving each time, provides a FWHM of 0.03 mm (0.14λ) for both implementations at a depth of 40 mm. This value is more than 20 times lower than the one achieved by conventional beamforming. The corresponding values of PSL are -58 dB and -63 dB for time and frequency domain MV beamformers, while a value no lower than -50 dB can be obtained from either Boxcar or Hanning weights. Interestingly, a single emission with central element #64 as the transmitting aperture provides results comparable to the full sequence. The values of FWHM are 0.04 mm and 0.03 mm and those of PSL are -42 dB and -46 dB for temporal and subband approaches. From a cyst phantom and for 128 emissions, the contrast level is calculated at -54 dB and -63 dB for time and frequency domain MV beamformers, while a value no lower than -50 dB can be obtained from either Boxcar or Hanning weights. Interestingly, a single emission with central element #64 as the transmitting aperture provides results comparable to the full sequence. The values of FWHM are 0.04 mm and 0.03 mm and those of PSL are -42 dB and -46 dB for temporal and subband approaches. From a cyst phantom and for 128 emissions, the contrast level is calculated at -54 dB and -63 dB for time and frequency domain MV beamformers, while a value no lower than -50 dB can be obtained from either Boxcar or Hanning weights. Interestingly, a single emission with central element #64 as the transmitting aperture provides results comparable to the full sequence. The values of FWHM are 0.04 mm and 0.03 mm and those of PSL are -42 dB and -46 dB for temporal and subband approaches. From a cyst phantom and for 128 emissions, the contrast level is calculated at -54 dB and -63 dB for time and frequency domain MV beamformers, while a value no lower than -50 dB can be obtained from either Boxcar or Hanning weights. Interestingly, a single emission with central element #64 as the transmitting aperture provides results comparable to the full sequence. The values of FWHM are 0.04 mm and 0.03 mm and those of PSL are -42 dB and -46 dB for temporal and subband approaches. From a cyst phantom and for 128 emissions, the contrast level is calculated at -54 dB and -63 dB for time and frequency domain MV beamformers, while a value no lower than -50 dB can be obtained from either Boxcar or Hanning weights. Interestingly, a single emission with central element #64 as the transmitting aperture provides results comparable to the full sequence. The values of FWHM are 0.04 mm and 0.03 mm and those of PSL are -42 dB and -46 dB for temporal and subband approaches. From a cyst phantom and for 128 emissions, the contrast level is calculated at -54 dB and -63 dB for time and frequency domain MV beamformers, while a value no lower than -50 dB can be obtained from either Boxcar or Hanning weights. Interestingly, a single emission with central element #64 as the transmitting aperture provides results comparable to the full sequence. The values of FWHM are 0.04 mm and 0.03 mm and those of PSL are -42 dB and -46 dB for temporal and subband approaches. From a cyst phantom and for 128 emissions, the contrast level is calculated at -54 dB and -63 dB for time and frequency domain MV beamformers, while a value no lower than -50 dB can be obtained from either Boxcar or Hanning weights. Interestingly, a single emission with central element #64 as the transmitting aperture provides results comparable to the full sequence. The values of FWHM are 0.04 mm and 0.03 mm and those of PSL are -42 dB and -46 dB for temporal and subband approaches.
Adaptive Multi-Lag for Synthetic Aperture Vector Flow Imaging

The range of detectable velocities in ultrasound flow imaging is linked to the user selection of pulse repetition frequency. Whenever a region with large differences in velocity magnitude is visualized, a trade-off has to be made. This work suggests an adaptive spatio-temporally independent, multi-lag method, which is performed in synthetic aperture vector flow data. Measurements are made on laminar and pulsatile, transverse flow profiles. A 7 MHz linear array is connected to the SARUS research, and acquisitions are made on a vessel phantom with recirculating blood mimicking fluid driven by a software controlled pump. A multi-lag velocity estimation is performed, and a lag is adaptively selected for every estimation point. Results from the constant flow compared to a true parabolic profile show an improvement in relative bias from 76.99% to 0.91% and standard deviation from 13.60% to 1.83% for the low velocity flow of 0.04 m/s; and relative bias from -2.23% to -1.87% and standard deviation from 3.71% to 2.29% for the high velocity flow of 0.4 m/s.

Advanced 3-D Ultrasound Imaging: 3-D Synthetic Aperture Imaging and Row-column Addressing of 2-D Transducer Arrays

The main purpose of the PhD project was to develop methods that increase the 3-D ultrasound imaging quality available for the medical personnel in the clinic. Acquiring a 3-D volume gives the medical doctor the freedom to investigate the measured anatomy in any slice desirable after the scan has been completed. This allows for precise measurements of organs dimensions and makes the scan more operator independent. Real-time 3-D ultrasound imaging is still not as widespread in use in the clinics as 2-D imaging. A limiting factor has traditionally been the low image quality achievable using a channel limited 2-D transducer array and the conventional 3-D beamforming technique, Parallel Beamforming. The
first part of the scientific contributions demonstrate that 3-D synthetic aperture imaging achieves a better image quality than the Parallel Beamforming technique. Data were obtained using both Field II simulations and measurements with the ultrasound research scanner SARUS and a 3.5MHz 1024 element 2-D transducer array. In all investigations, 3-D synthetic aperture imaging achieved a smaller main-lobe, lower sidelobes, higher contrast, and better signal to noise ratio than parallel beamforming. This is achieved partly because synthetic aperture imaging removes the limitation of a fixed transmit focal depth and instead enables dynamic transmit focusing. Lately, the major ultrasound companies have produced ultrasound scanners using 2-D transducer arrays with enough transducer elements to produce high quality 3-D images. Because of the large matrix transducers with integrated custom electronics, these systems are extremely expensive. The relatively low price of ultrasound scanners is one of the factors for the widespread use of ultrasound imaging. The high price tag on the high quality 3-D scanners is limiting their market share. Row-column addressing of 2-D transducer arrays is a low cost alternative to fully addressed 2-D arrays, for 3-D ultrasound imaging. Using row-column addressing, the number of transducer elements is dramatically reduced. This reduces the interconnection cost and removes the need to integrate custom made electronics into the probe. A downside of row-column addressing 2-D arrays is the creation of secondary temporal lobes, or ghost echoes, in the point spread function. In the second part of the scientific contributions, row-column addressing of 2-D arrays was investigated. An analysis of how the ghost echoes can be attenuated was presented. Attenuating the ghost echoes were shown to be achieved by minimizing the first derivative of the apodization function. In the literature, a circular symmetric apodization function was proposed. A new apodization layout that addresses the drawbacks of the circular symmetric apodization function was proposed and described. The new layout was shown to be effective in both simulations and with measurements on in-house produced CMUT arrays. The measurements included both intensity measurements of the edge waves and imaging of a wire phantom. New methods of integrating arbitrary apodization functions into the transducer array were proposed. The main part of the thesis consists of eight scientific papers submitted for international conferences and journals during the PhD project.

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Authors: Rasmussen, M. F. (Intern), Jensen, J. A. (Intern)
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A graphical simulator for active learning of MRI basics
This paper presents a MATLAB-based graphical user interface (GUI) for simulation of a simple magnetic resonance imaging (MRI) scanner that the student can operate and obtain results with. It is intended for the students in an introductory course in medical imaging and provides the students with a supplement to conventional text books.

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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Wilhjelm, J. E. (Intern), Duun-Henriksen, J. (Intern), Hanson, L. G. (Intern)
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A Mouse Model that Recapitulates Cardinal Features of the 15q13.3 Microdeletion Syndrome Including Schizophrenia- and Epilepsy-Related Alterations

Background: Genome-wide scans have uncovered rare copy number variants conferring high risk of psychiatric disorders. The 15q13.3 microdeletion is associated with a considerably increased risk of idiopathic generalized epilepsy, intellectual disability, and schizophrenia. Methods: A 15q13.3 microdeletion mouse model (Df[h15q13]/) was generated by hemizygous deletion of the orthologous region and characterized with focus on schizophrenia- and epilepsy-relevant parameters. Results: Df[h15q13]/ mice showed marked changes in neuronal excitability in acute seizure assays, with increased propensity to develop myoclonic and absence-like seizures but decreased propensity for clonic and tonic seizures. Furthermore, they had impaired long-term spatial reference memory and a decreased theta frequency in hippocampus and prefrontal cortex. Electroencephalogram characterization revealed auditory processing deficits similar to those observed in schizophrenia. Gamma band power was increased during active state, but evoked gamma power following auditory stimulus (40 Hz) was dramatically reduced, mirroring observations in patients with schizophrenia. In addition, Df[h15q13]/ mice showed schizophrenia-like decreases in amplitudes of auditory evoked potentials. Although displaying a grossly normal behavior, Df[h15q13]/ mice are more aggressive following exposure to mild stressors, similar to what is described in human deletion carriers. Furthermore, Df[h15q13]/ mice have increased body weight, and a similar increase in body weight was subsequently found in a sample of human subjects with 15q13.3 deletion. Conclusions: The Df[h15q13]/ mouse shows similarities to several alterations related to the 15q13.3 microdeletion syndrome, epilepsy, and schizophrenia, offering a novel tool for addressing the underlying biology of these diseases.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Neuroscience Research, deCODE Genetics, Technical University of Denmark, Copenhagen University Hospital
Authors: Fejgin, K. (Ekstern), Nielsen, J. (Ekstern), Birknow, M. R. (Ekstern), Bastlund, J. F. (Ekstern), Nielsen, V. (Ekstern), Lauridsen, J. B. (Ekstern), Stefansson, H. (Ekstern), Steinberg, S. (Ekstern), Sørensen, H. B. D. (Intern), Mortensen, T. E. (Ekstern), Larsen, P. H. (Ekstern), Klewe, I. V. (Ekstern), Rasmussen, S. V. (Ekstern), Stefansson, K. (Ekstern), Werge, T. M. (Ekstern), Kallunki, P. (Ekstern), Christensen, K. V. (Ekstern), Didriksen, M. (Ekstern)
Number of pages: 10
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Publication date: 2014
Main Research Area: Technical/natural sciences
Publication information
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Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 6.96 SJR 5.49 SNIP 2.337
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 7.63 SJR 6.204 SNIP 2.33
A Multi-threaded Version of Field II

A multi-threaded version of Field II has been developed, which automatically can use the multi-core capabilities of modern CPUs. The memory allocation routines were rewritten to minimize the number of dynamic allocations and to make pre-allocations possible for each thread. This ensures that the simulation job can be automatically partitioned and the interdependence between threads minimized. The new code has been compared to Field II version 3.22, October 27, 2013 (latest free-ware version). A 64 element 5 MHz focused array transducer was simulated. One million point scatterers randomly distributed in a plane of 20 x 50 mm (width x depth) with random Gaussian amplitudes were simulated using the command calc scat. Dual Intel Xeon CPU E5-2630 2.60 GHz CPUs were used under Ubuntu Linux 10.02 and Matlab version 2013b. Each CPU holds 6 cores with hyper-threading, corresponding to a total of 24 hyper-threading cores. The averaged simulation time for 10 realizations for the old version was 85.1 s. A single thread run for the new version took 27.7 s; a speed-up of 3.1. Employing all 24 cores gave a simulation time of 3.27 s for the one million scatterers corresponding to a speed-up factor of 26 times. The speed-up in general depends on the transducer, scatterers and simulation, and it varies across applications between 13 and 30. The program is fully compatible with older versions, and only a single command has been added for setting the number of threads to use. The division of labor is automatically handled by the program. For a phantom with 100,000 scatterers, it is now possible to simulate a full 128 line image in around 42 seconds with full precision.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Jensen, J. A. (Intern)
A new RF tagging pulse based on the Frank poly-phase perfect sequence

Radio frequency (RF) spectrally selective multiband pulses or tagging pulses, are applicable in a broad range of magnetic resonance methods. We demonstrate through simulations and experiments a new phase-modulation-only RF pulse for RF tagging based on the Frank poly-phase perfect sequence. In addition, we introduce an extended version with a WURST modulation (Frank-WURST). The new pulses exhibit interesting and flexible spin tagging properties and are easily implemented in existing MR sequences, where they can substitute slice-selective pulses with no additional alterations.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Aarhus University, University College Dublin
Authors: Laustsen, C. (Ekstern), Greferath, M. (Ekstern), Ringgaard, S. (Ekstern), Nielsen, N. C. (Ekstern), Ardenkjær-Larsen, J. H. (Intern)
Number of pages: 4
Pages: 50-53
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Magnetic Resonance
Volume: 247
ISSN (Print): 1090-7807
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.963 SJR 1.182 CiteScore 2.57
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.37 SJR 1.016 SNIP 0.983
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.111 SNIP 1.07 CiteScore 2.88
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.113 SNIP 1.013 CiteScore 2.26
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.103 SNIP 0.937 CiteScore 2.41
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.117 SNIP 1.046 CiteScore 2.28
ISI indexed (2012): ISI indexed yes
A phantom study on temporal and subband Minimum Variance adaptive beamforming

This paper compares experimentally temporal and subband implementations of the Minimum Variance (MV) adaptive beamformer for medical ultrasound imaging. The performance of the two approaches is tested by comparing wire phantom measurements, obtained by the research ultrasound scanner SARUS. A 7 MHz BK8804 linear transducer was used to scan a wire phantom in which wires are separated by 10 mm. Performance is then evaluated by the lateral Full-Width-Half-Maximum (FWHM), the Peak Sidelobe Level (PSL), and the computational load. Beamformed single emission responses are also compared with those from conventional Delay-and-Sum (DAS) beamformer. FWHM measured at the depth of 46.6 mm, is 0.02 mm (0.09λ) for both adaptive methods while the corresponding values for Hanning and Boxcar weights are 0.64 and 0.44 mm respectively. Between the MV beamformers a -2 dB difference in PSL is noticed in favor of the subband approach (-31 and -33 dB), whereas values from conventional are not lower than -29 dB. This slight improvement in the case of the subband implementation comes at the expense of increased computational cost; 3.7 TFLOPs per image are required in contrast to 130 GFLOPs of the temporal one, when only 0.5 GFLOPs are needed in DAS beamforming.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Heriot-Watt University, University of Edinburgh
Authors: Diamantis, K. (Ekstern), Voxen, I. H. (Intern), Greenaway, A. H. (Ekstern), Anderson, T. (Ekstern), Jensen, J. A. (Intern), Sboros, V. (Ekstern)
Pages: 1702-1705
Publication date: 2014

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Publisher: IEEE
ISBN (Electronic): 978-1-4799-7049-0
Apparent rate constant mapping using hyperpolarized [1-(13) C]pyruvate.

Hyperpolarization of [1-13C]pyruvate in solution allows real-time measurement of uptake and metabolism using MR spectroscopic methods. After injection and perfusion, pyruvate is taken up by the cells and enzymatically metabolized into downstream metabolites such as lactate, alanine, and bicarbonate. In this work, we present comprehensive methods for the quantification and interpretation of hyperpolarized 13C metabolite signals. First, a time-domain spectral fitting method is described for the decomposition of FID signals into their metabolic constituents. For this purpose, the required chemical shift frequencies are automatically estimated using a matching pursuit algorithm. Second, a time-discretized formulation of the two-site exchange kinetic model is used to quantify metabolite signal dynamics by two characteristic rate constants in the form of (i) an apparent build-up rate (quantifying the build-up of downstream metabolites from the pyruvate substrate) and (ii) an effective decay rate (summarizing signal depletion due to repetitive excitation, T1-relaxation and backward conversion). The presented spectral and kinetic quantification were experimentally verified in vitro and in vivo using hyperpolarized [1-13C]pyruvate. Using temporally resolved IDEAL spiral CSI, spatially resolved apparent rate constant maps are also extracted. In comparison to single metabolite images, apparent build-up rate constant maps provide improved contrast by emphasizing metabolically active tissues (e.g. tumors) and suppression of high perfusion regions with low conversion (e.g. blood vessels). Apparent build-up rate constant mapping provides a novel quantitative image contrast for the characterization of metabolic activity. Its possible implementation as a quantitative standard will be subject to further studies. Copyright © 2014 John Wiley & Sons, Ltd.
A Transverse Oscillation Approach for Estimation of Three-Dimensional Velocity Vectors, Part I: Concept and Simulation Study

A method for 3-D velocity vector estimation using transverse oscillations is presented. The method employs a 2-D transducer and decouples the velocity estimation into three orthogonal components, which are estimated simultaneously and from the same data. The validity of the method is investigated by conducting simulations emulating a 32 × 32 matrix transducer. The results are evaluated using two performance metrics related to precision and accuracy. The study includes several parameters including 49 flow directions, the SNR, steering angle, and apodization types. The 49 flow directions cover the positive octant of the unit sphere. In terms of accuracy, the median bias is −2%. The precision of \( v_x \) and \( v_y \) depends on the flow angle \( \beta \) and ranges from 5% to 31% relative to the peak velocity magnitude of 1 m/s. For comparison, the range is 0.4 to 2% for \( v_z \). The parameter study also reveals that the velocity estimation breaks down with an SNR between −6 and −3 dB. In terms of computational load, the estimation of the three velocity components requires 0.75 billion floating point operations per second (0.75 Gflops) for a realistic setup. This is well within the capability of modern scanners.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Pihl, M. J. (Intern), Jensen, J. A. (Intern)
Pages: 1599-1607

BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.635 SNIP 1.162 CiteScore 3.45
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.681 SNIP 1.31 CiteScore 3.9
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.628 SNIP 1.24 CiteScore 3.47
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.394 SNIP 1.344 CiteScore 3.37
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.351 SNIP 1.186
Scopus rating (2009): SJR 1.597 SNIP 1.539
Scopus rating (2008): SJR 1.874 SNIP 1.465
Web of Science (2010): Indexed yes
Scopus rating (2007): SJR 1.734 SNIP 1.408
Scopus rating (2006): SJR 1.386 SNIP 1.289
Scopus rating (2005): SJR 1.653 SNIP 1.587
Scopus rating (2004): SJR 1.229 SNIP 1.273
Scopus rating (2003): SJR 1.78 SNIP 1.28
Scopus rating (2002): SJR 1.084 SNIP 0.868
Scopus rating (2001): SJR 1.005 SNIP 0.926
Scopus rating (2000): SJR 0.987 SNIP 0.861
Scopus rating (1999): SJR 1.057 SNIP 1.101

Original language: English
hyperpolarized 13C, [1-13C]pyruvate, dynamic metabolic imaging, MRSI, metabolic exchange rate, kinetic modeling

DOIs: 10.1002/nbm.3174
A Transverse Oscillation Approach for Estimation of Three-Dimensional Velocity Vectors, Part II: Experimental Validation

The 3-D transverse oscillation method is investigated by estimating 3-D velocities in an experimental flowrig system. Measurements of the synthesized transverse oscillating fields are presented as well. The method employs a 2-D transducer; decouples the velocity estimation; and estimates the axial, transverse, and elevation velocity components simultaneously. Data are acquired using a research ultrasound scanner. The velocity measurements are conducted with steady flow in sixteen different directions. For a specific flow direction with \([\alpha,\beta]=[45,15]^\circ\), the mean estimated velocity vector at the center of the vessel is \((v_x,v_y,v_z) = (33.8,34.5,15.2) \pm (4.6,5.0,0.6)\text{cm/s}\) where the expected velocity is \((34.2,34.2,13.0)\text{cm/s}\). The velocity magnitude is \(50.6 \pm 5.2\text{cm/s}\) with a bias of \(0.7\text{cm/s}\). The flow angles \(\alpha\) and \(\beta\) are estimated as \(45.6 \pm 4.9^\circ\) and \(17.6 \pm 1.0^\circ\). Subsequently, the precision and accuracy are calculated over the entire velocity profiles. On average for all direction, the relative mean bias of the velocity magnitude is \(-0.08\%\). For \(\alpha\) and \(\beta\), the mean bias is \(-0.2^\circ\) and \(-1.5^\circ\). The relative standard deviations of the velocity magnitude ranges from 8 to 16%. For the flow angles, the ranges of the mean angular deviations are 5° to 16° and 0.7° and 8°.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Pihl, M. J. (Intern), Stuart, M. B. (Intern), Tomov, B. G. (Intern), Rasmussen, M. F. (Intern), Jensen, J. A. (Intern)
Pages: 1608-1618
Publication date: 2014
Main Research Area: Technical/natural sciences
Automatic detection and classification of artifacts in single-channel EEG

Ambulatory EEG monitoring can provide medical doctors important diagnostic information, without hospitalizing the patient. These recordings are however more exposed to noise and artifacts compared to clinically recorded EEG. An automatic artifact detection and classification algorithm for single-channel EEG is proposed to help identifying these artifacts. Features are extracted from the EEG signal and wavelet subbands. Subsequently a selection algorithm is applied in order to identify the best discriminating features. A non-linear support vector machine is used to discriminate among different artifact classes using the selected features. Single-channel (Fp1-F7) EEG recordings are obtained from experiments with 12 healthy subjects performing artifact inducing movements. The dataset was used to construct and validate the model. Both subject-specific and generic implementation, are investigated. The detection algorithm yield an average sensitivity and specificity above 95% for both the subject-specific and generic models. The classification algorithm show a mean accuracy of 78 and 64% for the subject-specific and generic model, respectively. The classification model was additionally validated on a reference dataset with similar results.

General information
State: Published
Automatic quality classification of entire electrocardiographic recordings obtained with a novel patch type recorder

Recently, new patch type electrocardiogram (ECG) recorders have reached the market. These new devices possess a number of advantages compared to the traditional Holter recorders. This forms the basis of questions related to benefits and drawbacks of different ambulatory ECG recording techniques. One of the important questions is the ability to obtain high clinical quality of the recordings during the entire monitoring period. It is thus desirable to be able to obtain an automatic estimate of the global quality of entire ECG recordings. The purpose of this pilot study is therefore to design an algorithm for automatic classification of entire ECG recordings into the groups “noisy” and “clean” recordings. This novel algorithm is based on three features and a simple Bayes classifier. The algorithm was tested on 40 ECG recordings in a five-fold cross validation scheme and it obtained an average accuracy of 90% on the test data.

Automatic sleep classification using a data-driven topic model reveals latent sleep states

Background: The golden standard for sleep classification uses manual scoring of polysomnography despite points of criticism such as oversimplification, low inter-rater reliability and the standard being designed on young and healthy subjects. New method: To meet the criticism and reveal the latent sleep states, this study developed a general and automatic sleep classifier using a data-driven approach. Spectral EEG and EOG measures and eye correlation in 1 s windows were calculated and each sleep epoch was expressed as a mixture of probabilities of latent sleep states by using the topic model Latent Dirichlet Allocation. Model application was tested on control subjects and patients with periodic leg movements (PLM) representing a non-neurodegenerative group, and patients with idiopathic REM sleep behavior disorder (iRBD) and Parkinson's Disease (PD) representing a neurodegenerative group. The model was optimized using 50
subjects and validated on 76 subjects. Results: The optimized sleep model used six topics, and the topic probabilities changed smoothly during transitions. According to the manual scorings, the model scored an overall subject-specific accuracy of 68.3 +/- 7.44 (% mu +/-sigma) and group specific accuracies of 69.0 +/- 4.62 (control), 70.1 +/- 5.10 (PLM), 67.2 +/- 8.30 (iRBD) and 67.7 +/- 9.07 (PD). Comparison with existing method: Statistics of the latent sleep state content showed accordances to the sleep stages defined in the golden standard. However, this study indicates that sleep contains six diverse latent sleep states and that state transitions are continuous processes. Conclusions: The model is generally applicable and may contribute to the research in neurodegenerative diseases and sleep disorders. (C) 2014 Elsevier B.V. All rights reserved.
Biomechanical symmetry of a hip joint altered by Perthes' disease

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen
Authors: Salmingo, R. A. (Intern), Skytte, T. (Ekstern), Traberg, M. S. (Intern), Henneberg, K. (Intern), Hindse, K. (Ekstern), Wong, C. (Ekstern)
Publication date: 2014
Event: Abstract from DOS Kongressen 2014, København, Denmark.
Main Research Area: Technical/natural sciences
Electronic versions:
Abstracts_2014.pdf
Source: PublicationPreSubmission
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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Brain-computer interface
A computer-implemented method of providing an interface between a user and a processing unit, the method comprising:
presenting one or more stimuli to a user, each stimulus varying at a respective stimulation frequency, each stimulation frequency being associated with a respective user-selectable input; receiving at least one signal indicative of brain activity of the user; and determining, from the received signal, which of the one or more stimuli the user attends to and selecting the user-selectable input associated with the stimulation frequency of the determined stimuli as being a user-selected input.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Sørensen, H. B. D. (Intern), Puthusserypady, S. (Intern), Vilic, A. (Intern), Kjaer, T. W. (Ekstern), Thomsen, C. E. (Intern)
Publication date: 2014

Publication information
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Patent number: WO2014207008
Date: 31/12/2014
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Original language: English
Electronic versions:
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Brain-computer interface using P300 and virtual reality: A gaming approach for treating ADHD

This paper presents a novel brain-computer interface (BCI) system aiming at the rehabilitation of attention-deficit/hyperactive disorder in children. It uses the P300 potential in a series of feedback games to improve the subjects’ attention. We applied a support vector machine (SVM) using temporal and template-based features to detect these P300 responses. In an experimental setup using five subjects, an average error below 30% was achieved. To make it more challenging the BCI system has been embedded inside an immersive 3D virtual reality (VR) classroom with simulated distractions, which was created by combining a low-cost infrared camera and an “off-axis perspective projection” algorithm. This system is intended for kids by operating with four electrodes, as well as a non-intrusive VR setting. With the promising results, and considering the simplicity of the scheme, we hope to encourage future studies to adapt the techniques presented in this study.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Rohani, D. A. (Intern), Sørensen, H. B. D. (Intern), Puthusserypady, S. (Intern)
Pages: 3606-3609
Publication date: 2014

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Publisher: IEEE
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Main Research Area: Technical/natural sciences
Bioengineering, Animals, Electrodes, Electroencephalography, Feature extraction, Games, Training, Visualization
DOIs:
10.1109/EMBC.2014.6944403
Source: FindIt
Source-ID: 272559198
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

Classification of acute stress using linear and non-linear heart rate variability analysis derived from sternal ECG

Chronic stress detection is an important factor in predicting and reducing the risk of cardiovascular disease. This work is a pilot study with a focus on developing a method for detecting short-term psychophysiological changes through heart rate variability (HRV) features. The purpose of this pilot study is to establish and to gain insight on a set of features that could be used to detect psychophysiological changes that occur during chronic stress. This study elicited four different types of arousal by images, sounds, mental tasks and rest, and classified them using linear and non-linear HRV features from electrocardiograms (ECG) acquired by the wireless wearable ePatch® recorder. The highest recognition rates were acquired for the neutral stage (90%), the acute stress stage (80%) and the baseline stage (80%) by sample entropy, detrended fluctuation analysis and normalized high frequency features. Standardizing non-linear HRV features for each subject was found to be an important factor for the improvement of the classification results.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, DELTA
Authors: Tanev, G. (Ekstern), Saadi, D. B. (Intern), Hoppe, K. (Ekstern), Sørensen, H. B. D. (Intern)
Pages: 3386-3389
Publication date: 2014

Host publication information
Title of host publication: 2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society
Publisher: IEEE
Main Research Area: Technical/natural sciences
Bioengineering, Educational institutions, Electrocardiography, Entropy, Heart rate variability, Standards, Stress, Videos
DOIs:
10.1109/EMBC.2014.6944349
Clinical evaluation of Synthetic Aperture Sequential Beamforming and Tissue Harmonic Imaging

This study determines if the data reduction achieved by the combination Synthetic Aperture Sequential Beamforming (SASB) and Tissue Harmonic Imaging (THI) affects image quality. SASB-THI was evaluated against the combination of Dynamic Received Focusing and Tissue Harmonic Imaging (DFR-THI). A BK medical UltraView 800 ultrasound scanner equipped with a research interface and an abdominal 3.5 MHz 3.5CL192-3ML convex array transducer was used and connected to a stand alone PC. SASB-THI and DFR-THI scan sequences were recorded interleaved and processed offline. Nineteen patients diagnosed with focal liver pathology were scanned to set a clinical condition, where ultrasonography is often performed. A total of 114 sequences were recorded and evaluated by five radiologists. The evaluators were blinded to the imaging technique, and each sequence was shown twice with different left-right positioning, resulting in 1140 evaluations. The program Image Quality Assessment Program (IQap) and a Visual Analog Scale (VAS) were applied for the evaluation. The scale ranged from -50 to 50, where positive values favored SASB-THI. SASB-THI and DFR-THI were evaluated alike in 49% of the evaluations, 28% favored SASB-THI and 23% favored DFR-THI. The average rating was 0.70 (Cl: -0.80 to 2.19). The statistical analysis, where the hypothesis of no differences between the techniques was tested, yielded a p-value of p=0.64, indicating no preference to any technique. This study demonstrates that SASB-THI and DFR-THI have equally good image quality although a data reduction of 64 times is achieved with SASB-THI.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital, University of Copenhagen
Authors: Brandt, A. H. (Ekstern), Hemmsen, M. C. (Intern), Hansen, P. M. (Ekstern), Lindskov Hansen, K. (Ekstern), Lange, T. (Ekstern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
Pages: 1312 - 1315
Publication date: 2014

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Publisher: IEEE
Main Research Area: Technical/natural sciences
Imaginate quality evaluation, Synthetic Aperture Sequential Beamforming Tissue Harmonic Imaging, Comparison of techniques
Electronic versions:
conf_paper_v4.pdf
DOIs:
10.1109/ULTSYM.2014.0324
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

Clinical evaluation of synthetic aperture sequential beamforming ultrasound in patients with liver tumors

Medical ultrasound imaging using synthetic aperture sequential beamforming (SASB) has for the first time been used for clinical patient scanning. Nineteen patients with cancer of the liver (hepatocellular carcinoma or colorectal liver metastases) were scanned simultaneously with conventional ultrasound and SASB using a commercial ultrasound scanner and abdominal transducer. SASB allows implementation of the synthetic aperture technique on systems with restricted data handling capabilities due to a reduction in the data rate in the scanner by a factor of 64. The image quality is potentially maintained despite the data reduction. A total of 117 sequences were recorded and evaluated blinded by five radiologists from a clinical perspective. Forty-eight percent of the evaluations were in favor of SASB, 33% in favor of conventional ultrasound and 19% were equal, that is, a clear, but non-significant trend favoring SASB over conventional ultrasound (p 5 0.18), despite the substantial data reduction. © 2014 World Federation for Ultrasound in Medicine & Biology.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Copenhagen University Hospital, University of Copenhagen
Authors: Hansen, P. M. (Intern), Hemmsen, M. C. (Intern), Brandt, A. H. (Ekstern), Rasmussen, J. (Intern), Lange, T. (Ekstern), Krohn, P. S. (Ekstern), Lönn, L. (Ekstern), Jensen, J. A. (Intern), Bachmann Nielsen, M. (Ekstern)
Pages: 2805-2810
Publication date: 2014
Main Research Area: Technical/natural sciences
Comparative study of T-amplitude features for fitness monitoring using the ePatch® ECG recorder

This study investigates ECG features, focusing on T-wave amplitude, from a wearable ECG device as a potential method for fitness monitoring in exercise rehabilitation. An automatic T-peak detection algorithm is presented that uses local baseline detection to overcome baseline drift without the need for preprocessing, and offers adequate performance on data recorded in noisy environments. The algorithm is applied to 24 hour data recordings from two subject groups with different physical activity histories. Results indicate that, while mean heart rate (HR) differs most significantly between the groups, T-amplitude features could be useful depending on the disparities in fitness level, and require further investigation on an individual basis.

General information
State: Published
Organisations: Department of Management Engineering, Production and Service Management, Engineering Systems Group, Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, University of Copenhagen, Frederiksborg Hospital, Køge hospital, DELTA
Authors: Thorpe, J. R. (Intern), Saida, T. (Ekstern), Mehlsen, J. (Ekstern), Mehlsen, A. (Ekstern), Langberg, H. (Ekstern), Hoppe, K. (Ekstern), Sørensen, H. B. D. (Intern)
Pages: 4172-4175
Publication date: 2014

Comparison of 3-D Synthetic Aperture Phased-Array Ultrasound Imaging and Parallel Beamforming

This paper demonstrates that synthetic aperture imaging (SAI) can be used to achieve real-time 3-D ultrasound phased-array imaging. It investigates whether SAI increases the image quality compared with the parallel beam-forming (PB) technique for real-time 3-D imaging. Data are obtained using both simulations and measurements with an ultrasound research scanner and a commercially available 3.5-MHz 1024-element 2-D transducer array. To limit the probeable thickness, 256 active elements are used in transmit and receive for both techniques. The two imaging techniques were designed for cardiac imaging, which requires sequences designed for imaging down to 15cm of depth and a frame rate of at least 20Hz. The imaging quality of the two techniques is investigated through simulations as a function of depth and angle. SAI improved the full-width at half-maximum (FWHM) at low steering angles by 35%, and the 20-dB cystic resolution by up to 62%. The FWHM of the measured line spread function (LSF) at 80mm depth showed a difference of 20% in favor of SAI. SAI reduced the cyst radius at 60mm depth by 39% in measurements. SAI improved the contrast-to-noise ratio measured on anechoic cysts embedded in a tissue-mimicking material by 29% at 70mm depth. The estimated penetration depth on the same tissue-mimicking phantom shows that SAI increased the penetration by 24% compared with PB. Neither SAI nor PB achieved the design goal of 15cm penetration depth. This is likely due to the limited transducer surface area and a low SNR of the experimental scanner used.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Rasmussen, M. F. (Intern), Jensen, J. A. (Intern)
Pages: 1638-1650
Publication date: 2014
Main Research Area: Technical/natural sciences
Comparison of Diagnostic Information from Regular Telemetry Equipment and a Novel Patch Type Electrocardiogram Recorder

The purpose of this pilot study is to compare the diagnostic information obtained using regular telemetry equipment and the novel ePatch heart monitor. The comparison was conducted by a cardiologist on 24-hour recordings from 11 admitted patients. For all 11 recordings, the same diagnostic information was found using the two recording techniques.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Odense University Hospital, DELTA
Authors: Saadi, D. B. (Intern), Egstrup, K. (Ekstern), Hoppe, K. (Ekstern), Sørensen, H. B. D. (Intern)
Publication date: 2014

Comparison of Vector Velocity Imaging using Directional Beamforming and Transverse Oscillation for a Convex Array Transducer

Vector velocity imaging can reveal both the magnitude and direction of the blood velocity. Several techniques have been suggested for estimating the velocity, and this paper compares the performance for directional beamforming and transverse oscillation (TO) vector flow imaging (VFI). Data have been acquired using the SARUS experimental ultrasound scanner connected to a BK 8820e (BK Medical, Herlev, Denmark) convex array probe with 192 active elements. A duplex sequence with 129 B-mode emissions interleaved with 129 flow emissions has been made. The flow was generated in a recirculating flow rig with a stationary, laminar flow, and the volume flow was measured by a MAG 3000 (Danfos, Sønderborg, Denmark) magnetic flow meter for reference. Data were beamformed with an optimized transverse oscillation scheme for the TO VFI, and standard fourth-order estimators were employed for the velocity estimation. Directional RF lines were beamformed along the flow direction and cross-correlation employed to estimate the velocity magnitude. The velocities were determined for beam-to-flow angles of 60, 75 and 90 degrees. Using 32 emissions the standard deviation relative to the peak velocity for TO estimation was 7.0% at a beam-to-flow angle of 75. This was 3.8% for directional beamforming and at 60 it was 2.2%. The general improvement, however, comes at an increase by a factor of roughly 11 in the number of calculations for the directional beamformation compared to the TO method.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Jensen, J. A. (Intern)
Publication date: 2014
 Connectivity between Right Inferior Frontal Gyrus and Supplementary Motor Area Predicts After-Effects of Right Frontal Cathodal tDCS on Picture Naming Speed

Background: Cathodal transcranial direct current stimulation (tDCS) of the right frontal cortex improves language abilities in post-stroke aphasic patients. Yet little is known about the effects of right frontal cathodal tDCS on normal language function. Objective/hypothesis: To explore the cathodal tDCS effects of the right-hemispheric homologue of Broca’s area on picture naming in healthy individuals. We hypothesized that cathodal tDCS improves Picture naming and that this effect is determined by the anatomical and functional connectivity of the targeted region. Methods: Cathodal and sham tDCS were applied to the right inferior frontal gyrus in 24 healthy subjects before a picture-naming task. All participants were studied with magnetic resonance imaging at pre-interventional baseline. Probabilistic tractography and dynamic causal modeling of functional brain activity during a word repetition task were applied to characterize anatomical and functional connectivity. Results: Subjects named pictures faster after cathodal relative to sham tDCS. The accelerating effect of tDCS was explained by a reduced frequency of very slow responses. tDCS-induced acceleration of Picture naming correlated with larger volumes of the tract connecting the right Broca’s area and the supplementary motor area (SMA) and greater functional coupling from the right SMA to the right Broca’s area.

Conclusions: The results support the notion that the after-effects of tDCS on brain function are at least in part determined by the anatomical and functional connectivity of the targeted region.
Consequence of reduced necrotic bone elastic modulus in a Perthes’ hip

Introduction
Perthes is a destructive hip joint disorder characterized as a malformation of the femoral head which affects young children. Several studies have shown the change of mechanical properties of the femoral head in Perthes’ disease. However, the consequence of the changes in bone mechanical properties in a Perthes’ hip is not well established. Due to the material differences, changes in bone mechanical properties might lead to localization of stress and deformation. Thus, the objective of this study was to investigate the effects of reduced elastic modulus of necrotic bone in the femoral head using Finite Element Analysis (FEA).

Methods
The femoral and necrotic bone of the affected hip of a Perthes’ patient was segmented from the MR images using Simpleware. The segmented parts were exported to SolidWorks to build the 3D solid model and Comsol for FEA. A load of 750 N (300% body weight) was applied on the top of the femoral head. The distal part of the femur was fixed. The same Poisson’s ratio 0.3 was set for the femoral and necrotic bone. The elastic modulus (E) of femoral bone was 500 MPa. To investigate the effects of reduced elastic modulus, the necrotic bone E was reduced as 400 MPa, 100 MPa, 10 MPa and 1 MPa.

Results
The results show that the bone deformation markedly increased when the necrotic bone E was 1 MPa. The maximum displacements were 1.79 mm, 1.80 mm, 1.92 mm and 3.74 mm for E = 400 MPa, E = 100 MPa, E = 10 MPa and E = 1 MPa, respectively. The displacement patterns were uniformly distributed when the necrotic bone E was 400 MPa and 100 MPa. Conversely, the displacements were more localized (concentrated at the necrotic bone) when the necrotic bone E was 10 MPa and 1 MPa.

Conclusions
The deformation patterns of a Perthes’ hip reveals that the disease may be more aggravated due to localization of bone deformation as a result of reduction of the elastic modulus of necrotic bone. The method in this study may be useful in surgical planning.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Wind Energy, Composites and Materials Mechanics, University of Copenhagen
Authors: Salmingo, R. A. (Intern), Skytte, T. L. (Intern), Mikkelsen, L. P. (Intern), Henneberg, K. (Intern), Wong, C. (Ekstern)
Publication date: 2014
Event: Abstract from Nordic Orthopaedic Federation Congress 2014, Helsinki, Finland.
Main Research Area: Technical/natural sciences

Bibliographical note
Presented as oral presentation at Nordic Orthopaedic Federation Congress 2014, 7-9 May 2014, Helsinki, Finland.
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014
Cortical N-acetyl aspartate is a predictor of long-term clinical disability in multiple sclerosis

Objective: To evaluate the prognostic value of the cortical N-acetyl aspartate to creatine ratio (NAA/Cr) in early relapsing-remitting multiple sclerosis (RRMS). Methods: Sixteen patients with newly diagnosed RRMS were studied by serial MRI and MR spectroscopic imaging (MRSI) once every 6 months for 24 months. Clinical examinations, including the expanded disability status scale (EDSS), were performed at baseline, month 24, and at year 7. Results: Baseline cortical NAA/Cr correlated inversely with EDSS at month 24 ($r = -0.61$, $P <0.05$), and patients with EDSS $\geq 4$ had a lower baseline cortical NAA/Cr compared to those with EDSS less than 4 ($P <0.05$). Baseline cortical NAA/Cr also correlated inversely with EDSS at the 7-year follow-up ($r = -0.56$, $P <0.05$), and patients with EDSS $\geq 4$ had a lower baseline cortical NAA/Cr compared to those with EDSS less than 4 ($P <0.05$). Baseline brain parenchymal fraction (BPF) correlated inversely with EDSS at month 24 ($r = -0.61$, $P <0.05$), but not with EDSS at year 7. Discussion: Cortical NAA/Cr in early RRMS correlated with clinical disability after 2 and 7 years and may be used as a predictor of long-term disease outcome.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen
Authors: Wu, X. (Ekstern), Hanson, L. G. (Intern), Skimminge, A. J. M. (Ekstern), Sorensen, P. S. (Ekstern), Paulson, O. B. (Ekstern), Mathiesen, H. K. (Ekstern), Blinkenberg, M. (Ekstern)
Pages: 701-708
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Main Research Area: Technical/natural sciences

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BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.591 SJR 0.592 CiteScore 1.48
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.633 SNIP 0.615 CiteScore 1.54
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.793 SNIP 0.673 CiteScore 1.62
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.649 SNIP 0.669 CiteScore 1.53
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.571 SNIP 0.675 CiteScore 1.63
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.527 SNIP 0.624 CiteScore 1.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.668 SNIP 0.684 CiteScore 1.55
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.672 SNIP 0.692
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.848 SNIP 0.772
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.728 SNIP 0.681
Scopus rating (2007): SJR 0.759 SNIP 0.742
Scopus rating (2006): SJR 0.787 SNIP 0.749
Scopus rating (2005): SJR 0.687 SNIP 0.837
Data adaptive estimation of transversal blood flow velocities

The examination of blood flow inside the body may yield important information about vascular anomalies, such as possible indications of, for example, stenosis. Current Medical ultrasound systems suffer from only allowing for measuring the blood flow velocity along the direction of irradiation, posing natural difficulties due to the complex behaviour of blood flow, and due to the natural orientation of most blood vessels. Recently, a transversal modulation scheme was introduced to induce also an oscillation along the transversal direction, thereby allowing for the measurement of also the transversal blood flow. In this paper, we propose a novel data-adaptive blood flow estimator exploiting this modulation scheme. Using realistic Field II simulations, the proposed estimator is shown to achieve a notable performance improvement as compared to current state-of-the-art techniques.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Lund University
Authors: Pirnia, E. (Ekstern), Jakobsson, A. (Ekstern), Gudmundson, E. (Ekstern), Jensen, J. A. (Intern)
Pages: 6637-6641
Publication date: 2014

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Main Research Area: Technical/natural sciences
Transversal blood velocity estimation, Spectral estimation, BIAA, Medical ultrasound
Electronic versions:
icassp14_biaa_final.pdf
DOI:
10.1109/ICASSP.2014.6854884
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

Data-driven modeling of sleep EEG and EOG reveals characteristics indicative of pre-Parkinson's and Parkinson's disease

Background: Manual scoring of sleep relies on identifying certain characteristics in polysomnograph (PSG) signals. However, these characteristics are disrupted in patients with neurodegenerative diseases. New method: This study evaluates sleep using a topic modeling and unsupervised learning approach to identify sleep topics directly from electroencephalography (EEG) and electrooculography (EOG). PSG data from control subjects were used to develop an EOG and an EEG topic model. The models were applied to PSG data from 23 control subjects, 25 patients with periodic leg movements (PLMs), 31 patients with idiopathic REM sleep behavior disorder (iRBD) and 36 patients with Parkinson's disease.

Electronic versions:

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disease (PD). The data were divided into training and validation datasets and features reflecting EEG and EOG characteristics based on topics were computed. The most discriminative feature subset for separating iRBD/PD and PLM/controls was estimated using a Lasso-regularized regression model. Results: The features with highest discriminability were the number and stability of EEG topics linked to REM and N3, respectively. Validation of the model indicated a sensitivity of 91.4% and a specificity of 68.8% when classifying iRBD/PD patients. Comparison with existing method: The topics showed visual accordance with the manually scored sleep stages, and the features revealed sleep characteristics containing information indicative of neurodegeneration. Conclusions: This study suggests that the amount of N3 and the ability to maintain NREM and REM sleep have potential as early PD biomarkers. Data-driven analysis of sleep may contribute to the evaluation of neurodegenerative patients. (C) 2014 Elsevier B.V. All rights reserved.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis, University of Copenhagen, H. Lundbeck A/S
Authors: Christensen, J. A. E. (Intern), Zoetmulder, M. (Ekstern), Koch, H. (Ekstern), Frandsen, R. (Ekstern), Arvastson, L. J. (Intern), Christensen, S. R. (Ekstern), Jennum, P. (Ekstern), Sørensen, H. B. D. (Intern)
Pages: 262-276
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Main Research Area: Technical/natural sciences

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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.52 SJR 1.132 SNIP 0.997
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.202 SNIP 0.958 CiteScore 2.44
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.039 SNIP 0.85 CiteScore 2.25
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.197 SNIP 1.033 CiteScore 2.52
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.123 SNIP 0.97 CiteScore 2.38
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.208 SNIP 1.041 CiteScore 2.57
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.269 SNIP 0.932
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.248 SNIP 0.959
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.124 SNIP 0.885
Scopus rating (2007): SJR 1.098 SNIP 1.053
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.052 SNIP 1.039
Scopus rating (2005): SJR 1.036 SNIP 0.932
Scopus rating (2004): SJR 1.112 SNIP 0.854
Decreased sleep spindle density in patients with idiopathic REM sleep behavior disorder and patients with Parkinson’s disease

Objective To determine whether sleep spindles (SS) are potentially a biomarker for Parkinson’s disease (PD).

Methods Fifteen PD patients with REM sleep behavior disorder (PD+RBD), 15 PD patients without RBD (PD−RBD), 15 idiopathic RBD (iRBD) patients and 15 age-matched controls underwent polysomnography (PSG). SS were scored in an extract of data from control subjects. An automatic SS detector using a Matching Pursuit (MP) algorithm and a Support Vector Machine (SVM) was developed and applied to the PSG recordings. The SS densities in N1, N2, N3, all NREM combined and REM sleep were obtained and evaluated across the groups. Results The SS detector achieved a sensitivity of 84.7% and a specificity of 84.5%. At a significance level of α=1%, the iRBD and PD+RBD patients had a significantly lower SS density than the control group in N2, N3 and all NREM stages combined. At a significance level of α=5%, PD−RBD had a significantly lower SS density in N2 and all NREM stages combined. Conclusions The lower SS density suggests involvement in pre-thalamic fibers involved in SS generation. SS density is a potential early PD biomarker. Significance It is likely that an automatic SS detector could be a supportive diagnostic tool in the evaluation of iRBD and PD patients.
Design of a New MR Compatible Haptic Interface with Six Actuated Degrees of Freedom

Functional magnetic resonance imaging is an often adopted tool to study human motor control mechanisms. Highly controlled experiments as required by this form of analysis can be realized with haptic interfaces. Their design is challenging because of strong safety and MR compatibility requirements. Existing MR-compatible haptic interfaces are restricted to maximum three actuated degrees of freedom. We propose an MR-compatible haptic interface with six actuated degrees of freedom to be able to study human brain mechanisms of natural pick-and-place movements including arm transport. In this work, we present its mechanical design, kinematic and dynamic model, as well as report on its model-based characterization. A novel hybrid control scheme for the employed ultrasonic motors is introduced. Preliminary MR compatibility tests based on one complete actuator-sensor module are performed. No measurable noise is found and thus, bidirectional compatibility of the six DoF interface can be expected.

General information
State: Published
Detection of K-complexes based on the wavelet transform

Sleep scoring needs computational assistance to reduce execution time and to assure high quality. In this pilot study a semi-automatic K-Complex detection algorithm was developed using wavelet transformation to identify pseudo-K-Complexes and various feature thresholds to reject false positives. The algorithm was trained and tested on sleep EEG from two databases to enhance its general applicability. When testing on data from subjects from the DREAMS© database, a mean true positive rate of 74 % and a positive predictive value of 65 % were achieved. After adjusting a few thresholds to adapt to the second database, the Danish Center for Sleep Medicine, a similar performance was achieved. The algorithm performs at the level of the State of the Art and surpasses the inter-rater agreement rate.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, University of Copenhagen
Authors: Krohne, L. K. (Ekstern), Hansen, R. B. (Ekstern), Christensen, J. A. E. (Intern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern)
Pages: 5450-5453
Publication date: 2014

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Main Research Area: Technical/natural sciences
Bioengineering, Databases, Electroencephalography, Feature extraction, Prediction algorithms, Sleep, Visualization, Wavelet transforms
DOIs: 10.1109/EMBC.2014.6944859

Relations
Activities:
36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society
Source: FindIt
Source-ID: 272559063
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

Detection of tonic epileptic seizures based on surface electromyography

The purpose of this project was to design an algorithm for detection of tonic seizures based on surface electromyography signals from the deltoids. A successful algorithm has a future prospect of being implemented in a wearable device as part of an alarm system. This has already been done for generalized tonic-clonic seizures, and the hypothesis was that some of the same characteristics could be found for tonic seizures. The signals were pre-processed by a high-pass filter to remove low frequency noise such as movement artifacts. Several different features were investigated, including kurtosis, median frequency, zero crossing rate and approximate entropy. These features were used as input in the random forest classifier to decide if a data segment was from a seizure or not. The goal was to develop a generic algorithm for all tonic
seizures, but better results were achieved when certain parameters were adapted specifically for each patient. With patient specific parameters the algorithm obtained a sensitivity of 100% for four of six patients with false detection rates between 0.08 and 7.90 per hour.

**General information**

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, IctalCare A/S, Danish Epilepsy Center
Authors: Larsen, S. N. (Ekstern), Conradsen, I. (Ekstern), Beniczky, S. (Ekstern), Sørensen, H. B. D. (Intern)
Pages: 942-945
Publication date: 2014

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ISBN (Print): 978-1-4244-7929-0
Main Research Area: Technical/natural sciences
Bioengineering, Alarm systems, Electroencephalography, Epilepsy, Feature extraction, Radio frequency, Sensitivity, Vegetation
DOIs: 10.1109/EMBC.2014.6943747
Source: FindIt
Source-ID: 272560590
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

**Determining inter-fractional motion of the uterus using 3D ultrasound imaging during radiotherapy for cervical cancer**

Uterine positional changes can reduce the accuracy of radiotherapy for cervical cancer patients. The purpose of this study was to: 1) Quantify the inter-fractional uterine displacement using a novel 3D ultrasound (US) imaging system, and 2) Compare the result with the bone match shift determined by Cone-Beam CT (CBCT) imaging. Five cervical cancer patients were enrolled in the study. Three of them underwent weekly CBCT imaging prior to treatment and bone match shift was applied. After treatment delivery they underwent a weekly US scan. The transabdominal scans were conducted using a Clarity US system (Clarity® Model 310C00). Uterine positional shifts based on soft-tissue match using US was performed and compared to bone match shifts for the three directions. Mean value (±1 SD) of the US shifts were (mm); anterior-posterior (A/P): (3.8±5.5), superior-inferior (S/I) (-3.5±5.2), and left-right (L/R): (0.4±4.9). The variations were larger than the CBCT shifts. The largest inter-fractional displacement was from -2 mm to +14 mm in the AP-direction for patient 3. Thus, CBCT bone matching underestimates the uterine positional displacement due to neglecting internal uterine positional change to the bone structures. Since the US images were significantly better than the CBCT images in terms of soft-tissue visualization, the US system can provide an optional image-guided radiation therapy (IGRT) system. US imaging might be a better IGRT system than CBCT, despite difficulty in capturing the entire uterus. Uterine shifts based on US imaging contains relative uterus-bone displacement, which is not taken into consideration using CBCT bone match.

**General information**

State: Published
Organisations: Center for Nuclear Technologies, Biomedical Engineering, Center for Fast Ultrasound Imaging, Department of Electrical Engineering, Copenhagen University Hospital
Authors: Baker, M. (Intern), Jensen, J. A. (Intern), Behrens, C. F. (Ekstern)
Number of pages: 10
Publication date: 2014

**Host publication information**

Title of host publication: Proceedings of SPIE
Volume: 9040
Publisher: SPIE - International Society for Optical Engineering
Article number: 90400Y
Main Research Area: Technical/natural sciences
Conference: SPIE Medical Imaging 2014, San Diego, California, United States, 15/02/2014 - 15/02/2014
DOIs: 10.1117/12.2043173
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Source-ID: u::10780
**Dimensional Scaling for Optimized CMUT Operations**

This work presents a dimensional scaling study using numerical simulations, where gap height and plate thickness of a CMUT cell is varied, while the lateral plate dimension is adjusted to maintain a constant transmit immersion center frequency of 5 MHz. Two cell configurations have been simulated, one with a single square cell and one with an infinite array of square cells. It is shown how the radiation impedance from neighboring cells has a significant impact on the design process. For transmit optimization, both plate dimensions and gap height should be increased. For receive mode, the gap height should be increased while the effect of plate dimensions is ambiguous depending on if the array design is closest to a single cell or infinite array of cells. The findings of the simulations are verified by acoustical measurements on two CMUT arrays with different plate dimensions.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, MEMS-Applied Sensors, Department of Electrical Engineering, Biomedical Engineering
Authors: Lei, A. (Intern), Diederichsen, S. E. (Intern), la Cour, M. F. (Intern), Stuart, M. B. (Intern), Christiansen, T. L. (Intern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)
Pages: 2595-2598
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Publisher: IEEE
ISBN (Print): 978-1-4799-0490
Main Research Area: Technical/natural sciences
DOI: 10.1109/ULTSYM.2014.0648
Source: PublicationPreSubmission
Source-ID: 100182196
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

**Enhanced performance large volume dissolution-DNP**

A systematic study of the performance of the dissolution process in dissolution-DNP is presented. A relatively simple set of modifications is made to the standard Hypersense dissolution system to enable polarization of large volume samples. These consist of a large volume sample cup along with supporting modifications to the dissolution head and related components. Additional modifications were made to support the mapping of the temperature/pressure space of the dissolution process as well as enabling the use of large volumes of solvent and improving the robustness of the system. No loss of polarization was observed as sample size was increased to the 1g capacity of the large volume cup and for a dilution factor as low as 1:10.

**General information**

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Bowen, S. (Intern), Ardenkjær-Larsen, J. H. (Intern)
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**Publication information**

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Volume: 240
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Scopus rating (2016): CiteScore 2.37 SJR 1.016 SNIP 0.983
NMR, Hyperpolarization, Dynamic nuclear polarization

DOIs:
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Source-ID: n:oai:DTIC-ART:elsevier/437084895::38200
Publication: Research - peer-review › Journal article – Annual report year: 2014

**ePatch® - A Clinical Overview**

**General Information**
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, OUH Svendborg Hospital, Copenhagen University Hospital, DELTA
Authors: Saadi, D. B. (Intern), Sørensen, H. B. D. (Intern), Hansen, I. H. (Ekstern), Egstrup, K. (Ekstern), Jennum, P. (Forskerdatabase), Hoppe, K. (Ekstern)
Number of pages: 12
Publication date: 2014
First report on intraoperative vector flow imaging of the heart among patients with healthy and diseased aortic valves

The vector velocity method Transverse Oscillation (TO) implemented on a conventional ultrasound (US) scanner (ProFocus, BK Medical, Herlev, Denmark) can provide real-time, angle-independent estimates of the cardiac blood flow. During cardiac surgery, epicardial US examination using TO was performed on (A) 3 patients with healthy aortic valve and (B) 3 patients with aortic valve stenosis. In group B, the systolic flow of the ascending aorta had higher velocities, was more aliased and chaotic. The jet narrowed to 44% of the lumen compared to 75% in group A and with a vector concentration, a measure of flow complexity, of 0.41 compared to 0.87 in group A. The two groups had similar secondary flow of the ascending aorta with an average rotation frequency of 4.8 Hz. Simultaneous measurements were obtained with spectral Doppler (SD) and a thermodilution technique (TD). The mean difference in peak systolic velocity compared to SD in group A was 22% and 45% in B, while the mean difference in volume flow compared to TD in group A was 30% and 32% in B. TO can potentially reveal new information of cardiac blood flow, and may become a valuable diagnostic tool in the evaluation of patients with cardiovascular diseases.
High altitude may alter oxygen availability and renal metabolism in diabetics as measured by hyperpolarized $^{1-13}$Cpyruvate magnetic resonance imaging

The kidneys account for about 10% of the whole body oxygen consumption, whereas only 0.5% of the total body mass. It is known that intrarenal hypoxia is present in several diseases associated with development of kidney disease, including diabetes, and when renal blood flow is unaffected. The importance of deranged oxygen metabolism is further supported by deterioration of kidney function in patients with diabetes living at high altitude. Thus, we argue that reduced oxygen availability alters renal energy metabolism. Here, we introduce a novel magnetic resonance imaging (MRI) approach to monitor metabolic changes associated with diabetes and oxygen availability. Streptozotocin diabetic and control rats were given reduced, normal, or increased inspired oxygen in order to alter tissue oxygenation. The effects on kidney oxygen metabolism were studied using hyperpolarized $^{1-13}$Cpyruvate MRI. Reduced inspired oxygen did not alter renal metabolism in the control group. Reduced oxygen availability in the diabetic kidney altered energy metabolism by increasing lactate and alanine formation by 23% and 34%, respectively, whereas the bicarbonate flux was unchanged. Thus, the increased prevalence and severity of nephropathy in patients with diabetes at high altitudes may originate from the increased sensitivity toward inspired oxygen. This increased lactate production shifts the metabolic routes toward hypoxic pathways.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Uppsala University, Linköping University, Aarhus University
Authors: Laustsen, C. (Ekstern), Lycke, S. (Ekstern), Palm, F. (Ekstern), Østergaard, J. A. (Ekstern), Bibby, B. M. (Ekstern), Nørregaard, R. (Ekstern), Nørregaard, R. (Ekstern), Flyvbjerg, A. (Ekstern), Pedersen, M. (Ekstern), Ardenkjær-Larsen, J. H. (Intern)
Pages: 67-74
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Kidney International
Hyperpolarized H2O MR angiography

The aim of this study was to demonstrate that dissolution- dynamic nuclear polarization is capable of hyperpolarizing water protons and that the signal from the hyperpolarized bolus injection can be exploited in angiographic applications. We hyperpolarized water/glycerol using dynamic nuclear polarization followed by dissolution in D2O. A water 1H signal enhancement of 77 times compared with 4.7 Tesla was obtained. This corresponds to a polarization of 3.5% for the 3.9 mol/L 1H in D2O. Moreover, a T1 in excess of 20 s was achieved. The use of hyperpolarized water as a contrast agent presents a new opportunity to obtain MRA images with high contrast-to-noise in a fraction of a second. Magn Reson Med 71:50–56, 2014. © 2013 Wiley Periodicals, Inc.
Several diseases of the heart have been linked to an insufficient ability to generate enough energy (ATP) to sustain proper heart function. Hyperpolarized magnetic resonance (MR) is a novel technique that can visualize and quantify myocardial energy metabolism. Hyperpolarization enhances the MR signal from a biological molecule of interest by more than 10,000 times, making it possible to measure its cellular uptake and conversion in specific enzymatic pathways in real time. We review the role of hyperpolarized MR in identifying changes in cardiac metabolism in vivo, and present the extensive literature on hyperpolarized pyruvate that has been used to characterize cardiac disease in various in vivo models, such as myocardial ischemia, hypertension, diabetes, hyperthyroidism and heart failure. The technical aspects of the technique are presented as well as the challenges of translating the technique into clinical practice. Hyperpolarized MR has the prospect of transforming diagnostic cardiology by offering new insights into cardiac disease and potentially even to contribute to personalized therapy based on a thorough understanding of the individual intracellular metabolism.

**General information**
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, University of Copenhagen
Authors: Lauritzen, M. H. (Ekstern), Søgaard, L. V. (Ekstern), Madsen, P. L. (Ekstern), Ardenkjær-Larsen, J. H. (Intern)
Pages: 6162-6170
Publication date: 2014
Main Research Area: Technical/natural sciences

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- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 2
- Scopus rating (2017): CiteScore 2.61 SJR 0.883 SNIP 0.726
- Web of Science (2017): Indexed Yes
- BFI (2016): BFI-level 2
- Scopus rating (2016): CiteScore 2.82 SJR 1.069 SNIP 0.817
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 2
- Scopus rating (2015): SJR 1.242 SNIP 0.904 CiteScore 3.01
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 1.292 SNIP 0.959 CiteScore 3.26
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 1.295 SNIP 0.99 CiteScore 3.41
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- Scopus rating (2011): SJR 1.414 SNIP 1.112 CiteScore 3.96
Impact of ultrasound probe pressure on uterine positional displacement in gynecologic cancer patients.

Aim: The aim of this study was to quantify the uterine positional displacement induced by ultrasound probe pressure on a phantom and address the daily uterine motion in a healthy volunteer. Materials & methods: The phantom mimics the female pelvic region. The incorporated organs were subjected to displacement. A total of 42 phantom scans and 16 volunteer scans were acquired. The uterine shifts were measured in three directions. Results & discussion: The difference of uterine positional displacements, using pressure versus without pressure on the phantom, was not statistically significant. The daily uterine positional variations of the volunteer were larger than the probe pressure induced displacements. Conclusion: The larger daily uterine shifts of the volunteer outweighed the submillimeter impact of the probe pressure in all directions.

General information
State: Published
Organisations: Center for Nuclear Technologies, Radiation Physics, Department of Electrical Engineering, Biomedical Engineering, University Hospital Herlev
Authors: Baker, M. (Intern), Juhler-Nøttrup, T. (Ekstern), Behrens, C. F. (Ekstern)
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Scopus rating (2012): SJR 0.646 SNIP 0.706 CiteScore 1.32
Scopus rating (2011): SJR 0.526 SNIP 0.341 CiteScore 1.22
Implementation of synthetic aperture imaging on a hand-held device

This paper presents several implementations of Synthetic Aperture Sequential Beamforming (SASB) on commercially available hand-held devices. The implementations include real-time wireless reception of ultrasound radio frequency signals and GPU processing for B-mode imaging. The proposed implementation demonstrates that SASB can be executed in-time for real-time ultrasound imaging. The wireless communication between probe and processing device satisfies the required bandwidth for real-time data transfer with current 802.11ac technology. The implementation is evaluated using four different hand-held devices all with different chipsets and a BK Medical UltraView 800 ultrasound scanner emulating a wireless probe. The wireless transmission is benchmarked using an imaging setup consisting of 269 scan lines x 1472 complex samples (1.58 MB pr. frame, 16 frames per second). The measured data throughput reached an average of 28.8 MB/s using a LG G2 mobile device, which is more than the required data throughput of 25.3 MB/s. Benchmarking the processing performance for B-mode imaging showed a total processing time of 18.9 ms (53 frames/s), which is less than the acquisition time (62.5 ms).

Increasing the Dynamic Range of Synthetic Aperture Vector Flow Imaging

In current ultrasound systems, the dynamic range of detectable velocities is susceptible to the selected pulse repetition frequency, thus limiting the dynamic range of flow mapping. To establish the feasibility of extending the range of detectable velocities towards low velocity vessels, results are presented using synthetic aperture which increases the frame-to-frame signal correlation of the scatterer displacement while providing continuous data. In this paper, recursive synthetic aperture acquisition, directional beamforming, and cross-correlation are used to produce B-mode and vector velocity images. The emissions for the two imaging modes are interleaved 1-to-1 ratio, providing a high frame rate equal to the effective pulse repetition frequency of each imaging mode. The direction of the flow is estimated, and the velocity is then determined in that direction. This method works for all angles, including fully axial and transverse flows. The method is investigated using Field II simulations and data from the experimental ultrasound scanner SARUS, acquired from a circulating flow rig with a parabolic flow. A 7 MHz linear array transducer is used, and several pulse repetition frequencies are synthesized in a simulated flow phantom with linearly increasing velocity and in a dual-vessel phantom with laminar flow with peak velocities of 0.05 m/s and 0.5 m/s. The experimental measurements are made with laminar flow as in the simulations. For the simulated and experimental vessel with peak velocity of 0.05 m/s and flow angle of 75°, the relative bias is -0.29% and -3.19%, and the relative standard deviations are 2.39% and 5.75% respectively. For the simulated and experimental vessel with peak velocity of 0.5 m/s and flow angle of -90°, the relative biases are -4.30% and -7.37%, and the relative standard deviations are 1.59% and 6.12%, respectively. The presented method can improve the estimates by
Insufficient insulin administration to diabetic rats increases substrate utilization and maintains lactate production in the kidney

Good glycemic control is crucial to prevent the onset and progression of late diabetic complications, but insulin treatment often fails to achieve normalization of glycemic control to the level seen in healthy controls. In fact, recent experimental studies indicate that insufficient treatment with insulin, resulting in poor glycemic control, has an additional effect on progression of late diabetic complications, than poor glycemic control on its own. We therefore compared renal metabolic alterations during conditions of poor glycemic control with and without suboptimal insulin administration, which did not restore glycemic control, to streptozotocin (STZ)-diabetic rats using noninvasive hyperpolarized 13C-pyruvate magnetic resonance imaging (MRI) and blood oxygenation level–dependent (BOLD) 1H-MRI to determine renal metabolic flux and oxygen availability, respectively. Suboptimal insulin administration increased pyruvate utilization and metabolic flux via both anaerobic and aerobic pathways in diabetic rats even though insulin did not affect kidney oxygen availability, HbA1c, or oxidative stress. These results imply direct effects of insulin in the regulation of cellular substrate utilization and metabolic fluxes during conditions of poor glycemic control. The study demonstrates that poor glycemic control in combination with suboptimal insulin administration accelerates metabolic alterations by increasing both anaerobic and aerobic metabolism resulting in increased utilization of energy substrates. The results demonstrate the importance of tight glycemic control in insulinopenic diabetes, and that insulin, when administered insufficiently, adds an additional burden on top of poor glycemic control.
Influence of implant rod curvature on sagittal correction of scoliosis deformity

BACKGROUND CONTEXT: Deformation of in vivo–implanted rods could alter the scoliosis sagittal correction. To our knowledge, no previous authors have investigated the influence of implanted-rod deformation on the sagittal deformity correction during scoliosis surgery. PURPOSE: To analyze the changes of the implant rod’s angle of curvature during surgery and establish its influence on sagittal correction of scoliosis deformity. STUDY DESIGN: A retrospective analysis of the preoperative and postoperative implant rod geometry and angle of curvature was conducted. PATIENT SAMPLE: Twenty adolescent idiopathic scoliosis patients underwent surgery. Average age at the time of operation was 14 years. OUTCOME MEASURES: The preoperative and postoperative implant rod angle of curvature expressed in degrees was obtained for each patient. METHODS: Two implant rods were attached to the concave and convex side of the spinal deformity.

The preoperative implant rod geometry was measured before surgical implantation. The postoperative implant rod geometry after surgery was measured by computed tomography. The implant rod angle of curvature at the sagittal plane was obtained from the implant rod geometry. The angle of curvature between the implant rod extreme ends was measured before implantation and after surgery. The sagittal curvature between the corresponding spinal levels of healthy adolescents obtained by previous studies was compared with the implant rod angle of curvature to evaluate the sagittal curve correction. The difference between the postoperative implant rod angle of curvature and normal spine sagittal curvature of the corresponding instrumented level was used to evaluate over or under correction of the sagittal deformity.

RESULTS: The implant rods at the concave side of deformity of all patients were significantly deformed after surgery. The average degree of rod deformation Dq at the concave and convex sides was 15.8 and 1.6, respectively. The average preoperative and postoperative implant rod angle of curvature at the concave side was 33.6 and 17.8, respectively. The average preoperative and postoperative implant rod angle of curvature at the convex side was 25.5 and 23.9, respectively. A significant relationship was found between the degree of rod deformation and preoperative implant rod angle of curvature (r50.60, p!.005). The implant rods at the convex side of all patients...
Investigation of PDMS as coating on CMUTs for Imaging

A protective layer is necessary for Capacitive Micromachined Ultrasonic Transducers (CMUTs) to be used for imaging purpose. The layer should both protect the device itself and the patient while maintaining the performance of the device. In this work Sylgard 170 PDMS is tested as coating material for CMUTs through comparison of transmit pressure and receive sensitivity in immersion of coated and uncoated elements. It is seen that the transmitted pressure decreases with 27% and the receive sensitivity decreases 35 % when applying the coating using a dam and fill principle. This matches well with the estimated value of 31 %. With the coating, the center frequency was found to be decreased from 4.5 MHz to 4.1 MHz and the fractional bandwidth was increased from 77 % to 84 % in transmit. In receive the center frequency was found to decrease from 4.4 MHz to 3.9 MHz and the fractional bandwidth was decreased from 108 % to 92 %, when applying the PDMS coating.
In vivo Convex Array Vector Flow Imaging

In vivo VFI scans obtained from the abdomen of a human volunteer using a convex array transducers and transient oscillation vector flow imaging (VFI) are presented. A 3 MHz BK Medical 8820e (Herlev, Denmark) 192-element convex array probe is used with the SARUS experimental ultrasound scanner. A sequence with a 129-line B-mode image is followed by a VFI sequence in 17 directions with 32 emissions in each direction. The pulse repetition frequency was set to 5 kHz, and the intensity and MI were measured with the Acoustic Intensity Measurement System AIMS III (Onda, Sunnyvale, California, USA). The derated Ispta:3 was 79.7 mW/m2 and MI was 1.32, which are within FDA limits for abdominal scans. The right liver lobe of a 28-year healthy volunteer was scanned with a view of the main portal vein and vena cava inferior at a frame rate of 7.4 Hz. Thirty frames were acquired, giving 4 seconds of data. For this volunteer the duration corresponded to roughly 3 heartbeats. The velocities were found at a beam-to-flow angle of 72°, where a conventional CFM scan would yield poor results. Three VF images from the same position in the cardiac cycle were investigated and the mean lateral velocities were -0.079, -0.081 and -0.080 m/s showing the consistence of the in vivo results.

In vivo measurement of apparent diffusion coefficients of hyperpolarized 13C-labeled metabolites

The combination of hyperpolarized MRS with diffusion weighting (dw) allows for determination of the apparent diffusion coefficient (ADC), which is indicative of the intra- or extracellular localization of the metabolite. Here, a slice-selective pulsed-gradient spin echo sequence was implemented to acquire a series of dw spectra from rat muscle in vivo to determine the ADCs of multiple metabolites after a single injection of hyperpolarized [1-13C]pyruvate. An optimal control optimized universal-rotation pulse was used for refocusing to minimize signal loss caused by B1 imperfections. Non-dw spectra were acquired interleaved with the dw spectra and these were used to correct for signal decay during the acquisition as a result of T1 decay, pulse imperfections, flow etc. The data showed that the ADC values for [1-13C]lactate (0.4–0.7 μm2/ms) and [1-13C]alanine (0.4–0.9 μm2/ms) were about a factor of two lower than the ADC of [1-13C]pyruvate (1.1–1.5 μm2/ms). This indicates a more restricted diffusion space for the former two metabolites consistent with lactate and alanine being intracellular. The higher ADC for pyruvate (similar to the proton ADC) reflected that the injected substance was not confined inside the muscle cells but also present extracellular. Copyright © 2014 John Wiley & Sons,
In-Vivo Synthetic Aperture and Plane Wave High Frame Rate Cardiac Imaging

A comparison of synthetic aperture imaging using spherical and plane waves with low number of emission events is presented. For both wave types, a 90 degree sector is insonified using 15 emission events giving a frame rate of 200 frames per second. Field II simulations of point targets show similar resolution of approximately one wavelength radially and one degree angularly for both wave types. The use of spherical waves is found to have higher signal strength and better cystic resolution than plane waves. Measurements on wires in water yield similar results to simulations with similar resolution between the two wave types but better cystic resolution for spherical waves. Measurements on tissue mimicking phantoms show that both wave types penetrate down to 11 cm. Intensity measurements show an I spta: 3 of 18.4 mW/cm² for spherical waves and 22.7 mW/cm² for plane waves. The derated MI is 0.43 for spherical and 0.70 for plane waves. All measures are well within FDA limits for cardiac imaging. In-vivo images of the heart of a healthy 28-year old volunteer are shown.

Local pH domains regulate NHE3-mediated Na⁺ reabsorption in the renal proximal tubule

The proximal tubule Na⁺/H⁺ exchanger 3 (NHE3), located in the apical dense microvilli (brush border), plays a major role in the reabsorption of NaCl and water in the renal proximal tubule. In response to a rise in blood pressure NHE3 redistributes in the plane of the plasma membrane to the base of the brush border, where NHE3 activity is reduced. This NHE3 redistribution is assumed to provoke pressure natriuresis; however, it is unclear how NHE3 redistribution per se reduces NHE3 activity. To investigate if the distribution of NHE3 in the brush border can change the reabsorption rate, we constructed a spatiotemporal mathematical model of NHE3-mediated Na⁺ reabsorption across a proximal tubule cell and compared the model results with in vivo experiments in rats. The model predicts that when NHE3 is localized exclusively at the base of the brush border, it creates local pH microdomains that reduce NHE3 activity by >30%. We tested the model's prediction experimentally: the rat kidney cortex was loaded with the pH-sensitive fluorescent dye BCECF, and cells of the proximal tubule were imaged in vivo using confocal fluorescence microscopy before and after an increase of blood pressure by ~50 mmHg. The experimental results supported the model by demonstrating that a rise of blood pressure induces the development of pH microdomains near the bottom of the brush border. These local changes in pH reduce NHE3 activity, which may explain the pressure natriuresis response to NHE3 redistribution.
Mapping and correcting respiration-induced field changes in the brain using fluorine field probes

**General information**

**State:** Published

**Organisations:** Department of Electrical Engineering, Biomedical Engineering, University Medical Centre Utrecht, Leiden University, Copenhagen University Hospital

**Authors:** Andersen, M. (Intern), Madsen, K. (Ekstern), Hanson, L. G. (Intern), Boer, V. (Ekstern), van der Velden, T. (Ekstern), Klomp, D. (Ekstern), Wezel, J. (Ekstern), van Osch, M. (Ekstern), Versluis, M. (Ekstern)

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Method for detection of an abnormal sleep pattern in a person

The present disclosure relates to a method for detection of an abnormal sleep pattern based on a dataset of Electrooculography (EOG) signals obtained from a sleeping subject over a time interval, the method comprising the steps of dividing the time interval into a plurality of subintervals, each subinterval preferably corresponding to a sleep epoch, classifying each subinterval in terms of sleep stages, thereby obtaining a temporal sleep stage pattern, wherein a subject having an uncharacteristic temporal distribution of sleep stages is characterized as having an abnormal sleep pattern.

**General information**

**State:** Published

**Organisations:** Department of Electrical Engineering, Biomedical Engineering, Department of Applied Mathematics and Computer Science, Statistics and Data Analysis

**Authors:** Sørensen, H. B. D. (Intern), Christensen, J. A. E. (Intern), Jennum, P. J. (Ekstern), Rahn Christensen, S. (Ekstern), Arvastson, L. J. (Intern)

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Micromachined Integrated Transducers for Ultrasound Imaging

The purpose of this project is to develop capacitive micromachined ultrasonic transducers (CMUTs) for medical imaging. Medical ultrasound transducers used today are fabricated using piezoelectric materials and bulk processing. To fabricate transducers capable of delivering a higher imaging resolution it is however necessary to develop new fabrication methods that allows fabrication of transducer elements with smaller
dimensions. By using microfabrication technology it is possible to push the dimensions down and provide higher design flexibility.

This project is part of a large ultrasound project and collaboration with a lot of partners to improve medical ultrasound imaging. The focus in this part of the project is to design, fabricate and characterize 1D CMUT arrays. Two versions of 1D transducers are made, one at Stanford University and one at DTU. Electrical and acoustical characterizations are carried out successfully for both types of arrays. The arrays made at Stanford is found to suffer from low breakdown voltage of the supporting oxide and was not useful for medical imaging.

The arrays made at DTU are used for various tests, both of the design, performance, possible packaging, and post-processing. The electrical characterization shows serious charging effects in the device which is shown to be reduced by reversing the bias polarity. Furthermore, the wirebonding and glob top packaging scheme shows to cause loose connection for several elements. This is still under investigation, but two possible solutions are suggested. Two devices are assembled into probe handles and initial acoustical characterizations are promising. Even though the sensitivity is currently low, images are produced with recognizable features both on phantoms and volunteers. It can be mentioned that a -6 dB fractional bandwidth of 100-110 % is measured.

**Modal radiation patterns of baffled circular plates and membranes**

The far field velocity potential and radiation pattern of baffled circular plates and membranes are found analytically using the full set of modal velocity profiles derived from the corresponding equation of motion. The derivation is valid for a plate or membrane subjected to an external excitation force, which is used as a sound receiver in any medium or as a sound transmitter in a gaseous medium. A general, concise expression is given for the radiation pattern of any mode of the membrane and the plate with arbitrary boundary conditions. Specific solutions are given for the four special cases of a plate with clamped, simply supported, and free edge boundary conditions as well as for the membrane. For all non-axisymmetric modes, the velocity potential along the axis of the radiator is found to be strictly zero. In the long wavelength limit, the radiation pattern of all axisymmetric modes approaches that of a monopole, while the non-axisymmetric modes exhibit multipole behavior. Numerical results are also given, demonstrating the implications of having non-axisymmetric excitation using both a point excitation with varying eccentricity and a homogeneous excitation acting on half of the circular radiator.
Noninvasive estimation of 2-D pressure gradients in steady flow using ultrasound

A noninvasive method for estimating 2-D pressure gradients from ultrasound vector velocity data is presented. It relies on vector velocity fields acquired using the transverse oscillation method during steady flow conditions. The pressure gradients are calculated from the velocity fields using the Navier-Stokes equations. Scans of a carotid bifurcation phantom with a 70% constriction are performed using a linear transducer connected to a scanner. The performance of the estimator is evaluated by comparing its results to those of a computational fluid dynamics model of the carotid bifurcation phantom. The geometry of the model is determined from magnetic resonance imaging. The presented study is conducted assuming steady flow using velocity data acquired at 16 frames per second. The proposed method shows pressure gradients at the constricted region from -8 kPa/m to 9 kPa/m, with a maximum bias of -7% for the axial component and -8% for the lateral component. The relative standard deviation of the estimator is 5% (axial component) and 30% (lateral component) when studying the pressure gradient across the constriction using 3 velocity frames per pressure estimate. The study shows that 2-D pressure gradients can be achieved noninvasively using ultrasound data in a constant flow environment.
This paper investigates how pressure gradients in a pulsatile flow environment can be measured non-invasively using ultrasound. The presented set-up is based on vector velocity fields measured on a blood mimicking fluid moving at a peak flow rate of 1 ml/s through a constricted vessel. Fields of pressure gradients are calculated using the Navier-Stokes equations. Flow data are acquired to a depth of 3 cm using directional synthetic aperture flow imaging on a linear array transducer producing 1500 image frames of velocity estimates per second. Scans of a carotid bifurcation phantom with a 70% constriction are performed using an experimental scanner. The performance of the presented estimator is evaluated by comparing its results to a numerical simulation model, which geometry is reconstructed from MRI data. The study showed pressure gradients varying from 0 kPa/m to 4.5 kPa/m with a maximum bias and standard deviation of 10% and 13%, respectively, relative to peak estimated gradient. The paper concludes that maps of pressure gradients can be measured non-invasively using ultrasound with a precision of more than 85%.
Novel flow quantification of the carotid bulb and the common carotid artery with vector flow ultrasound.

Abnormal blood flow is usually assessed using spectral Doppler estimation of the peak systolic velocity. The technique, however, only estimates the axial velocity component, and therefore the complexity of blood flow remains hidden in conventional ultrasound examinations. With the vector ultrasound technique transverse oscillation the blood velocities of both the axial and the transverse directions are obtained and the complexity of blood flow can be visualized. The aim of the study was to determine the technical performance and interpretation of vector concentration as a tool for estimation of flow complexity. A secondary aim was to establish accuracy parameters to detect flow changes/patterns in the common carotid artery (CCA) and the carotid bulb (CB). The right carotid bifurcation including the CCA and CB of eight healthy volunteers were scanned in a longitudinal plane with vector flow ultrasound (US) using a commercial vector flow ultrasound scanner (ProFocus, BK Medical, Denmark) with a linear 5 MHz transducer transverse oscillation vector flow software. CCA and CB areas were marked in one cardiac cycle from each volunteer. The complex flow was assessed by medical expert evaluation and by vector concentration calculation. A vortex with complex flow was found in all carotid bulbs, whereas the CCA had mainly laminar flow. The medical experts evaluated the flow to be mainly laminar in the CCA (0.82 +/- 0.14) and mainly complex (0.23 +/- 0.22) in the CB. Likewise, the estimated vector concentrations in CCA (0.96 +/- 0.16) indicated mainly laminar flow and in CB (0.83 +/- 0.07) indicated mainly turbulence. Both methods were thus able to clearly distinguish the flow patterns of CCA and CB in systole. Vector concentration from angle-independent vector velocity estimates is a quantitative index, which is simple to calculate and can differentiate between laminar and complex flow. (C) 2014 World Federation for Ultrasound in Medicine & Biology.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, University of Copenhagen, BK Medical Aps
Authors: Pedersen, M. M. (Intern), Pihl, M. J. (Intern), Haugaard, P. (Ekstern), Hansen, K. L. (Intern), Lange, T. (Ekstern), Lonn, L. (Ekstern), Nielsen, M. B. (Intern), Jensen, J. A. (Intern)
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Scopus rating (2014): SJR 1.054 SNIP 1.407 CiteScore 2.65
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Novel method for detection of Sleep Apnoea using respiration signals

Polysomnography (PSG) studies are considered the “gold standard” for the diagnosis of Sleep Apnoea (SA). Identifying cessations of breathing from long-lasting PSG recordings manually is a labour-intensive and time-consuming task for sleep specialist, associated with inter-scorer variability. In this study a simplified, semi-automatic, three-channel method for detection of SA patients is proposed in order to increase analysis reliability and diagnostic accuracy in the clinic. The method is based on characteristic features, such as respiration stoppages pr. hour and the total number of oxygen desaturations > 3%, extracted from the thorax and abdomen respiration effort belts, and the oxyhemoglobin saturation (SaO2), fed to an Elastic Net classifier and validated according to American Academy of Sleep Medicine (AASM) using the patients’ AHI value. The method was applied to 109 patient recordings and resulted in a very high SA classification with accuracy of 97.9%. The proposed method reduce the time spent on manual analysis of respiration stoppages and the inter- and intra-scorer variability, and may serve as an alternative screening method for SA.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen
Authors: Nielsen, K. C. (Intern), Kempfner, L. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern)
Carotid strain imaging in 3D is not possible with conventional focused imaging, because the frame rate is too low. Plane wave ultrasound provides sufficiently high frame rates, albeit at the cost of image quality, especially in the off-axis direction due to the lack of focusing. Multiple techniques have been developed to cope with the low off-axis imaging quality when performing 2D (and in future 3D) motion estimation: cross correlation with directional beamforming (with or without RF (coherent) compounding) and displacement compounding. This study compares the precision of these techniques using linear array ultrasound data of a pulsating concentric homogeneous artery simulated using Field II. The transducer (fc = 9 MHz, pitch = 197.9 μm, 192 elements, fs = 180 MHz) transmitted plane waves at 3 sequentially alternating angles (0°, +θ, -θ) at a PRF of 2 kHz. Simulations were repeated for θ ranging from 1° to 20° with increments of 1°. Displacements were estimated for frame intervals of 1/15th s, tracked, and cumulated from diastole to systole using either displacement compounding, or directional beamforming optionally enhanced by RF compounding. 1D directional beamforming with RF compounding and 2D displacement compounding with θ = ~20° performed equally and best with a relative root-mean-squared error of ~2% with respect to the analytical solution. The mean and standard deviation of the estimated motion direction for 2D displacement compounding with θ = 20° was 0.03° ± 1.43°. Since displacement compounding requires no assumptions regarding the motion direction, this technique seems the best option for plane wave carotid strain imaging.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Radboud University Nijmegen
Authors: Hansen, H. H. (Ekstern), Stuart, M. B. (Intern), Villagómez Hoyos, C. A. (Intern), Jensen, J. A. (Intern), de Korte, C. L. (Ekstern)
Pages: 1814-1817
Publication date: 2014

Rapid eye movement sleep behavior disorder as an outlier detection problem
OBJECTIVE: Idiopathic rapid eye movement (REM) sleep behavior disorder is a strong early marker of Parkinson’s disease and is characterized by REM sleep without atonia and/or dream enactment. Because these measures are subject to individual interpretation, there is consequently need for quantitative methods to establish objective criteria. This study proposes a semiautomatic algorithm for the early detection of Parkinson's disease. This is achieved by distinguishing...
between normal REM sleep and REM sleep without atonia by considering muscle activity as an outlier detection problem.

**METHODS:** Sixteen healthy control subjects, 16 subjects with idiopathic REM sleep behavior disorder, and 16 subjects with periodic limb movement disorder were enrolled. Different combinations of five surface electromyographic channels, including the EOG, were tested. A muscle activity score was automatically computed from manual scored REM sleep. This was accomplished by the use of subject-specific features combined with an outlier detector (one-class support vector machine classifier).

**RESULTS:** It was possible to correctly separate idiopathic REM sleep behavior disorder subjects from healthy control subjects and periodic limb movement subjects with an average validation area under the receiver operating characteristic curve of 0.993 when combining the anterior tibialis with submentalis. Additionally, it was possible to separate all subjects correctly when the final algorithm was tested on 12 unseen subjects. **CONCLUSIONS:** Detection of idiopathic REM sleep behavior disorder can be regarded as an outlier problem. Additionally, the EOG channels can be used to detect REM sleep without atonia and is discriminative better than the traditional submentalis. Furthermore, based on data and methodology, arousals and periodic limb movements did only have a minor influence on the quantification of the muscle activity. Analysis of muscle activity during nonrapid eye movement sleep may improve the separation even further.

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Rapid Measurements of Intensities for Safety Assessment of Advanced Imaging Sequences

FDA requires that intensity and safety parameters are measured for all imaging schemes for clinical imaging. This is often cumbersome, since the scan sequence has to be broken apart, measurements conducted for the individually emitted beams, and the final intensity levels calculated by combining the intensities from the individual beams. This paper suggests a fast measurement scheme using the multi-line sampling capability of modern scanners and research systems. The hydrophone is connected to one sampling channel in the research system, and the intensity is measured for all imaging lines in one emission sequence. This makes it possible to map out the pressure field and hence intensity level for all imaging lines in a single measurement. The approach has several advantages: the scanner does not have to be re-programmed and can use the scan sequence without modification. The measurements are orders of magnitude faster (minutes rather than hours) and the final intensity level calculation can be made generic and reused for any kind of scan sequence by just knowing the number of imaging lines and the pulse repetition time. The scheme has been implemented on the Acoustic Intensity Measurement System AIMS III (Onda, Sunnyvale, California, USA). The research scanner SARUS is used for the experiments, where one of the channels is used for the hydrophone signal. A 3 MHz BK 8820e (BK Medical, Herlev, Denmark) convex array with 192 elements is used along with an Onda HFL-0400 hydrophone connected to a AH-2010 pre-amplifier (Onda Corporation, Sunnyvale, USA). A single emission sequence is employed for testing and calibrating the approach. The measurements using the AIMS III and SARUS systems after calibration agree within a relative standard deviation of 0.24%. A duplex B-mode and flow sequence is also investigated. The complex intensity map is measured and the time averaged spatial peak intensity is found. A single point measurement takes 3.43 seconds and the whole sequence can be characterized on the acoustical axis in around 6 minutes.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Jensen, J. A. (Intern), Rasmussen, M. F. ( Intern), Stuart, M. B. (Intern), Tomov, B. G. ( Intern)
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Real-Time GPU Implementation of Transverse Oscillation Vector Velocity Flow Imaging

Rapid estimation of blood velocity and visualization of complex flow patterns are important for clinical use of diagnostic ultrasound. This paper presents real-time processing for two-dimensional (2-D) vector flow imaging which utilizes an off-the-shelf graphics processing unit (GPU). In this work, Open Computing Language (OpenCL) is used to estimate 2-D vector velocity flow in vivo in the carotid artery. Data are streamed live from a BK Medical 2202 Pro Focus UltraView Scanner to a workstation running a research interface software platform. Processing data from a 50 millisecond frame of a duplex vector flow acquisition takes 2.3 milliseconds seconds on an Advanced Micro Devices Radeon HD 7850 GPU card. The detected velocities are accurate to within the precision limit of the output format of the display routine. Because this tool was developed as a module external to the scanner’s built-in processing, it enables new opportunities for prototyping novel algorithms, optimizing processing parameters, and accelerating the path from development lab to clinic.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Technical University of Denmark, BK Medical Aps
Authors: Bradway, D. (Intern), Pihl, M. J. (Intern), Krebs, A. (Ekstern), Tomov, B. G. (Intern), Kjær, C. S. (Ekstern), Nikolov, S. I. (Ekstern), Jensen, J. A. (Intern)
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Row-Column Addressed 2-D CMUT Arrays with Integrated Apodization

Experimental results from row-column addressed capacitive micromachined ultrasonic transducers (CMUTs) with integrated apodization are presented. The apodization is applied by varying the density of CMUT cells in the array with the objective of damping the edge waves originating from the element ends. Two row-column addressed 32+32 CMUT arrays are produced using a wafer-bonding technique, one with and one without integrated apodization. Hydrophone measurements of the emitted pressure field from the array with integrated apodization show a reduction in edge wave energy of 8.4 dB (85 %) compared to the array without integrated apodization. Field II simulations yield a corresponding reduction of 13.0 dB (95 %). The simulations are able to replicate the measured pressure field, proving the predictability of the technique.

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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Christiansen, T. L. (Intern), Rasmussen, M. F. (Intern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)
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Row-Column Addressed 2-D CMUT Arrays with Integrated Apodization

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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering
Authors: Christiansen, T. L. (Intern), Rasmussen, M. F. (Intern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)
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Simulation and Efficient Measurements of Intensities for Complex Imaging Sequences
It is investigated how linear simulation can be used to predict both the magnitude of the intensities as well as the placement of the peak values. An ultrasound sequence is defined through the normal setup routines for the experimental SARUS scanner, and Field II is then used automatically on the sequence to simulate both intensity and mechanical index (MI) according to FDA rules. A 3 MHz BK Medical 8820e convex array transducer is used with the SARUS scanner. An Onda HFL-0400 hydrophone and the Onda AIMS III system measures the pressure field for three imaging schemes: a fixed focus, single emission scheme, a duplex vector flow scheme, and finally a vector flow imaging scheme. The hydrophone is connected to a receive channel in SARUS, which automatically measures the emitted pressure for the complete imaging sequence. MI can be predicted with an accuracy of 16.4 to 38 %. The accuracy for the intensity is from -17.6 to 9.7 %, although the measured fields are highly non-linear (several MPa) and linear simulation is used. Linear simulation can, thus, be used to accurately predict intensity levels for any advanced imaging sequence and is an efficient tool in predicting the energy distribution.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Jensen, J. A. (Intern), Rasmussen, M. F. (Intern), Stuart, M. B. (Intern), Tomov, B. G. (Intern)
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Publication: Research - peer-review › Article in proceedings – Annual report year: 2014
Simulation Study of Real Time 3-D Synthetic Aperture Sequential Beamforming for Ultrasound Imaging

This paper presents a new beamforming method for real-time three-dimensional (3-D) ultrasound imaging using a 2-D matrix transducer. To obtain images with sufficient resolution and contrast, several thousand elements are needed. The proposed method reduces the required channel count from the transducer to the main imaging system, by including electronics in the transducer handle. The reduction of element channel count is achieved using a sequential beamforming scheme. The beamforming scheme is a combination of a fixed focus beamformer in the transducer and a second dynamic focus beamformer in the main system. The real-time imaging capability is achieved using a synthetic aperture beamforming technique, utilizing the transmit events to generate a set of virtual elements that in combination can generate an image. The two core capabilities in combination is named Synthetic Aperture Sequential Beamforming (SASB).

Simulations are performed to evaluate the image quality of the presented method in comparison to Parallel beamforming utilizing 16 receive beamformers. As indicators for image quality the detail resolution and Cystic resolution are determined for a set of scatterers at a depth of 90mm for elevation and azimuth angles from 0 to 25. Simulations show that the acoustic performance of the proposed method is less angle dependent than Parallel beamforming. The Cystic resolution is shown to be more than 50% improved, with a detail resolution on the same order as Parallel Beamforming.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Hemmsen, M. C. (Intern), Rasmussen, M. F. (Intern), Stuart, M. B. (Intern), Jensen, J. A. (Intern)
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Simultaneous Multiaagent Hyperpolarized $^{13}$C Perfusion Imaging

Purpose: To demonstrate simultaneous hyperpolarization and imaging of three $^{13}$C-labeled perfusion MRI contrast agents with dissimilar molecular structures ($[^{13}$C]urea, $[^{13}$C]hydroxymethyl cyclopropane, and $[^{13}$C]-butanol) and correspondingly variable chemical shifts and physiological characteristics, and to exploit their varying diffusibility for simultaneous measurement of vascular permeability and perfusion in initial preclinical studies. Methods: Rapid and efficient dynamic multislice imaging was enabled by a novel pulse sequence incorporating balanced steady state free precession excitation and spectral-spatial readout by multiband frequency encoding, designed for the wide, regular spectral separation of these compounds. We exploited the varying bilayer permeability of these tracers to quantify vascular permeability and perfusion parameters simultaneously, using perfusion modeling methods that were investigated in simulations. "Tripolarized" perfusion MRI methods were applied to initial preclinical studies with differential conditions of vascular permeability, in normal mouse tissues and advanced transgenic mouse prostate tumors. Results: Dynamic imaging revealed clear differences among the individual tracer distributions. Computed permeability maps demonstrated differential permeability of brain tissue among the tracers, and tumor perfusion and permeability were both elevated over values expected for normal tissues. Conclusion: Tripolarized perfusion MRI provides new molecular imaging measures for specifically monitoring permeability, perfusion, and transport simultaneously in vivo.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of California, San Francisco
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Main Research Area: Technical/natural sciences
Size of quorum sensing communities

Ensembles of bacteria are able to coordinate their phenotypic behavior in accordance with the size, density, and growth state of the ensemble. This is achieved through production and exchange of diffusible signal molecules in a cell–cell regulatory system termed quorum sensing. In the generic quorum sensor a positive feedback in the production of signal molecules defines the conditions at which the collective behavior switches on. In spite of its conceptual simplicity, a proper measure of biofilm colony “size” appears to be lacking. We establish that the cell density multiplied by a geometric factor which incorporates the boundary conditions constitutes an appropriate size measure. The geometric factor is the square of the radius for a spherical colony or a hemisphere attached to a reflecting surface. If surrounded by a rapidly exchanged medium, the geometric factor is divided by three. For a disk-shaped biofilm the geometric factor is the horizontal dimension multiplied by the height, and the square of the height of the biofilm if there is significant flow above the biofilm. A remarkably simple factorized expression for the size is obtained, which separates the all-or-none ignition caused by the positive feedback from the smoother activation outside the switching region.

General information

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Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Cellular Signal Integration, Department of Electrical Engineering, Biomedical Engineering
Authors: Ferkinghoff-Borg, J. (Intern), Sams, T. (Intern)
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Web of Science (2016): Indexed yes
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Web of Science (2014): Indexed yes
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Scopus rating (2012): SJR 1.625 SNIP 0.882 CiteScore 3.43
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BFI (2011): BFI-level 1
Sleep-spindle detection: crowdsourcing and evaluating performance of experts, non-experts and automated methods

Sleep spindles are discrete, intermittent patterns of brain activity observed in human electroencephalographic data. Increasingly, these oscillations are of biological and clinical interest because of their role in development, learning and neurological disorders. We used an Internet interface to crowdsource spindle identification by human experts and non-experts, and we compared their performance with that of automated detection algorithms in data from middle- to older-aged subjects from the general population. We also refined methods for forming group consensus and evaluating the performance of event detectors in physiological data such as electroencephalographic recordings from polysomnography. Compared to the expert group consensus gold standard, the highest performance was by individual experts and the non-expert group consensus, followed by automated spindle detectors. This analysis showed that crowdsourcing the scoring of sleep data is an efficient method to collect large data sets, even for difficult tasks such as spindle identification. Further refinements to spindle detection algorithms are needed for middle- to older-aged subjects.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Stanford University, California Institute of Technology, University of Wisconsin-Madison, Copenhagen University Hospital
Authors: Warby, S. C. (Ekstern), Wendt, S. L. (Intern), Welinder, P. (Ekstern), Munk, E. G. (Ekstern), Carrillo, O. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern), Peppard, P. E. (Ekstern), Perona, P. (Ekstern), Mignot, E. (Ekstern)
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Sleep spindle scoring: performance of humans versus machines

General information
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Organisations: Department of Applied Electronics, Department of Electrical Engineering, Biomedical Engineering, Center for Sleep Sciences and Medicine, Danish Center for Sleep Medicine
Authors: Wendt, S. L. (Intern), Warby, S. (Ekstern), Welinder, P. (Ekstern), Sørensen, H. B. D. (Intern), E. Peppard, P. (Ekstern), Mignot, E. (Ekstern), Jennum, P. (Ekstern)
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Sleep spindle scoring: performance of humans versus machines
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Sources of the brain activation in visual attention: a novel feature for electroencephalography-based brain computer interface

General information
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SSVEP-modulation by covert and overt attention: Novel features for BCI in attention neuro-rehabilitation

In this pilot study the effect of attention (covert and overt) on the signal detection and classification of steady-state visual-evoked potential (SSVEP) were investigated. Using the SSVEP-based paradigm, data were acquired from 4 subjects using 3 scalp electroencephalography (EEG) electrodes located on the visual area. Subjects were instructed to perform the attention task in which they attended covertly or overtly to either of the stimuli flickering with different frequencies (6, 7, 8 and 9Hz). We observed a decrease in signal power in covert compared to the overt attention. However, there was a consistent pattern in covert attention causing an increase in the power of the 2\textsuperscript{nd} harmonic of the attended frequency. Encouraging results of this preliminary study indicates that it can be adapted and implemented in the brain-computer interface (BCI) system which could potentially be used as a neuro-rehabilitation tool for individuals with attention deficit.

Statistical Discriminability Estimation for Pattern Classification Based on Neural Incremental Attribute Learning

Feature ordering is a significant data preprocessing method in Incremental Attribute Learning (IAL), a novel machine learning approach which gradually trains features according to a given order. Previous research has shown that, similar to feature selection, feature ordering is also important based on each feature's discrimination ability, and should be sorted in a descending order of their discrimination ability. However, such an ordering is crucial for the performance of IAL. As the number of feature dimensions in IAL is increasing, feature discrimination ability also should be calculated in the corresponding incremental way. Based on Single Discriminability (SD), where only the feature discrimination ability is computed, a new filter statistical feature discrimination ability predictive metric, called the Accumulative Discriminability (AD), is designed for the dynamical feature discrimination ability estimation. Moreover, a criterion that summarizes all the produced values of AD is employed with a GA (Genetic Algorithm)-based approach to obtain the optimum feature ordering for classification problems based on neural networks by means of IAL. Compared with the feature ordering obtained by other approaches, the method proposed in this paper exhibits better performance in the final classification results. Such a phenomenon indicates that, (i) the feature discrimination ability should be incrementally estimated in IAL, and (ii) the feature ordering derived by AD and its corresponding approaches are applicable with IAL.
Storage of magnetization as singlet order by optimal control designed pulses

The use of hyperpolarization to enhance the sensitivity of MRI has so far been limited by the decay of the polarization through T1 relaxation. Recently, methods have been proposed that extend the lifetime of the hyperpolarization by storing the spin order in slowly relaxing singlet states. With this aim, optimal control theory was applied to create pulses that for near-equivalent spins accomplish transfers in and out of the singlet state with maximum efficiency while ensuring robustness toward variations in the nuclear spin system Hamiltonian (chemical shift, J-couplings, B1 and B magnetic field inhomogeneity). The pulses are designed to accomplish efficient transfer with low B1 amplitude, essential for applications on preclinical and clinical MR scanners. It is demonstrated that significantly improved efficiency and robustness can be obtained within the limitations of typical MR scanner performance. Magn Reson Med 71:921–926, 2014. © 2013 Wiley Periodicals, Inc.
Synthetic Aperture Sequential Beamforming implemented on multi-core platforms

This paper compares several computational approaches to Synthetic Aperture Sequential Beamforming (SASB) targeting consumer level parallel processors such as multi-core CPUs and GPUs. The proposed implementations demonstrate that ultrasound imaging using SASB can be executed in real-time with a significant headroom for post-processing. The CPU implementations are optimized using Single Instruction Multiple Data (SIMD) instruction extensions and multithreading, and the GPU computations are performed using the APIs, OpenCL and OpenGL. The implementations include refocusing (dynamic focusing) of a set of fixed focused scan lines received from a BK Medical UltraView 800 scanner and subsequent image processing for B-mode imaging and rendering to screen. The benchmarking is performed using a clinically evaluated imaging setup consisting of 269 scan lines x 1472 complex samples (1.58 MB per frame, 16 frames per second) on an Intel Core i7 2600 CPU with an AMD HD7850 and a NVIDIA GTX680 GPU. The fastest CPU and GPU implementations use 14% and 1.3% of the real-time budget of 62 ms/frame, respectively. The maximum achieved processing rate is 1265 frames/s.
Thermal Oxidation of Structured Silicon Dioxide

The topography of thermally oxidized, structured silicon dioxide is investigated through simulations, atomic force microscopy, and a proposed analytical model. A 357 nm thick oxide is structured by removing regions of the oxide in a masked etch with either reactive ion etching or hydrofluoric acid. Subsequent thermal oxidation is performed in both dry and wet ambients in the temperature range 950\degree C to 1100\degree C growing a 205 ± 12 nm thick oxide in the etched mask windows. Lifting of the original oxide near the edge of the mask in the range 6 nm to 37 nm is seen with increased lifting for increasing processing temperatures. Oxides structured by reactive ion etching are lifted on average a factor of four more than oxides etched in hydrofluoric acid. Both simulations and the analytical model successfully predict the oxide topography qualitatively, showing that the mask lifting phenomenon is governed mainly by diffusion and the geometry of the oxide. Simulations also predict the oxide topography quantitatively, with an average root mean square deviation of 1.2 nm and a maximum deviation of 13 nm (39%) from the mean of the measured values.
Tissue Harmonic Synthetic Aperture Ultrasound Imaging

Synthetic aperture sequential beamforming (SASB) and tissue harmonic imaging (THI) are combined to improve the image quality of medical ultrasound imaging. The technique is evaluated in a comparative study against dynamic receive focusing (DRF). The objective is to investigate if SASB combined with THI improves the image quality compared to DRF-THI. The major benefit of SASB is a reduced bandwidth between the probe and processing unit. A BK Medical 2202 Ultraview ultrasound scanner was used to acquire beamformed RF data for offine evaluation. The acquisition was made interleaved between methods, and data were recorded with and without pulse inversion for tissue harmonic imaging. Data were acquired using a Sound Technology 192 element convex array transducer from both a wire phantom and a tissue mimicking phantom to investigate spatial resolution and penetration. In-vivo scans were also performed for a visual comparison. The spatial resolution for SASB-THI is on average 19% better than DRF-THI, and the investigation of penetration showed equally good signal-to-noise ratio. In-vivo B-mode scans were made and compared. The comparison showed that SASB-THI reduces the artefact and noise interference and improves image contrast and spatial resolution.
Transverse Spectral Velocity Estimation

A transverse oscillation (TO)-based method for calculating the velocity spectrum for fully transverse flow is described. Current methods yield the mean velocity at one position, whereas the new method reveals the transverse velocity spectrum as a function of time at one spatial location. A convex array probe is used along with two different estimators based on the correlation of the received signal. They can estimate the velocity spectrum as a function of time as for ordinary spectrograms, but they also work at a beam-to-flow angle of 90°. The approach is validated using simulations of pulsatile flow using the Womersly–Evans flow model. The relative bias of the mean estimated frequency is 13.6% and the mean relative standard deviation is 14.3% at 90°, where a traditional estimator yields zero velocity. Measurements have been conducted with an experimental scanner and a convex array transducer. A pump generated artificial femoral and carotid artery flow in the phantom. The estimated spectra degrade when the angle is different from 90°, but are usable down to 60° to 70°. Below this angle the traditional spectrum is best and should be used. The conventional approach can automatically be corrected for angles from 0° to 70° to give fully quantitative velocity spectra without operator intervention.
Ultrasound Evaluation of an Abdominal Aortic Fluid-Structure Interaction Model

Ultrasound measurements are used for evaluating biomechanics of the abdominal aorta (AA) predicted by a fluid-structure interaction (FSI) simulation model. FSI simulation models describe the complete arterial physiology by quantifying the mechanical response in the vessel wall caused by the percolating pulsating blood. But the predictability of FSI models needs validation for these to be usable for diagnostic purposes. Ultrasound measurements are suitable for such an evaluation as the wall displacement can be measured in vivo and compared to the wall displacement simulated in the FSI model. Spectral Doppler velocity data from 3 healthy male volunteers were used to construct inlet profiles for the FSI model. Simultaneously, wall movement was tracked and used for comparison to FSI model results. Ultrasound data were acquired using a scanner equipped with a research interface. The wall displacement was estimated by time shift estimation obtained from cross-correlation of signals to a fixed reference. The FSI model was constructed as a 2D axisymmetric pipe with lumen diameter predicted by B-mode images from each volunteer. Visual comparison of wall displacement over 1 cardiac cycle show agreement except for 1 volunteer (Male, 23 yrs.). The magnitude of the displacement in simulation, $u_{fsi}$, and in vivo, $u_{iv}$, is within the same order of magnitude for the young ($u_{iv} = 0.48$ mm, $u_{fsi} = 0.12$ mm) and middle-aged volunteer ($u_{iv} = 0.783$ mm, $u_{fsi} = 0.31$ mm). For the elderly volunteer the simulated displacement ($u_{fsi} = 0.975$ mm) is different from the in vivo measurement ($u_{iv} = 0.975$ mm).

Video surveillance of epilepsy patients using color image processing

This paper introduces a method for tracking patients under video surveillance based on a color marker system. The patients are not restricted in their movements, which requires a tracking system that can overcome non-ideal scenes e.g. occlusions, very fast movements, lighting issues and other moving objects. The suggested marker system consists of twelve unique markers that are located at each joint. By using a color marker system, each marker (if visible) can be found in every frame disregarding the possibility that it was occluded in the previous frame, compared to other tracking systems.
Volume Flow in Arteriovenous Fistulas Using Vector Velocity Ultrasound

Volume flow in arteriovenous fistulas for hemodialysis was measured using the angle-independent ultrasound technique Vector Flow Imaging and compared with flow measurements using the ultrasound dilution technique during dialysis. Using an UltraView 800 ultrasound scanner (BK Medical, Herlev, Denmark) with a linear transducer, 20 arteriovenous fistulas were scanned directly on the most superficial part of the fistula just before dialysis. Vector Flow Imaging volume flow was estimated with two different approaches, using the maximum and the average flow velocities detected in the fistula. Flow was estimated to be 242 mL/min and 404 mL/min lower than the ultrasound dilution technique estimate, depending on the approach. The standard deviations of the two Vector Flow Imaging approaches were 175.9 mL/min and 164.8 mL/min compared with a standard deviation of 136.9 mL/min using the ultrasound dilution technique. The study supports that Vector Flow Imaging is applicable for volume flow measurements.
Three dimensional (3d) transverse oscillation vector velocity ultrasound imaging.
An ultrasound imaging system (300) includes a transducer array (302) with a two-dimensional array of transducer elements configured to transmit an ultrasound signal and receive echoes, transmit circuitry (304) configured to control the transducer array to transmit the ultrasound signal so as to traverse a field of view, and receive circuitry (306) configured to receive a two dimensional set of echoes produced in response to the ultrasound signal traversing structure in the field of view, wherein the structure includes flowing structures such as flowing blood cells, organ cells etc. A beamformer (312) configured to beamform the echoes, and a velocity processor (314) configured to separately determine a depth velocity component, a transverse velocity component and an elevation velocity component, wherein the velocity components are determined based on the same transmitted ultrasound signal and the same received set of two dimensional echoes form part of the imaging system.

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3D cardiac Chemical Shift Imaging of [1-13C] hyperpolarized acetate and pyruvate in pigs

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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Luca, M. (Ekstern), Francesca, F. (Ekstern), Alessandra, F. (Ekstern), Vincenzo, L. (Ekstern), Matteo, L. (Ekstern), Giulio, G. (Ekstern), Giacomo, B. (Ekstern), L, R. S. (Ekstern), Vincenzo, P. (Ekstern), Ardenkjær-Larsen, J. H. (Intern), F, S. R. (Ekstern), A, R. F. (Ekstern), Luigi, L. (Ekstern), Maria, S. (Ekstern), Massimo, L. (Ekstern)
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.42
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 5.71
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 4.44
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 3.86
ISI indexed (2013): ISI indexed no
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BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 3.28
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Scopus rating (2011): CiteScore 3.1
ISI indexed (2011): ISI indexed yes
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BFI (2010): BFI-level 1
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BFI (2008): BFI-level 1
Scopus rating (2007): SNIP 1.184 SJR 0.301
Scopus rating (2006): SNIP 0.521 SJR 0.318
Scopus rating (2005): SNIP 0.201 SJR 0.178
Scopus rating (2004): SNIP 0.282 SJR 0.248
Scopus rating (2003): SNIP 0.191 SJR 0.106
Scopus rating (2002): SNIP 0.362
Scopus rating (2001): SNIP 0.314
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3D_cardiac_Chemical_Shift_Imaging.pdf

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3D CMR Mapping of Metabolism by Hyperpolarized 13C-Pyruvate in Ischemia–Reperfusion

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Main Research Area: Technical/natural sciences

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Scopus rating (2017): SNIP 2.682 SJR 4.66 CiteScore 3.85
Web of Science (2017): Indexed Yes
Scopus rating (2016): SJR 5.038 SNIP 2.685 CiteScore 4.36
Scopus rating (2015): SJR 3.694 SNIP 2.251 CiteScore 4.11
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Scopus rating (2013): SJR 3.917 SNIP 2.155 CiteScore 3.67
ISI indexed (2013): ISI indexed yes
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ISI indexed (2012): ISI indexed yes
Scopus rating (2011): SJR 3.525 SNIP 1.846 CiteScore 3.73
ISI indexed (2011): ISI indexed no
Scopus rating (2010): SJR 3.11 SNIP 1.896
Scopus rating (2009): SJR 1.761 SNIP 1.219
Original language: English
3-D Ultrasound Imaging Performance of a Row-Column Addressed 2-D Array Transducer: A Measurement Study

A real-time 3-D ultrasound measurement using only 32 elements and 32 emissions is presented. The imaging quality is compared to a conventionally fully addressed array using 1024 elements and 256 emissions. The main-lobe of the measured line spread function is almost identical, but the side-lobe levels are higher for the row-column addressed array. The cystic resolution sampled at a relative intensity difference of 20 dB shows a cyst size of 5.00 mm for the row-column addressed array and 2.39 mm for the fully sampled array. A simulation study is carried out which compares how the imaging quality of the two addressing methods scales with the number of beamforming channels used. It is shown that for any fixed number of active elements, a row-column addressed array achieves a better image quality than fully addressing the array. When using 128 channels, the mainlobe when fully addressing the array is 510% larger than when row-column addressing the array. The cyst radius needed to achieve -20 dB intensity in the cyst is 396% larger for the fully addressed array compared to the row-column addressed array. The measurements were made using the experimental ultrasound scanner SARUS and a 32x32 element ultrasound probe made by Vermon S.A.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Rasmussen, M. F. (Intern), Jensen, J. A. (Intern)
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3-D Ultrasound Imaging Performance of a row-column addressed 2D array transducer: a simulation study

This paper compares the imaging performance of a 128+128 element row-column addressed array with a fully addressed 1616 2D array. The comparison is made via simulations of the point spread function with Field II. Both arrays have lambda-pitch, a center frequency of 3.5 MHz and use 256 active elements. The row-column addressed array uses 128 transmit channels and 128 receive channels, whereas the fully addressed array uses 256 channels in both transmit and receive. The large size of the emulated row and column elements in the row-column addressed array causes ghost echoes to appear. The ghost echoes are shown to be suppressed when the sub-elements within each of the emulated row and column elements are apodized. The maximum ghost intensity is suppressed by 22:2 dB compared to using no apodization. With apodization applied, the full-width-at-half-maximum in the lateral direction for the fully addressed array is 2.81 mm, and 1.01 mm for the row-column addressed array. This shows that the detail resolution can be more than doubled using the row-column addressed array instead of the fully addressed array. The row column addressed array achieves a R20 dB cystic resolution of 0.76 mm, compared to 3.16 mm for the fully addressed array. The significantly smaller R20 dB-value for the row-column addressed array indicates that it can achieve a much higher contrast resolution than the fully addressed array.

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State: Published
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Authors: Rasmussen, M. F. (Intern), Jensen, J. A. (Intern)
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A Delta-Sigma beamformer with integrated apodization

This paper presents a new design of a discrete time Delta-Sigma (ΔΣ) oversampled ultrasound beamformer which integrates individual channel apodization by means of variable feedback voltage in the Delta-Sigma analog to digital (A/D) converters. The output bit-width of each oversampled A/D converter remains the same as in an unmodified one. The outputs of all receiving channels are delayed and summed, and the resulting multi-bit sample stream is filtered and decimated to become an image line. The simplicity of this beamformer allows the production of high-channel-count or very compact beamformers suitable for 2-D arrays or compact portable scanners. The new design is evaluated using measured data from the research scanner SARUS and a BK-8811 192 element linear array transducer (BK Medical, Herlev, Denmark), insonifying a water-filled wire phantom containing four wires orthogonal to the image plane. The data are acquired using 12-bit flash A/D converters at a sampling rate of 70 MHz, and are then upsampled off-line to 560 MHz for input to the simulated ΔΣ beamformer. The latter generates a B-mode image which is compared to that produced by a digital beamformer that uses 10-bit A/D converters. The performance is evaluated by comparing the width of the wire images at half amplitude and the noise level of the images. The ΔΣ beamformer resolution has been found to be identical to that of the multi-bit A/D beamforming architecture, while the noise floor is elevated by approximately 6 dB.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Tomov, B. G. (Intern), Stuart, M. B. (Intern), Hemmisen, M. C. (Intern), Jensen, J. A. (Intern)
Number of pages: 7
Publication date: 2013

A new attempt for deformity correction: Mechanical analysis of scoliosis correction by finite element method

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Abe, Y. (Ekstern), Ito, M. (Ekstern), Abumi, K. (Ekstern), Salmingo, R. A. (Intern), Tadano, S. (Ekstern)
Pages: 201-208
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Hokkaido Seikei Saigai Geka Gakkai Zasshi
Volume: 54
Apparatus and method for motion tracking in brain imaging

Disclosed is apparatus and method for motion tracking of a subject in medical brain imaging. The method comprises providing a light projector and a first camera; projecting a first pattern sequence (S1) onto a surface region of the subject with the light projector, wherein the subject is positioned in a scanner borehole of a medical scanner, the first pattern sequence comprising a first primary pattern (P1,1) and/or a first secondary pattern (P1,2); detecting the projected first pattern sequence (S1') with the first camera; determining a second pattern sequence (S2) comprising a second primary pattern (P2,1) based on the detected first pattern sequence (S1'); projecting the second pattern sequence (S2) onto a surface region of the subject with the light projector; detecting the projected second pattern sequence (S2') with the first camera; and determining motion tracking parameters based on the detected second pattern sequence (S2').

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Image Analysis & Computer Graphics, Biomedical Engineering
Authors: Olesen, O. V. (Intern), Larsen, R. (Intern), Paulsen, R. R. (Intern), Hejgaard, L. (Intern)
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Original language: English

Bibliographical note
Assessment of early diabetic renal changes with hyperpolarized [1-\textsuperscript{13}C]pyruvate

This experimental study explores a novel magnetic resonance imaging/spectroscopic (MRI/MRS) method that measures changes in renal metabolism in a diabetic rat model. This hyperpolarized metabolic MRI/MRS method allows monitoring of metabolic processes in seconds by >10 000-fold enhancement of the MR signal. The method has shown that the conversion of pyruvate to bicarbonate, i.e. pyruvate dehydrogenase (PDH) activity, is significantly altered in the myocardium already at the onset of diabetes, and the predominant Warburg effect is a valuable cancer maker via the lactate dehydrogenase (LDH) activity. We hypothesize that a similar change in PDH and LDH could be found in the early diabetic kidney. In a streptozotocin rat model of type 1 diabetes, hyperpolarized 13C-MRI and blood oxygenation level-dependent 1H-MRI was employed to investigate the changes in renal metabolism in the diabetic and the control kidneys in vivo. The diabetic kidney showed a 149% increase in the lactate/pyruvate ratio compared with the control rat kidney, whereas the bicarbonate/pyruvate ratio was unchanged between the diabetic and the control rat kidneys, consistent with literature findings. These metabolic findings paralleled a reduced intrarenal oxygen availability as found by blood oxygenation level-dependent MRI. Hyperpolarized 13C-MRI shows promise in the diagnosis and monitoring of early renal changes associated with diabetes, with the pyruvate/lactate ratio as an imaging biomarker for regional renal changes.

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Attenuated Heart Rate Response is Associated with Hypocretin Deficiency in Patients with Narcolepsy.

Our results show that autonomic dysfunction is part of the narcoleptic phenotype, and that hypocretin-1 deficiency is the primary predictor of this dysfunction. This finding suggests that the hypocretin system participates in the modulation of cardiovascular function at rest. CITATION: Sorensen GL; Knudsen S; Petersen ER; Kempfner J; Gammeltoft S; Sorensen HBD; Jennum P. Attenuated heart rate response is associated with hypocretin deficiency in patients with narcolepsy. SLEEP 2013;36(1):91-98.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Sørensen, G. L. (Intern), Knudsen, S. (Forskerdatabase), Petersen, E. R. (Ekstern), Kempfner, J. (Intern), Gammeltoft, S. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. (Forskerdatabase)
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BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.783 SJR 2.37 CiteScore 4.64
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.1 SJR 2.436 SNIP 1.713
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.668 SNIP 1.754 CiteScore 4.29
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.434 SNIP 2.039 CiteScore 4.22
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Automatic characterization of dynamics in Absence Epilepsy

Dynamics of the spike-wave paroxysms in Childhood Absence Epilepsy (CAE) are automatically characterized using novel approaches. Features are extracted from scalograms formed by Continuous Wavelet Transform (CWT). Detection algorithms are designed to identify an estimate of the temporal development of frequencies in the paroxysms. A database of 106 paroxysms from 26 patients was analyzed. The database is large compared to other known studies in the field of dynamics in CAE. CWT is more efficient than the widely used Fourier transform due to CWT's ability to recognize smaller discontinuities and variations. The use of scalograms and the detection algorithms result in a potentially usable clinical tool for dividing CAE patients into subsets. Differences between the grouped paroxysms may turn out to be useful from a clinical perspective as a prognostic indicator or when adjusting drug treatment.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, Copenhagen University Hospital, University of Copenhagen
Authors: Petersen, K. N. H. (Forskerdatabase), Nielsen, T. N. (Ekstern), Kjær, T. W. (Ekstern), Thomsen, C. E. (Ekstern), Sorensen, H. B. D. (Intern)
Pages: 4283 - 4286
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Main Research Area: Technical/natural sciences
Conference: 35th Annual International Conference of the IEEE EMBS, Osaka, Japan, 03/07/2013 - 03/07/2013
drugs, electroencephalography, feature extraction, Fourier transforms, medical disorders, medical signal detection, paediatrics, patient treatment, wavelet transforms, Engineered Materials, Dielectrics and Plasmas

Automatic SLEEP staging: From young adults to elderly patients using multi-class support vector machine

Aging is a process that is inevitable, and makes our body vulnerable to age-related diseases. Age is the most consistent factor affecting the sleep structure. Therefore, new automatic sleep staging methods, to be used in both of young and
elderly patients, are needed. This study proposes an automatic sleep stage detector, which can separate wakefulness, rapid-eye-movement (REM) sleep and non-REM (NREM) sleep using only EEG and EOG. Most sleep events, which define the sleep stages, are reduced with age. This is addressed by focusing on the amplitude of the clinical EEG bands, and not the affected sleep events. The age-related influences are then reduced by robust subject-specific scaling. The classification of the three sleep stages are achieved by a multi-class support vector machine using the one-versus-rest scheme. It was possible to obtain a high classification accuracy of 0.91. Validation of the sleep stage detector in other sleep disorders, such as apnea and narcolepsy, should be considered in future work.

**General information**

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Kempfner, J. (Intern), Jennum, P. (Forskerdatabase), Sorensen, H. B. D. (Intern), Christensen, J. A. E. (Intern), Nikolic, M. (Forskerdatabase)
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Main Research Area: Technical/natural sciences
diseases, electro-oculography, electroencephalography, geriatrics, medical disorders, medical signal detection, signal classification, sleep, support vector machines, Engineered Materials, Dielectrics and Plasmas
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**BCI using imaginary movements: The simulator**

Over the past two decades, much progress has been made in the rapidly evolving field of Brain Computer Interface (BCI). This paper presents a novel concept: a BCI-simulator, which has been developed for the Hex-O-Spell interface, using the sensory motor rhythms (SMR) paradigm. With the simulator, it is possible to evaluate how the model parameters such as error classifications, delay between classifications and success rate affect the communication rate. Another advantage of the simulator is that it allows us to study for more classes than most online BCI systems which are limited to only two classes. Results show that the BCI simulator is able to give a deeper understanding of the feedback systems. We also find that a 3-class system is more efficient than a 2-class system if it obtains a success rate of at least 55% of the 2-class system.

**General information**

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Organisations: Department of Electrical Engineering, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering, Biomedical Engineering, Technical University of Denmark, Copenhagen University Hospital, University of Copenhagen
Authors: Rohani, D. A. (Intern), Henning, W. S. (Ekstern), Thomsen, C. E. (Intern), Kjaer, T. W. (Ekstern), Puthusserypady, S. (Intern), Sorensen, H. B. (Intern)
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Scopus rating (2017): SNIP 1.767 SJR 0.786 CiteScore 3.49
Web of Science (2017): Indexed Yes
Blood-Brain Barrier Permeability of Normal Appearing White Matter in Relapsing-Remitting Multiple Sclerosis

Background: Multiple sclerosis (MS) affects the integrity of the blood-brain barrier (BBB). Contrast-enhanced T1 weighted magnetic resonance imaging (MRI) is widely used to characterize location and extent of BBB disruptions in focal MS lesions. We employed quantitative T1 measurements before and after the intravenous injection of a paramagnetic contrast agent to assess BBB permeability in the normal appearing white matter (NAWM) in patients with relapsing-remitting MS (RR-MS). Methodology/Principal Findings: Fifty-nine patients (38 females) with RR-MS undergoing immunomodulatory treatment and nine healthy controls (4 females) underwent quantitative T1 measurements at 3 tesla before and after injection of a paramagnetic contrast agent (0.2 mmol/kg Gd-DTPA). Mean T1 values were calculated for NAWM in patients and total cerebral white matter in healthy subjects for the T1 measurements before and after injection of Gd-DTPA. The pre-injection baseline T1 of NAWM (945655 [SD] ms) was prolonged in RR-MS relative to healthy controls...
Gd-DTPA injection shortened T1 to a similar extent in both groups. Mean T1 of NAWM was 866647 ms in the NAWM of RR-MS patients and 824613 ms in the white matter of healthy controls. The regional variability of T1 values expressed as the coefficient of variation (CV) was comparable between the two groups at baseline, but not after injection of the contrast agent. After intravenous Gd-DTPA injection, T1 values in NAWM were more variable in RR-MS patients (CV = 0.19860.046) compared to cerebral white matter of healthy controls (CV = 0.16660.018, p = 0.046).

Conclusions/Significance: We found no evidence of a global BBB disruption within the NAWM of RR-MS patients undergoing immunomodulatory treatment. However, the increased variation of T1 values in NAWM after intravenous Gd-DTPA injection points to an increased regional inhomogeneity of BBB function in NAWM in relapsing-remitting MS.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Lund, H. (Ekstern), Krakauer, M. (Ekstern), Skimminge, A. (Ekstern), Sellebjerg, F. (Ekstern), Garde, E. (Ekstern), Siebner, H. R. (Ekstern), Paulson, O. B. (Ekstern), Hesse, D. (Ekstern), Hanson, L. G. (Intern)
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BFI (2017): BFI-level 1
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.11 SJR 1.236 SNIP 1.101
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.427 SNIP 1.136 CiteScore 3.32
Web of Science (2015): Indexed yes
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Scopus rating (2014): SJR 1.559 SNIP 1.148 CiteScore 3.54
Web of Science (2014): Indexed yes
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ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.982 SNIP 1.156 CiteScore 4.15
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BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.425 SNIP 1.233 CiteScore 4.58
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Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.705 SNIP 1.178
Web of Science (2010): Indexed yes
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Scopus rating (2009): SJR 2.614 SNIP 1.046
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Cerebral angiography in rats: comparison of 1h tof-mra, spio enhancement and hyperpolarized 13c bssfp

General information
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Organisations: Department of Micro- and Nanotechnology, Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Lipsø, H. K. W. (Intern), Magnusson, P. (Ekstern), Søgaard, L. V. (Ekstern), Ardenkjær-Larsen, J. H. (Intern)
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Classification of iRBD and Parkinson's disease patients based on eye movements during sleep
Patients suffering from the sleep disorder idiopathic rapid-eye-movement sleep behavior disorder (iRBD) have been observed to be in high risk of developing Parkinson's disease (PD). This makes it essential to analyze them in the search for PD biomarkers. This study aims at classifying patients suffering from iRBD or PD based on features reflecting eye movements (EMs) during sleep. A Latent Dirichlet Allocation (LDA) topic model was developed based on features extracted from two electrooculographic (EOG) signals measured as parts in full night polysomnographic (PSG) recordings from ten control subjects. The trained model was tested on ten other control subjects, ten iRBD patients and ten PD patients, obtaining a EM topic mixture diagram for each subject in the test dataset. Three features were extracted from the topic mixture diagrams, reflecting “certainty”, “fragmentation” and “stability” in the timely distribution of the EM topics. Using a Naive Bayes (NB) classifier and the features “certainty” and “stability” yielded the best classification result and the subjects were classified with a sensitivity of 95 %, a specificity of 80% and an accuracy of 90 %. This study demonstrates in a data-driven approach, that iRBD and PD patients may exhibit abnorm form and/or timely distribution of EMs during sleep.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Applied Mathematics and Computer Science , Technical University of Denmark, H. Lundbeck A/S, Copenhagen University Hospital, University of Copenhagen
Authors: Christensen, J. A. E. (Intern), Koch, H. (Ekstern), Frandsen, R. (Ekstern), Kempfner, J. (Intern), Arvastson, L. J. (Intern), Christensen, S. R. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. (Forskerdatabase)
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Main Research Area: Technical/natural sciences
Bayes methods, diseases, electro-oculography, feature extraction, medical disorders, medical signal processing, signal classification, sleep, Engineered Materials, Dielectrics and Plasmas
Classification of iRBD and Parkinson’s patients using a general data-driven sleep staging model built on EEG

Sleep analysis is an important diagnostic tool for sleep disorders. However, the current manual sleep scoring is time-consuming as it is a crude discretization in time and stages. This study changes Esbroeck and Westover’s [1] latent sleep staging model into a global model. The proposed data-driven method trained a topic mixture model on 10 control subjects and was applied on 10 other control subjects, 10 iRBD patients and 10 Parkinson’s patients. In that way 30 topic mixture diagrams were obtained from which features reflecting distinct sleep architectures between control subjects and patients were extracted. Two features calculated on basis of two latent sleep states classified subjects as “control” or “patient” by a simple clustering algorithm. The mean sleep staging accuracy compared to classical AASM scoring was 72.4% for control subjects and a clustering of the derived features resulted in a sensitivity of 95% and a specificity of 80%. This study demonstrates that frequency analysis of sleep EEG can be used for data-driven global sleep classification and that topic features separates iRBD and Parkinson’s patients from control subjects.

Design of a quadrature surface coil for hyperpolarized 13C MRS cardiac metabolism studies in pigs

This work describes the design of a quadrature surface coil constituted by a circular loop and a butterfly coil, employed in transmit/receive (TX/RX) mode for hyperpolarized 13C studies of pig heart with a clinical 3T scanner. The coil characterization is performed by developing an SNR model for coil performance evaluation in terms of coil resistance, sample-induced resistance and magnetic field pattern. Experimental SNR-vs.-depth profiles, extracted from the [1-13C]acetate phantom chemical shift image (CSI), showed good agreement with the theoretical SNR-vs.-depth profiles. Moreover, the performance of the quadrature coil was compared with the single TX/RX circular and TX/RX butterfly coil, in order to verify the advantage of the proposed configuration over the single coils throughout the volume of interest for cardiac imaging in pig. Finally, the quadrature surface coil was tested by acquiring metabolic maps with hyperpolarized [1-13C]pyruvate injected i.v. in a pig. © 2013 Wiley Periodicals, Inc.
Detection and Prediction of Epileptic Seizures

Approximately 50 million people worldwide suffer from epilepsy. Although 70% can control their seizures by anti-epileptic drugs, it is still a cumbersome disease to live with for a large group of patients. The current PhD dissertation investigates how these people can be helped by continuous monitoring of their brain waves. More specifically, three issues were investigated: The feasibility of automatic seizure prediction, optimization of automatic seizure detection algorithms, and the link between intra- and extracranial EEG. Regarding feasibility of automatic seizure prediction, neither the author nor any other in the seizure prediction society have yet obtained clinical applicable prediction results. However, this should not be taken as discouraging for the future. New large public databases have emerged during 2012 which might provide the means to identify patterns leading to reliable seizure prediction algorithms.

More promising results were obtained in the investigating of possible use of an outpatient EEG monitoring device for idiopathic generalized epilepsy patients. Combined with an automatic seizure detection algorithm such a device can give an objective account of the paroxysm frequency, duration, and time of occurrence. Based on standard EEG data from 20 patients recorded in the clinic, the log-sum of wavelet transform coefficients were used as feature input to a classifier consisting of a support vector machine. 97% of paroxysms lasting more than two seconds were correctly detected without any false positive detections. This was obtained using a generic algorithm on the signals from only a single frontal channel. Applying the same algorithm architecture on EEG data from two outpatient children monitored for approximately three entire days each, the sensitivity was 90% and the false detection rate was 0.12/h. When more recordings are collected, the outpatient algorithm can be further optimized and results should improve.

The final investigation examined the relationship between spontaneous, awake intra- and extracranial EEG. Seven patients with electrodes placed subdurally as well as subgaleally were used to estimate the field of vision of a single extracranial channel. By computation of the coherence between the channels, the well recognized hypothesis stating that the skull acts as an electroencephalographic averager was proven correct. Although coherence was significant in an accumulation area of 150 cm², only channels within a cortical area of approximately 30 cm² showed to increase the coherence. The increase seemed to progress linearly with an accumulation area up to 31 cm², where 50% of the maximal coherence was accumulated from only 2 cm² (corresponding to one channel), and 75% from 16 cm². The coherences of different frequency bands below 16 Hz all seem to have similar declines as a function of the Euclidean distance between channels. Frequencies between 16 and 30 Hz have a steeper decline and will only show coherent parts to cortical channels within 80 cm². There is no coherence for frequencies above 30 Hz at any distance.

A lot of patients with epilepsy still struggle with a dreadful fear of suddenly having a seizure. The current PhD study
identified topics where an EEG monitor could provide improvement in the patient’s quality of life. By algorithm development, implementation and testing, a step toward such a device is presented.

**General information**

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Duun-Henriksen, J. (Intern), Sørensen, H. B. D. (Intern), Kjaer, T. W. (Ekstern), Thomsen, C. E. (Intern)
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**Relations**

Projects:
Detection and Prediction of Epileptic Seizures
Publication: Research › Ph.D. thesis – Annual report year: 2013

Detection of a sleep disorder predicting Parkinson's disease
Idiopathic rapid eye-movement (REM) sleep behavior disorder (iRBD) has been found to be a strong early predictor for later development into Parkinson's disease (PD). iRBD is diagnosed by polysomnography but the manual evaluation is laborious, why the aims of this study are to develop supportive methods for detecting iRBD from electroencephalographic (EEG) signals recorded during REM sleep. This method classified subjects from their EEG similarity with the two classes iRBD patients and control subjects. The feature sets used for classifying subjects were based on the relative powers of the EEG signals in different frequency bands. The classification was based on the fast and classical K-means and Bayesian classifiers. With a subject-specific re-scaling of the feature set and the use of a Bayesian classifier the performance reached 90% in both sensitivity and specificity. For the purpose of reducing the feature count, the features were evaluated with the statistical Smith-Satterthwaite test and by using sequential forward selection a well-performing feature subset was found which contained only five features, while attaining a sensitivity and a specificity of both 80%.

**General information**

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, Copenhagen University Hospital
Authors: Hansen, I. H. (Ekstern), Marcussen, M. (Ekstern), Christensen, J. A. E. (Intern), Jennum, P. (Forskerdatabase), Sørensen, H. B. D. (Intern)
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biomechanics, diseases, electroencephalography, eye, feature extraction, medical disorders, medical signal processing, sensitivity, signal classification, sleep, statistical analysis, Engineered Materials, Dielectrics and Plasmas
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Publication: Research - peer-review › Article in proceedings – Annual report year: 2013

Detection of Epileptic Seizures with Multi-modal Signal Processing
The main focus of this dissertation lies within the area of epileptic seizure detection. Medically refractory epileptic patients suffer from the unawareness of when the next seizure sets in, and what the consequences will be. A wearable device based on uni- or multi-modalities able to detect and alarm whenever a seizure starts is of great importance to these
patients and their relatives, in the sense, that the alert of the seizure will make them feel more safe. Thus the objective of the project is to investigate the movements of convulsive epileptic seizures and design seizure detection algorithms for these based on uni- or multimodalities. Regarding seizure detection, the highest potential clinical relevance is for the generalized tonic-clonic (GTC) seizures, as these are associated with an increased risk for sudden unexpected death in epilepsy (SUDEP) in unsupervised patients.

Several methods have been applied in different studies in order to achieve the goal of reliable seizure detection. In the first study we present a method where the support vector machine classifier is applied on features based on wavelet bands. This was used on multi-modal data from control subjects, with the result that the inclusion of more modalities provided a better performance. We succeeded in performing a multi-modal recording of a GTC seizure from an epileptic patient, and a visual analysis of the data showed that it was similar to the data from our control subjects, only more pronounced. Based on this we expected the algorithm to perform better on the patient data as well if more modalities were used. The presented algorithm proved to be able to detect epileptic tonic and GTC seizures based on one modality, surface electromyography (sEMG), but it did not prove to be sufficient for the other convulsive seizures tested.

Another study was performed, involving quantitative parameters in the time and frequency domain. The study showed, that there are several differences between tonic seizures and the tonic phase of GTC seizures and furthermore revealed differences of the epileptic (tonic and tonic phase of GTC) and simulated seizures. This was valuable information concerning a seizure detection algorithm, and the findings from this research provided evidence for a change in the definition of these seizures by the International League Against Epilepsy (ILAE).

Our final study presents a novel seizure detection algorithm for GTC seizures based on sEMG from a single channel. The algorithm is simple, based on a high-pass filter and a count of zero-crossings, in order to ease the implementation into a small wireless sEMG device. The algorithm proved to be reliable, and was after minor changes implemented in a wireless sEMG device. A double-blind test on patients in the clinic, showed 100 % reliability for three of four patients, whereas it failed for the last patient, who had atypical GTC seizures.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Danish Epilepsy Center
Authors: Conradsen, I. (Intern), Sørensen, H. B. D. (Intern), Beniczky, S. (Ekstern), Sams, T. (Intern), Wolf, P. (Ekstern)
Number of pages: 200
Publication date: 2013

Detection of the quorum sensing signal molecule N-Dodecanoyl-DL-homoserine lactone below 1 nanomolar concentrations using surface enhanced Raman spectroscopy
To the best of our knowledge we here for the first time demonstrate surface enhanced Raman spectroscopy (SERS) to detect a quorum sensing (QS) signal molecule below 1 nM concentration in both ultrapure water and under physiological conditions. Based on our results, SERS shows promise as a highly suitable tool for in situ measurements of low Acyl-Homoserine Lactone (AHL) concentrations in biofilms containing QS bacteria. Signal molecules communicate information about their environment and coordinate certain physiological activities in QS systems that exist in many bacteria. SERS enables detection of different AHLs at low concentrations due to structural differences observed in the corresponding SERS spectra. Ag colloidal nanoparticles, produced by the hydroxylamine reducing method, were used for the SERS measurements. SERS spectra of C12-HSL suspended in ultrapure water and in supplemented minimal medium were collected for 5 concentrations ranging from 2 μM to 0.2 nM, and a comparison between the spectra from these two media is also presented. We have been able to detect biologically relevant concentrations of AHL molecules ranging from 1 nM to 1 μM using SERS.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Chemistry, Panum Institutet , University of Copenhagen
Authors: Claussen, A. (Intern), Abdali, S. (Ekstern), Berg, R. W. (Intern), Givskov, M. (Ekstern), Sams, T. (Intern)
Pages: 199--214
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DTU BCI speller: An SSVEP-based spelling system with dictionary support

In this paper, a new brain computer interface (BCI) speller, named DTU BCI speller, is introduced. It is based on the steady-state visual evoked potential (SSVEP) and features dictionary support. The system focuses on simplicity and user friendliness by using a single electrode for the signal acquisition and displays stimuli on a liquid crystal display (LCD). Nine healthy subjects participated in writing full sentences after a five minutes introduction to the system, and obtained an information transfer rate (ITR) of 21.94 ± 15.63 bits/min. The average amount of characters written per minute (CPM) is 4.90 ± 3.84 with a best case of 8.74 CPM. All subjects reported systematically on different user friendliness measures, and the overall results indicated the potentials of the DTU BCI Speller system. For subjects with high classification accuracies, the introduced dictionary approach greatly reduced the time it took to write full sentences.

Dynamic nuclear polarization and optimal control spatial-selective 13C MRI and MRS

Aimed at 13C metabolic magnetic resonance imaging (MRI) and spectroscopy (MRS) applications, we demonstrate that dynamic nuclear polarization (DNP) may be combined with optimal control 2D spatial selection to simultaneously obtain high sensitivity and well-defined spatial restriction. This is achieved through the development of spatial-selective single-shot spiral-readout MRI and MRS experiments combined with dynamic nuclear polarization hyperpolarized [1-13C]pyruvate on a 4.7T pre-clinical MR scanner. The method stands out from related techniques by facilitating anatomic shaped region-of-interest (ROI) single metabolite signals available for higher image resolution or single-peak spectra. The 2D spatial-selective rf pulses were designed using a novel Krotov-based optimal control approach capable of iteratively fast providing successful pulse sequences in the absence of qualified initial guesses. The technique may be important for early detection of abnormal metabolism, monitoring disease progression, and drug research.
Efficiency evaluation of a 13C Magnetic Resonance birdcage coil: Theory and comparison of four methods

Radiofrequency coils in Magnetic Resonance systems are used to produce a homogeneous $B_1$ field for exciting the nuclei and to pick up the signals emitted by the nuclei with high signal-to-noise ratio. Accordingly, coil performance affects strongly the quality of the obtained data and images. Coil efficiency, defined as the $B_1$ magnetic field induced at a given point on the square root of supplied power $P$, is an important parameter that characterizes coil performance, since by maximizing efficiency will also maximize the signal-to-noise ratio. This work describes and compares four methods for coil efficiency estimation, based on different theoretical approaches. Three methods allow efficiency measurement by using “probe techniques” (perturbing loop, perturbing sphere and pick-up coil), which can be used both on the bench and inside the scanner, while an “NMR technique” has been employed for comparison purpose. Methods were tested on a 13C birdcage coil tuned at 32.13 MHz.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, National Research Council of Italy, Fondazione G. Monasterio
Authors: Giovannetti, G. (Ekstern), Frijia, F. (Ekstern), Hartwig, V. (Ekstern), Menichetti, L. (Ekstern), Ardenkjaer-Larsen, J. H. (Intern), Marchi, D. D. (Ekstern), Positano, V. (Ekstern), Landini, L. (Ekstern), Lombardi, M. (Ekstern), Santarelli, M. F. (Ekstern)
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Scopus rating (2016): CiteScore 2.52 SJR 0.727 SNIP 1.685
Web of Science (2016): Indexed yes
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Electrical potentials in the myoendothelial junction

General information

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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Brasen, J. C. (Intern), Holstein-Rathlou, N. (Intern)
Publication date: 2013
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Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 99452659
Publication: Research - peer-review › Poster – Annual report year: 2014

Enhancing the [13C]bicarbonate signal in cardiac hyperpolarized [1-13C]pyruvate MRS studies by infusion of glucose, insulin and potassium

A change in myocardial metabolism is a known effect of several diseases. MRS with hyperpolarized 13C-labelled pyruvate is a technique capable of detecting changes in myocardial pyruvate metabolism, and has proven to be useful for the evaluation of myocardial ischaemia in vivo. However, during fasting, the myocardial glucose oxidation is low and the fatty acid oxidation (β-oxidation) is high, which complicates the interpretation of pyruvate metabolism with the technique. The aim of this study was to investigate whether the infusion of glucose, insulin and potassium (GIK) could increase the myocardial glucose oxidation in the citric acid cycle, reflected as an increase in the [13C]bicarbonate signal in cardiac hyperpolarized [1-13C]pyruvate MRS measurements in fasted rats. Two groups of rats were infused with two different doses of GIK and investigated by MRS after injection of hyperpolarized [1-13C]pyruvate. No [13C]bicarbonate signal could be detected in the fasted state. However, a significant increase in the [13C]bicarbonate signal was observed by the infusion of a high dose of GIK. This study demonstrates that a high [13C]bicarbonate signal can be achieved by GIK infusion in fasted rats. The increased [13C]bicarbonate signal indicates an increased flux of pyruvate through the pyruvate dehydrogenase enzyme complex and an increase in myocardial glucose oxidation through the citric acid cycle. Copyright © 2013 John Wiley & Sons, Ltd.

General information
EPR oxygen imaging and hyperpolarized (13) C MRI of pyruvate metabolism as noninvasive biomarkers of tumor treatment response to a glycolysis inhibitor 3-bromopyruvate.

The hypoxic nature of tumors results in treatment resistance and poor prognosis. To spare limited oxygen for more crucial pathways, hypoxic cancerous cells suppress mitochondrial oxidative phosphorylation and promote glycolysis for energy production. Thereby, inhibition of glycolysis has the potential to overcome treatment resistance of hypoxic tumors. Here, EPR imaging was used to evaluate oxygen dependent efficacy on hypoxia-sensitive drug. The small molecule 3-bromopyruvate blocks glycolysis pathway by inhibiting hypoxia inducible enzymes and enhanced cytotoxicity of 3-bromopyruvate under hypoxic conditions has been reported in vitro. However, the efficacy of 3-bromopyruvate was substantially attenuated in hypoxic tumor regions (pO(2) < 10 mmHg) in vivo using squamous cell carcinoma (SCC VII)-bearing mouse model. Metabolic MRI studies using hyperpolarized (13) C-labeled pyruvate showed that monocarboxylate transporter-1 is the major transporter for pyruvate and the analog 3-bromopyruvate in SCC VII tumor. The discrepant results between in vitro and in vivo data were attributed to biphasic oxygen dependent expression of monocarboxylate transporter-1 in vivo. Expression of monocarboxylate transporter-1 was enhanced in moderately hypoxic (8-15 mmHg) tumor regions but down regulated in severely hypoxic (<5 mmHg) tumor regions. These results emphasize the importance of noninvasive imaging biomarkers to confirm the action of hypoxia-activated drugs.
Experimental and Theoretical Investigation of Signaling in Quorum Sensing of Pseudomonas Aeruginosa

Quorum sensing (QS) is an intercellular communication system by which some bacterial cells are capable of indirectly monitoring their own population density through exchange of signal molecules. The expression of virulence factors is kept low until the population density (signal molecule concentration) reaches a threshold value, after which the host system is surprised by a stealth attack. The focus of this study is on the Quorum Sensing regulatory system of Pseudomonas aeruginosa called the Las system.

In this thesis, two distinct methods to obtain information about the system are considered. First, Surface Enhanced Raman Spectroscopy (SERS) is applied to the signal molecule known as N-dodecanoyl-L-homoserine lactone. To the best of our knowledge we here for the first time demonstrate SERS to detect a QS signal molecule below 1 nM concentration in both ultrapure water and under physiological conditions. Based on our results, SERS shows promise as a highly suitable tool for in situ measurements of low Acyl-Homoserine Lactone (AHL) concentrations in biofilms containing QS bacteria. Secondly, a conventional fluorescent monitor system is used to follow the response to signal molecules. A kinetic model is applied in order to extract knowledge about the interaction between signal molecule and regulator. In the model, the regulator monomer is decaying rapidly due to proteases while all dimerized regulators are protected against proteases. Moreover, the LasR regulator can fold into its stable dimer conformation in the absence of its cognate signal. In the presence of signal the dimer is activated through cooperative binding of the two signal molecules.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Claussen, A. (Intern), Givskov, M. C. (Intern), Sams, T. (Intern)
Number of pages: 120
Fast simulation of non-linear pulsed ultrasound fields using an angular spectrum approach

A fast non-linear pulsed ultrasound field simulation is presented. It is implemented based on an angular spectrum approach (ASA), which analytically solves the non-linear wave equation. The ASA solution to the Westervelt equation is derived in detail. The calculation speed is significantly increased compared to a numerical solution using an operator splitting method (OSM). The ASA has been modified and extended to pulsed non-linear ultrasound fields in combination with Field II, where any array transducer with arbitrary geometry, excitation, focusing and apodization can be simulated. The accuracy of the nonlinear ASA is compared to the non-linear simulation program – Abersim, which is a numerical solution to the Burgers equation based on the OSM. Simulations are performed for a linear array transducer with 64 active elements, focus at 40 mm, and excitation by a 2-cycle sine wave with a center frequency of 5 MHz. The speed is increased approximately by a factor of 140 and the calculation time is 12 min with a standard PC, when simulating the second harmonic pulse at the focal point. For the second harmonic point spread function the full width error is 1.5% at 6 dB and 6.4% at 12 dB compared to Abersim.
Field dependence of T1 for hyperpolarized [1-13C]pyruvate

In vivo metabolism of hyperpolarized pyruvate has been demonstrated to be an important probe of cellular glycolysis in diseases such as cancer. The usefulness of hyperpolarized 13C imaging is dependent on the relaxation rates of the 13C-enriched substrates, which in turn depend on chemical conformation and properties of the dissolution media such as buffer composition, solution pH, temperature and magnetic field. We have measured the magnetic field dependence of the spin–lattice relaxation time of hyperpolarized [1-13C]pyruvate using field-cycled relaxometry. [1-13C]pyruvate was hyperpolarized using dynamic nuclear polarization and then rapidly thawed and dissolved in a buffered solution to a concentration of 80 mmol l\(^{-1}\) and a pH of ~7.8. The hyperpolarized liquid was transferred within 8 s to a fast field-cycling relaxometer with a probe tuned for detection of 13C at a field strength of ~0.75 T. The magnetic field of the relaxometer was rapidly varied between relaxation and acquisition fields where the sample magnetization was periodically measured using a small flip angle. Data were recorded for relaxation fields varying between 0.237 mT and 0.705 T to map the T1 dispersion of the C-1 of pyruvate. Using similar methods, we also determined the relaxivity of the triarylmethyl radical (OX063; used for dynamic nuclear polarization) on the C-1 of pyruvate at field strengths of 0.001, 0.01, 0.1 and 0.5 T using 0.075, 1.0 and 2.0 mmol l\(^{-1}\) concentrations of OX063 in the hyperpolarized pyruvate solution.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Chattergoon, N. (Ekstern), Martnez-Santiesteban, F. (Ekstern), Handler, W. B. (Ekstern), Ardenkjær-Larsen, J. H. (Intern), Scholl, T. J. (Ekstern)
Pages: 57-62
Publication date: 2013
Main Research Area: Technical/natural sciences
Formulation and utilization of choline based samples for dissolution dynamic nuclear polarization

Hyperpolarization by the dissolution dynamic nuclear polarization (DNP) technique permits the generation of high spin polarization of solution state. However, sample formulation for dissolution-DNP is often difficult, as concentration and viscosity must be optimized to yield a dissolved sample with sufficient concentration, while maintaining polarization during the dissolution process. The unique chemical properties of choline permit the generation of highly soluble salts as well as deep eutectic mixtures with carboxylic acids and urea. We describe the formulation of these samples and compare their performance to more traditional sample formulations. Choline yields stable samples with exceptional polarization performance while simultaneously offering the capability to easily remove the choline after dissolution, perform experiments with the hyperpolarized choline, or anything in between.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Bowen, S. (Intern), Ardenkjær-Larsen, J. H. (Intern)
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Scopus rating (2015): SJR 1.111 SNIP 1.07 CiteScore 2.88
Heart rhythm analysis using ECG recorded with a novel sternum based patch technology

According to the World Health Organization, cardiovascular diseases are the number one cause of death globally. Early diagnosis and treatment of many of these patients depend on ambulatory electrocardiography recordings. Therefore a novel wireless patch technology has been designed for easy, reliable long-term ECG recordings. The device is designed for high compliance and low patient burden. This novel patch technology is CE approved for ambulatory ECG recording of two ECG channels on the sternum. This paper describes a clinical pilot study regarding the usefulness of these ECG signals for heart rhythm analysis. A clinical technician with experience in ECG interpretation selected 200 noise-free 7 seconds ECG segments from 25 different patients. These 200 ECG segments were evaluated by two medical doctors according to their usefulness for heart rhythm analysis. The first doctor considered 98.5% of the segments useful for rhythm analysis, whereas the second doctor considered 99.5% of the segments useful for rhythm analysis. The conclusion of this pilot study indicates that two channel ECG recorded on the sternum is useful for rhythm analysis and could be used as input to diagnosis together with other clinical tests and medical history.

General information
State: Published
High frame rate synthetic aperture duplex imaging

Conventional color flow images are limited in velocity range and can either show the high velocities in systole or be optimized for the lower diastolic velocities. The full dynamics of the flow is, thus, hard to visualize. The dynamic range can be significantly increased by employing synthetic aperture flow imaging as demonstrated in this paper. Synthetic aperture, directional beamforming, and cross-correlation are used to produce B-mode and vector velocity images at high frame rates. The frame rate equals the effective pulse repetition frequency of each imaging mode. Emissions for making the B-mode images and velocity maps are interleaved in a 1-to-1 ratio. This provides continuous data allowing a wide range of velocities to be estimated. Two cases are considered in the flow estimation: In the first case, the angle of the flow is determined from the B-mode image. In the other case, the angle is determined by estimating the flow velocity in all directions and choosing the one with the strongest correlation. The method works for all angles, including fully axial and fully transverse flows. Field II simulations with a 192 element, 7 MHz linear array are made of laminar, transverse flow profiles. For a simulated peak velocity of 0.5 m/s, the relative bias is −6.8% and the relative standard deviation is 6.1%. The bias on the angle is 0.98 degrees with a standard deviation of 2.39 degrees when using the flow estimator to determine the angle. For a peak velocity of 0.05 m/s, the relative bias of the velocity estimation is −1.8% and the relative standard deviation 5.4%. The approach can thus estimate both high and low velocities with equal accuracy and thereby makes it possible to present vector flow images with a high dynamic range. Measurements are made using the SARUS research scanner, a linear array transducer similar to the simulated one, and a recirculating flow rig with a blood mimicking fluid and a parabolic flow profile with a peak velocity of approximately 0.3 m/s. The relative bias of the velocity estimation is 0.19% and the mean relative standard deviation 4.9%. For the direction estimation, the bias is 3.2 degrees with a standard deviation of 1.6 degrees.
In-situ identification of marine organisms using high frequency, wideband ultrasound

Reliable remote fish identification would be an important improvement in resource management as well as in commercial fishing. Optical and acoustical methods could be used either in combination or separately. However, the acoustical methods have better detection ranges than any known optical methods. Conventional acoustical methods use frequencies in the range of 10 to 500 kHz and give reasonable estimations of size distribution, if the species is known, but can only significantly support the determination of the actual species, if there are only a few known species available. It is expected that higher frequencies and broader bandwidths than used until now will give more information useful for fish species identification.

The objective of this Ph.D. study has been to develop a method to investigate the possibility of in-situ identification of fish with high-frequency, wideband ultrasound. The approach was to build a 1 MHz wideband single-element transducer system to obtain range profiles of fish, and to do fish species identification by comparing measured range profiles with libraries of reference range profiles as it is done in some radar systems used to identify aircraft. To do this, it is also necessary to investigate the properties of ultrasound backscatter of fish in the MHz frequency range to help the interpretation of the range profiles. Three case studies were investigated in this Ph.D. study.

The first case study was to investigate the ultrasound backscatter of fish in the MHz frequency range using empirical methods. Measurements using a BK Medical ultrasound scanner equipped with a dedicated research interface were performed on a saithe (Pollachius virens) and three cods (Gadus morhua) at different frequencies as well as angles between the center line of the transducer beams and the fish bodies. The frequencies are 2, 3.5, and 6 MHz. The angles are -30°, -15°, 0°, 15°, and 30°. The results show that even though there are variations, a scan of the ultrasound backscatter along a fish of a specific species contains patterns that are characteristic for that species. This is true at all frequencies in the low MHz range. The part of a fish that contributes most is not necessarily the swimbladder as the results indicate that in the low MHz frequency range bone structures, and skin surfaces are more important.

The second case study was to develop a method to generate simulated ultrasound images from computed tomography images to build simulated ultrasound range profiles of fish. It can be observed from the first case study that shadow effects are normally pronounced in ultrasound images, so they should be included in the simulation. In this study, a method to capture the shadow effects has been developed, which makes the simulated ultrasound images appear more realistic. The method using a focused beam tracing model gives diffuse shadows that are similar to the ones observed in measurements on real objects.

The last case study was to do measurements of ultrasound range profiles of free-swimming fish using a 1 MHz wideband single-element transducer system. The portable system consists of a Reson TC3210 1 MHz single-element transducer, a BlueView P900-2250 dual-frequency multi-beam sonar, and three Oregon ATC9K cameras on a fixture. The positions, orientations, and lengths of the fish were estimated by three-dimensional image analysis, while species were identified manually from the video sequences. Ex-situ experiments were performed on fish that have swimbladder (cod, European sea bass (Dicentrarchus labrax), gilthead sea bream (Sparus aurata), and Atlantic horse mackerel (Trachurus trachurus)) as well as on fish that do not have swimbladder (Atlantic mackerel (Scomber scombrus)). There are indications that the variations in the range profiles seem to have some unique details to discriminate between species like mackerel and sea bream. In some cases the range profiles also indicate whether the head or the tail is closest to the transducer. It has also been shown that the surface areas of the fish are the most important elements that decide how much energy is backscattered in the low MHz frequency range.

In conclusion, the ultrasound backscatter from fish in the MHz frequency range was investigated empirically as well as by simulation and the 1 MHz wideband single-element transducer system was developed. The results data from the ex-situ experiments in a large aquarium tank presented in the last case study can be considered comparable to data obtained in in-situ experiments in a calm shallow sea area. The single-element transducer system can therefore be considered ready for preliminary in-situ experiments. Hereby the main objectives of the Ph.D. study have been reached.

General information
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Organisations: National Institute of Aquatic Resources, Department of Electrical Engineering, Section for Ecosystem Imaging, Marine Management, Section for Marine Living Resources, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Pham, A. H. (Intern), Lundgren, B. (Intern), Stage, B. (Intern), Jensen, J. A. (Intern)
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Internal strain estimation for quantification of human heel pad elastic modulus: A phantom study
Shock absorption is the most important function of the human heel pad. However, changes in heel pad elasticity, as seen in e.g. long-distance runners, diabetes patients, and victims of Falanga torture are affecting this function, often in a painful manner. Assessment of heel pad elasticity is usually based on one or a few strain measurements obtained by an external load-deformation system. The aim of this study was to develop a technique for quantitative measurements of heel pad elastic modulus based on several internal strain measures from within the heel pad by use of ultrasound images. Nine heel phantoms were manufactured featuring a combination of three heel pad stiffnesses and three heel pad thicknesses to model the normal human variation. Each phantom was tested in an indentation system comprising a 7MHz linear array ultrasound transducer, working as the indentor, and a connected load cell. Load-compression data and ultrasound B-mode images were simultaneously acquired in 19 compression steps of 0.1mm each. The internal tissue displacement was for each step calculated by a phase-based cross-correlation technique and internal strain maps were derived from these displacement maps. Elastic moduli were found from the resulting stress–strain curves. The elastic moduli made it possible to distinguish eight of nine phantoms from each other according to the manufactured stiffness and showed very little dependence of the thickness. Mean elastic moduli for the three soft, the three medium, and the three hard phantoms were 89kPa, 153kPa, and 168kPa, respectively. The combination of ultrasound images and force measurements provided an effective way of assessing the elastic properties of the heel pad due to the internal strain estimation.

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Scopus rating (2016): CiteScore 2.51 SJR 0.834 SNIP 1.728
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Scopus rating (2015): SJR 0.708 SNIP 1.655 CiteScore 2.23
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Scopus rating (2014): SJR 0.848 SNIP 2.156 CiteScore 2.41
Web of Science (2014): Indexed yes
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Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.675 SNIP 1.886 CiteScore 2.09
ISI indexed (2012): ISI indexed yes
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Scopus rating (2011): SJR 0.707 SNIP 1.72 CiteScore 2.2
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Inter-operator Variability in Defining Uterine Position Using Three-dimensional Ultrasound Imaging

In radiotherapy the treatment outcome of gynecological (GYN) cancer patients is crucially related to reproducibility of the actual uterine position. The purpose of this study is to evaluate the inter-operator variability in addressing uterine position using a novel 3-D ultrasound (US) system. The study is initiated by US-scanning of a uterine phantom (CIRS 404, Universal Medical, Norwood, USA) by seven experienced US operators. The phantom represents a female pelvic region, containing a uterus, bladder and rectal landmarks readily definable in the acquired US-scans. The organs are subjected to displacement by applied operator-pressure that mimics an actual GYN patient. The transabdominal scanning was performed using a 3D-US system (Clarity® Model 310C00, Elekta, Montreal, Canada). It consists of a US acquisition-station, workstation, and a 128- element 1D array curved probe. The iterated US-scans were performed in four subsequent sessions (totally 21 US-scans) in a period of four weeks to investigate the randomness of the inter-operator variability. An additionally US-scan was performed as a reference target volume to the consecutive scans. At first, the phantom was marked with ball bearings for daily laser alignment. In each session the US-scans were acquired by the seven operators. The uterus was outlined in each of the US imagesets using Clarity autosegmentation in the workstation. Further, the shifts in the uterine centre of mass relative to the reference were measured for the three orthogonal directions; left (+)-right (LR), anterior (+)-posterior (AP), and inferior (+)-superior (IS), respectively. The same operator delineated the target volumes. The average inter-operator deviation ±1SD of the daily US scans was (in mm); LR: day 1 (-0.4±0.9), day 2 (-0.3±0.6), day 3 (-1.0±1.2), day 4 (1.3±0.5); AP: day 1 (0.0±1.7), day 2 (0.1±0.7), day 3 (-1.0±0.9), day 4 (0.2±1.2); IS: day 1 (-1.5±2.6), day 2 (0.1±1.8), day 3 (0.1±1.1), day 4 (0.5±3.1), respectively. The largest inter-operator discordance was observed to be 4.7 mm in the IS-direction in day 4. Published studies report significantly larger inter-fractional uterine positional displacement, in some cases up to 20 mm, which outweighs the magnitude of current inter-operator variations. Thus, the current US-phantom-study suggests that the inter-operator variability in addressing uterine position is clinically irrelevant.
Intraoperative Cardiac Ultrasound Examination Using Vector Flow Imaging

Conventional ultrasound (US) methods for blood velocity estimation only provide onedimensional and angle-dependent velocity estimates; thus, the complexity of cardiac flow has been difficult to measure. To circumvent these limitations, the Transverse Oscillation (TO) vector flow method has been proposed. The vector flow method implemented on a Commercial scanner provided real-time, angle-independent estimates of cardiac blood flow. Epicardiac and epiaortic, intraoperative US examinations were performed on three patients with stenosed coronary arteries scheduled for bypass surgery. Repeating cyclic beat-to-beat flow patterns were seen in the ascending aorta and pulmonary artery of each patient, but these patterns varied between patients. Early systolic retrograde flow filling the aortic sinuses was seen in the ascending aorta as well as early systolic retrograde flow in the pulmonary artery. In diastole, stable vortices in aortic sinuses of the ascending aorta created central antegrade flow. A stable vortex in the right atrium was seen during the entire heart cycle. The measurements were compared with estimates obtained intraoperatively with conventional spectral Doppler US using a transesophageal and an epiaortic approach. Mean differences in peak systole velocity of 11% and 26% were observed when TO was compared with transesophageal echocardiography and epiaortic US, respectively. In one patient, the cardiac output derived from vector velocities was compared with pulmonary artery catheter thermodilution technique and showed a difference of 16%. Vector flow provides real-time, angle-independent vector velocities of cardiac blood flow. The technique can potentially reveal new information of cardiovascular physiology and give insight into blood flow dynamics.
Intraoperative Vector Flow Imaging of the Heart

The cardiac flow is complex and multidirectional, and difficult to measure with conventional Doppler ultrasound (US) methods due to the one-dimensional and angle-dependent velocity estimation. The vector velocity method Transverse Oscillation (TO) has been proposed as a solution to this. TO is implemented on a conventional US scanner (Pro Focus 2202 UltraView, BK Medical) using a linear transducer (8670, BK Medical) and can provide real-time, angle-independent vector velocity estimates of the cardiac blood flow. During cardiac surgery, epicardic US examinations using TO were performed on three patients. Antegrade central jet and retrograde flow near the vessel wall in the ascending aorta and the pulmonary artery were seen during systole, while stable vortices were seen in the aortic sinuses and complex flow patterns were seen around the valves during diastole. In the right atrium, a stable vortex was seen during the entire heart cycle. For comparison, simultaneous Measurements were obtained with conventional spectral Doppler (SD) and intravenous catheter thermodilution technique (TD). Peak systolic velocities were underestimated by 18% compared to SD and cardiac output was underestimated by 16% compared to TD. This is the first time TO measurements have been obtained of cardiac flow. TO can potentially reveal new information of cardiovascular physiology and blood flow dynamics, and become a valuable tool in cardiology.

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Investigation of an angular spectrum approach for pulsed ultrasound fields

An Angular Spectrum Approach (ASA) is formulated and employed to simulate linear pulsed ultrasound fields for high bandwidth signals. A geometrically focused piston transducer is used as the acoustic source. Signals are cross-correlated to find the true sound speed during the measurement to make the simulated and measured pulses in phase for comparisons. The calculated sound speed in the measurement is varied between 1487.45 m/s and 1487.75 m/s by using different initial values in the ASA simulation. Results from the pulsed ASA simulation using both Field II simulated and hydrophone measured acoustic sources are compared to the Field II simulated and hydrophone measured pulses, respectively. The total relative root mean square (RMS) errors of the pulsed ASA are investigated by using different time-point, zero-padding factors, spatial sampling interval and temporal sampling frequency in the simulation. Optimal parameters for the ASA are found in the simulation. The RMS error of the ASA simulation is reduced from 10.9% to 2.4% for the optimal parameters when comparing to Field II simulation. The comparison between the ASA calculated and measured pulses are illustrated and the corresponding RMS error is 25.4%.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps
Authors: Du, Y. (Intern), Jensen, H. (Ekstern), Jensen, J. A. (Intern)
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BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.675 SNIP 1.886 CiteScore 2.09
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Investigations on the visco-elastic behaviour of a human healthy heel pad: in vivo compression tests and numerical analysis

The aim of this study was to investigate the viscoelastic behaviour of the human heel pad by comparing the stress–relaxation curves obtained from a compression device used on an in vivo heel pad with those obtained from a three-dimensional computer-based subject-specific heel pad model subjected to external compression. The three-dimensional model was based on the anatomy revealed by magnetic resonance imaging of a 31-year-old healthy female. The calcaneal fat pad tissue was described with a viscohyperelastic model, while a fibre-reinforced hyperelastic model was formulated for the skin. All numerical analyses were performed to interpret the mechanical response of heel tissues, with loading conditions and displacement rate in agreement with experimental tests. The heel tissues showed a non-linear, viscoelastic behaviour described by characteristic hysteretic curves, stress–relaxation and viscous recovery phenomena. The reliability of the investigations was validated by the interpretation of the mechanical response of heel tissues under the application of three pistons with diameter of 15, 20 and 40 mm, at the same displacement rate of about 1.7 mm/s. The maximum and minimum relative errors were found to be less than 0.95 and 0.064, respectively.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Padua, University of Florence, Technical University of Denmark
Authors: Matteoli, S. (Intern), Fontanella, C. G. (Ekstern), Carniel, E. L. (Ekstern), Wilhjelm, J. E. (Intern), Virga, A. (Ekstern), Corbin, N. (Ekstern), Corvi, A. (Ekstern), Natali, A. N. (Ekstern)
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In Vivo Three-Dimensional Velocity Vector Imaging and Volumetric Flow Rate Measurements

The three-dimensional (3-D) Transverse Oscillation (TO) method is used to obtain 3-D velocity vector estimates in two orthogonal planes. The method is suitable for a real-time implementation. Data are acquired using a Vermon 3.0 MHz 32x32 element 2-D phased array and the experimental ultrasound scanner SARUS. Measurements are conducted on a carotid artery flow phantom from Danish Phantom Design, and 20 frames are acquired with a constant flow rate of 16.7±0.17 mL/s provided by a Shelley Medical Imaging Technologies CompuFlow 1000 system. The peak velocity magnitude in the vessel is found to be 52.3±8.1 m/s compared to an expected peak velocity of 53.6±0.54 cm/s. Based on the out-of-plane velocity component in the crosssectional plane, the estimated volumetric flow rates are 17.1±1.4 mL/s. The coefficient of variation is 8.3%, and the bias is 2.2%. An in vivo measurement of 3-D M-mode velocities is conducted over five heart beats. The peak systolic and end-diastolic velocities are 69±5.4 cm/s and 7.9±5.5 cm/s at the center of the vessel. For comparison, a commercial BK Medical ultrasound scanner using the spectral estimator yields 71.2 cm/s and
7.70 cm/s, respectively. The results demonstrate that the 3-D TO method can estimate 3-D velocities in two crossed planes, volumetric flow rates, and 3-D velocities in vivo.

**Kinetic Model for Signal Binding to the Quorum Sensing Regulator LasR**

We propose a kinetic model for the activation of the las regulon in the opportunistic pathogen Pseudomonas aeruginosa. The model is based on in vitro data and accounts for the LasR dimerization and consecutive activation by binding of two OdDHL signal molecules. Experimentally, the production of the active LasR quorum-sensing regulator was studied in an Escherichia coli background as a function of signal molecule concentration. The functional activity of the regulator was monitored via a GFP reporter fusion to lasB expressed from the native lasB promoter. The new data shows that the active form of the LasR dimer binds two signal molecules cooperatively and that the timescale for reaching saturation is independent of the signal molecule concentration. This favors a picture where the dimerized regulator is protected against proteases and remains protected as it is activated through binding of two successive signal molecules. In absence of signal molecules, the dimerized regulator can dissociate and degrade through proteolytic turnover of the monomer. This resolves the apparent contradiction between our data and recent reports that the fully protected dimer is able to “degrade” when the induction of LasR ceases.
Ligand Binding Kinetics of the Quorum Sensing Regulator PqsR

The Pseudomonas aeruginosa quinolone signal (PQS) is a quorum sensing molecule that plays an important role in regulating the virulence of this organism. We have purified the ligand binding domain of the receptor PqsRLBD for PQS and have used Förster resonance energy transfer fluorimetry and kinetic modeling to characterize the ligand binding in vitro. The dissociation constant for binding of PQS to a ligand binding site in (PqsRLBD)2 dimers was determined to be 1.2 ± 0.3 μM. We found no cooperativity in the consecutive binding of two ligand molecules to the dimer.
Magnetic resonance butterfly coils: Design and application for hyperpolarized 13C studies

Hyperpolarized 13C magnetic resonance spectroscopy in pig models enables cardiac metabolism assessment and provides a powerful tool for heart physiology studies, although the low molar concentration of derived metabolites gives rise to technological limitations in terms of data quality. The design of dedicated coils capable of providing large field of view with high Signal-to-Noise Ratio (SNR) data is of fundamental importance. This work presents magnetostatic simulations and tests of two butterfly coils with different geometries, both designed for 13C hyperpolarized studies of pig heart with a clinical 3T scanner. In particular, the paper provides details of the design, modeling, construction and application of the butterfly style coils. While both coils could be successfully employed in single configuration (linear mode), the second prototype was used to design a quadrature surface coil constituted by the butterfly and a circular loop both in receive (RX) mode while using a birdcage coil as transmitter (TX). The performance of this coils configuration was compared with the single TX/RX birdcage coil, in order to verify the advantage of the proposed configuration over the volume coil throughout the volume of interest for cardiac imaging in pig. Experimental SNR-vs-depth profiles, extracted from the [1-13C]acetate phantom chemical shift image (CSI), permitted to highlight the performance of the proposed coils configuration. © 2013 Elsevier Ltd. All rights reserved.
Magnetic resonance imaging of tumor oxygenation and metabolic profile

The tumor microenvironment is distinct from normal tissue as a result of abnormal vascular network characterized by hypoxia, low pH, high interstitial fluid pressure and elevated glycolytic activity. This poses a barrier to treatments including radiation therapy and chemotherapy. Imaging methods which can characterize such features non-invasively and repeatedly will be of significant value in planning treatment as well as monitoring response to treatment. The three techniques based on magnetic resonance imaging (MRI) are reviewed here. Tumor pO2 can be measured by two MRI methods requiring an exogenous contrast agent: electron paramagnetic resonance imaging (EPRI) and Overhauser magnetic resonance imaging (OMRI). Tumor metabolic profile can be assessed by a third method, hyperpolarized metabolic MR, based on injection of hyperpolarized biological molecules labeled with 13C or 15N and MR spectroscopic imaging. Imaging pO2 in tumors is now a robust pre-clinical imaging modality with potential for implementation clinically. Pre-clinical studies and an initial clinical study with hyperpolarized metabolic MR have been successful and suggest that the method may be part of image-guided radiotherapy to select patients for tailored individual treatment regimens.
Metabolic imaging of patients with prostate cancer using hyperpolarized \([1-\text{^13C}]\)pyruvate.

This first-in-man imaging study evaluated the safety and feasibility of hyperpolarized \([1-\text{^13C}]\)pyruvate as an agent for noninvasively characterizing alterations in tumor metabolism for patients with prostate cancer. Imaging living systems with hyperpolarized agents can result in more than 10,000-fold enhancement in signal relative to conventional magnetic resonance (MR) imaging. When combined with the rapid acquisition of in vivo \(^{13}\)C MR data, it is possible to evaluate the distribution of agents such as \([1-\text{^13C}]\)pyruvate and its metabolic products lactate, alanine, and bicarbonate in a matter of seconds. Preclinical studies in cancer models have detected elevated levels of hyperpolarized \([1-\text{^13C}]\)lactate in tumor, with the ratio of \([1-\text{^13C}]\)lactate/\([1-\text{^13C}]\)pyruvate being increased in high-grade tumors and decreased after successful treatment. Translation of this technology into humans was achieved by modifying the instrument that generates the hyperpolarized agent, constructing specialized radio frequency coils to detect \(^{13}\)C nuclei, and developing new pulse sequences to efficiently capture the signal. The study population comprised patients with biopsy-proven prostate cancer, with 31 subjects being injected with hyperpolarized \([1-\text{^13C}]\)pyruvate. The median time to deliver the agent was 66 s, and uptake was observed about 20 s after injection. No dose-limiting toxicities were observed, and the highest dose (0.43 ml/kg of 230 mM agent) gave the best signal-to-noise ratio for hyperpolarized \([1-\text{^13C}]\)pyruvate. The results were extremely promising in not only confirming the safety of the agent but also showing elevated \([1-\text{^13C}]\)lactate/\([1-\text{^13C}]\)pyruvate in regions of biopsy-proven cancer. These findings will be valuable for noninvasive cancer diagnosis and treatment monitoring in future clinical trials.
Modeling and Measurements of CMUTs with Square Anisotropic Plates

The conventional method of modeling CMUTs use the isotropic plate equation to calculate the deflection, leading to deviations from FEM simulations including anisotropic effects of around 10% in center deflection. In this paper, the deflection is found for square plates using the full anisotropic plate equation and the Galerkin method. Utilizing the symmetry of the silicon crystal, a compact and accurate expression for the deflection can be obtained. The deviation from FEM in center deflection is <0.1%. The deflection was measured on fabricated CMUTs using a white light interferometer. Fitting the anisotropic calculated deflection to the measurement a deviation of 0.5-1.5% is seen for the fitted values. Finally it was also measured how the device behaved under increasing bias voltage and it is observed that the model including anisotropic effects is within the uncertainty interval of the measurements.

General information
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Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Department of Electrical Engineering, Biomedical Engineering, Silicon Microtechnology, Department of Physics, Experimental Surface and Nanomaterials, Physics, Technical University of Denmark
Authors: la Cour, M. F. (Intern), Christiansen, T. L. (Intern), Dahl-Petersen, C. (Ekstern), Reck, K. (Intern), Hansen, O. (Intern), Jensen, J. A. (Intern), Thomsen, E. V. (Intern)
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New Developments in Vector Velocity Imaging using the Transverse Oscillation Approach

Vector velocity imaging using the Transverse Oscillation (TO) approach has recently been FDA approved for linear array transducers on a commercial platform. It can now be used clinically for studying the complex flow at e.g. bifurcations, valves, and the heart in real time. Several clinical examples from venous flow to rotational flow in the heart will be shown. The technique is also being further developed and adapted for convex and phased array probes, for spectral velocity estimation, pressure estimation, and for three dimensional velocity tensor imaging. It is shown how the methods are optimized using Field II simulations along with several examples of their performance.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Jensen, J. A. (Intern), Pihl, M. J. (Intern), Olesen, J. B. (Intern), Møller Hansen, P. (Ekstern), Lindskov Hansen, K. (Ekstern), Bachmann Nielsen, M. (Ekstern)
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Non-invasive Measurement of Pressure Gradients in Pulsatile Flow using Ultrasound

This paper demonstrates how pressure gradients in a pulsatile flow environment can be measured non-invasively using ultrasound. The proposed method relies on vector velocity fields acquired from ultrasound data. 2-D flow data are acquired at 18-23 frames/sec using the Transverse Oscillation approach. Pressure gradients are calculated from the measured velocity fields using the Navier-Stokes equation. Velocity fields are measured during constant and pulsating flow on a carotid bifurcation phantom and on a common carotid artery in-vivo. Scanning is performed with a 5 MHz BK8670 linear transducer using a BK Medical 2202 UltraView Pro Focus scanner. The calculated pressure gradients are validated through a finite element simulation of the constant flow model. The geometry of the flow simulation model is reproduced using MRI data, thereby providing identical flow domains in measurement and simulation. The proposed method managed to estimate pressure gradients that varied from 0 kPa/m–7 kPa/m during constant flow and from 0 kPa/m–200 kPa/m in the pulsatile flow environments. The estimator showed, in comparison to the simulation model, a bias of -9% and -8% given in reference to the peak gradient for the axial and lateral gradient component, respectively.

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Authors: Olesen, J. B. (Intern), Traberg, M. S. (Intern), Pihl, M. J. (Intern), Hansen, P. M. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Non-invasive measurement of pressure gradients using ultrasound

A non-invasive method for estimating 2-D pressure gradients from ultrasound vector velocity data is presented. The method relies on in-plane vector velocity fields acquired using the Transverse Oscillation method. The pressure gradients are estimated by applying the Navier-Stokes equations for isotropic fluids to the estimated velocity fields. The velocity fields were measured for a steady flow on a carotid bifurcation phantom (Shelley Medical, Canada) with a 70% constriction on the internal branch. Scanning was performed with a BK8670 linear transducer (BK Medical, Denmark) connected to a BK Medical 2202 UltraView Pro Focus scanner. The results are validated through finite element simulations of the carotid flow model where the geometry is determined from MR images. This proof of concept study was conducted at nine ultrasound frames per second. Estimated pressure gradients along the longitudinal direction of the constriction varied from 0 kPa/m to 10 kPa/m with a normalized bias of -9.1% for the axial component and -7.9% for the lateral component. The relative standard deviation of the estimator, given in reference to the peak gradient, was 28.4% in the axial direction and 64.5% in the lateral direction. A study made across the constriction was also conducted. This yielded magnitudes from 0 kPa/m to 7 kPa/m with a normalized bias of -5.7% and 13.9% for the axial and lateral component, respectively. The relative standard deviations of this study were 45.2% and 83.2% in the axial and lateral direction, respectively.

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Optimization of Transverse Oscillating Fields for Vector Velocity Estimation with Convex Arrays

A method for making Vector Flow Images using the transverse oscillation (TO) approach on a convex array is presented. The paper presents optimization schemes for TO fields for convex probes and evaluates their performance using Field II simulations and measurements using the SARUS experimental scanner. A 3 MHz 192 elements convex array probe (pitch 0.33 mm) is used in both simulations and measurements. An F-number of 5 is used in transmit and two 32 element wide peaks are used in receive separated by 96 elements between peaks. Parabolic velocity profiles are simulated at beam-to-flow angles from 90 to 45 degrees in steps of 15 degrees. The optimization routine changes the lateral oscillation period \(l_x\) to yield the best possible estimates based on the energy ratio between positive and negative spatial frequencies in the ultrasound field. The basic equation for \(l_x\) gives 1.14 mm at 40 mm, and 1.51 mm from the simulated point spread function. This results in a bias of 35% as \(l_x\) directly scales the estimated velocities. Optimizing the focusing yields a \(l_x\) of...
1.61 mm. The energy ratio is reduced from -12.8 dB to -20.1 dB and the spectral bandwidth from 115.1 m\(^{-1}\) to 96.5 m\(^{-1}\). \(I_x\) is maintained between 1.47 and 1.70 mm from 25 mm to 70 mm and is increased to 2.8 mm at a depth of 100 mm. Parabolic profiles are estimated using 16 missions. The optimization gives a reduction in std. from 8.5\% to 5.9\% with a reduction in bias from 35\% to 1.02\% at 90 degrees (transverse flow) at a depth of 40 mm. Measurements have been made using the SARUS experimental ultrasound scanner and a BK Medical 8820e convex array transducer. Sixty-four elements was used in transmit and 2 x 32 elements in receive for creating a color flow map image of a flow rig phantom with a laminar, parabolic flow. At 70 degrees a bias of less than 1\% was obtained.

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**PHAISTOS: A framework for Markov chain Monte Carlo simulation and inference of protein structure**

We present a new software framework for Markov chain Monte Carlo sampling for simulation, prediction, and inference of protein structure. The software package contains implementations of recent advances in Monte Carlo methodology, such as efficient local updates and sampling from probabilistic models of local protein structure. These models form a probabilistic alternative to the widely used fragment and rotamer libraries. Combined with an easily extendible software architecture, this makes PHAISTOS well suited for Bayesian inference of protein structure from sequence and/or experimental data. Currently, two force-fields are available within the framework: PROFASI and OPLS-AA/L, the latter including the generalized Born surface area solvent model. A flexible command-line and configuration-file interface allows users quickly to set up simulations with the desired configuration. PHAISTOS is released under the GNU General Public License v3.0. Source code and documentation are freely available from http://phaistos.sourceforge.net. The software is implemented in C++ and has been tested on Linux and OSX platforms. © 2013 Wiley Periodicals, Inc.

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Preliminary examples of 3D vector flow imaging

This paper presents 3D vector flow images obtained using the 3D Transverse Oscillation (TO) method. The method employs a 2D transducer and estimates the three velocity components simultaneously, which is important for visualizing complex flow patterns. Data are acquired using the experimental ultrasound scanner SARUS on a flow rig system with steady flow. The vessel of the flow-rig is centered at a depth of 30 mm, and the flow has an expected 2D circular-symmetric parabolic profile with a peak velocity of 1 m/s. Ten frames of 3D vector flow images are acquired in a cross-sectional plane orthogonal to the center axis of the vessel, which coincides with the y-axis and the flow direction. Hence, only out-of-plane motion is expected. This motion cannot be measured by typical commercial scanners employing 1D arrays. Each frame consists of 16 flow lines steered from -15 to 15 degrees in steps of 2 degrees in the ZX-plane. For the center line, 3200 M-mode lines are acquired yielding 100 velocity profiles. At the center of the vessel, the mean and standard deviation of the estimated velocity vectors are \( (v_x, v_y, v_z) = (0.026, 0.88, 0.84) \) cm/s compared to the expected \( (0.0, 0.0, 0.0) \) cm/s. Relative to the velocity magnitude this yields standard deviations of \( (9.1, 6.4, 0.88) \) %. Volumetric flow rates were estimated for all ten frames yielding 57.9 \pm 2.0 mL/s in comparison with 56.2 mL/s measured by a commercial magnetic flow meter. One frame of the obtained 3D vector flow data was presented and visualized using three alternative approaches. Practically no in-plane motion \( (v_x \text{ and } v_z) \) is measured, whereas the out-of-plane motion \( (v_y) \) and the velocity magnitude exhibit the expected 2D circular-symmetric parabolic shape. It shown that the ultrasound method is
suitable for real-time data acquisition as opposed to magnetic resonance imaging (MRI). The results demonstrate that the 3D TO method is capable of performing 3D vector flow imaging.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Pihl, M. J. (Intern), Stuart, M. B. (Intern), Tomov, B. G. (Intern), Hansen, J. M. (Intern), Rasmussen, M. F. (Intern), Jensen, J. A. (Intern)
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**Preliminary study of synthetic aperture tissue harmonic imaging on in-vivo data**

A method for synthetic aperture tissue harmonic imaging is investigated. It combines synthetic aperture sequential beamforming (SASB) with tissue harmonic imaging (THI) to produce an increased and more uniform spatial resolution and improved side lobe reduction compared to conventional B-mode imaging. Synthetic aperture sequential beamforming tissue harmonic imaging (SASB-THI) was implemented on a commercially available BK 2202 Pro Focus UltraView ultrasound system and compared to dynamic receive focused tissue harmonic imaging (DRF-THI) in clinical scans. The scan sequence that was implemented on the UltraView system acquires both SASB-THI and DRF-THI simultaneously. Twenty-four simultaneously acquired video sequences of in-vivo abdominal SASB-THI and DRF-THI scans on 3 volunteers of 4 different sections of liver and kidney tissues were created. Videos of the in-vivo scans were presented in double blinded studies to two radiologists for image quality performance scoring. Limitations to the systems transmit stage prevented user defined transmit apodization to be applied. Field II simulations showed that side lobes in SASB could be improved by using Hanning transmit apodization. Results from the image quality study show, that in the current configuration on the UltraView system, where no transmit apodization was applied, SASB-THI and DRF-THI produced equally good images. It is expected that given the use of transmit apodization, SASB-THI could be further improved.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Rasmussen, J. H. (Intern), Hemmsen, M. C. (Intern), Sloth Madsen, S. (Ekstern), Møller Hansen, P. (Ekstern), Bachmann Nielsen, M. (Ekstern), Jensen, J. A. (Intern)
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Real Time Deconvolution of In-Vivo Ultrasound Images

The axial resolution in medical ultrasound is directly linked to the emitted ultrasound frequency, which, due to tissue attenuation, is selected based on the depth of scanning. The resolution is determined by the transducers impulse response, which limits the attainable resolution to be between one and two wavelengths. This can be improved by deconvolution, which increase the bandwidth and equalizes the phase to increase resolution under the constraint of the electronic noise in the received signal. A fixed interval Kalman filter based deconvolution routine written in C is employed. It uses a state based model for the ultrasound pulse and can include a depth varying pulse and spatially varying signal-to-noise ration. An autoregressive moving average (ARMA) model of orders 8 and 9 is used for the pulse, and the ARMA parameters are determined as a function of depth using a minimum variance algorithm using averaging over several RF lines. In vivo data from a 3 MHz mechanically rotating probe is used and the received signal is sampled at 20 MHz and 12 bits. In-vivo data acquired from a 16th week old fetus is used along with a scan from the liver and right kidney of a 27 years old male. The axial resolution has been determined from the in-vivo liver image using the auto-covariance function. From the envelope of the estimated pulse the axial resolution at Full-Width-Half-Max is 0.581 mm corresponding to 1.13 l at 3 MHz. The algorithm increases the resolution to 0.116 mm or 0.227 l corresponding to a factor of 5.1. The basic pulse can be estimated in roughly 0.176 seconds on a single CPU core on an Intel i5 CPU running at 1.8 GHz. An in-vivo image consisting of 100 lines of 1600 samples can be processed in roughly 0.1 seconds making it possible to perform real-time deconvolution on ultrasound data by using dual or quad core CPUs for frame-rates of 20-40 Hz.

Recycling and imaging of nuclear singlet hyperpolarization

The strong enhancement of NMR signals achieved by hyperpolarization decays, at best, with a time constant of a few minutes. Here, we show that a combination of long-lived singlet states, molecular design, magnetic field cycling, and specific radiofrequency pulse sequences allows repeated observation of the same batch of polarized nuclei over a period of 30 min and more. We report a recycling protocol in which the enhanced nuclear polarization achieved by dissolution-DNP is observed with full intensity and then returned to singlet order. MRI experiments may be run on a portion of the available spin polarization, while the remaining is preserved and made available for a later use. An analogy is drawn with a "spin bank" or "resealable container" in which highly polarized spin order may be deposited and retrieved. © 2013 American Chemical Society.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Southampton, Aarhus University Hospital
Pages: 5084-5088
Publication date: 2013
Main Research Area: Technical/natural sciences
Reliability and responsiveness of dynamic contrast-enhanced magnetic resonance imaging in rheumatoid arthritis

Objectives: To investigate the responsiveness to treatment and the reliability of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) in rheumatoid arthritis (RA) knee joints. Methods: DCE-MRI was performed in 12 clinically active RA knee joints before and 1, 7, 30, and 180 days after intraarticular injection with 80 mg methylprednisolone. Using semi-automated image processing software, DCE-MRI parameters, including the initial rate of enhancement (IRE) and maximal enhancement (ME), were generated for three regions of interest (ROIs): ‘Whole slice’, ‘Quick ROI’, and ‘Precise ROI’. The smallest detectable difference (SDD), the smallest detectable change (SDC), and intra- and inter-reader intraclass correlation coefficients (ICCs) were used to assess the reliability of DCE-MRI. Responsiveness to treatment was assessed by the standardized response mean (SRM).

Results: In all patients clinical remission of the knee was achieved at day 7. All DCE-MRI parameters decreased from day 0 to day 7. Using the Quick and Precise ROI methods, respectively, IRE decreased by 63% and 69%, ME decreased by 11% and 11%, Nvoxel decreased by 55% and 57%, and IRE Nvoxel decreased by 84% and 85%. The intra- and inter-reader ICCs were very high (0.96–1.00). The decrease in DCE-MRI parameters was larger than the SDC for all patients.

SRM was large for all parameters, ranging from –1.04 to –2.40. When the Whole slice ROI method was used, no parameters were responsive to treatment.

Conclusions: DCE-MRI analysed using semi-automatic software is a reliable and responsive tool for assessing treatment in RA knees joints. Rough manual delineation of the joint to omit enhancement artefacts is necessary.
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ISI indexed (2013): ISI indexed yes
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BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.121 SNIP 0.924 CiteScore 2.02
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.111 SNIP 0.899 CiteScore 1.92
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.121 SNIP 0.888
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.111 SNIP 1.037
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.111 SNIP 1.189
Scopus rating (2007): SJR 0.686 SNIP 1.31
Scopus rating (2006): SJR 0.365 SNIP 0.472
Scopus rating (2005): SJR 0.326 SNIP 0.617
Scopus rating (2004): SJR 0.282 SNIP 1.223
Scopus rating (2003): SJR 0.354 SNIP 1.46
Scopus rating (2002): SJR 0.387 SNIP 1.384
Scopus rating (2001): SJR 0.224 SNIP 0.352
Scopus rating (2000): SJR 0.361 SNIP 0.85
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.301 SNIP 0.867
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DOIs: 10.3109/03009742.2012.723745
Source: dtu
Source-ID: u::6970
Publication: Research - peer-review › Journal article – Annual report year: 2013

SARUS: A Synthetic Aperture Real-Time Ultrasound System
The Synthetic Aperture Real-time Ultrasound System (SARUS) for acquiring and processing synthetic aperture (SA) data for research purposes is described. The specifications and design of the system are detailed, along with its performance for SA, nonlinear, and 3-D flow estimation imaging. SARUS acquires individual channel data simultaneously for up to 1024 transducer elements for a couple of heart beats, and is capable of transmitting any kind of excitation. The 64 boards in the system house 16 transmit and 16 receive channels each, where sampled channel data can be stored in 2 GB of RAM and processed using five field-programmable gate arrays (FPGAs). The fully parametric focusing unit calculates delays and apodization values in real time in 3-D space and can produce 350 million complex samples per channel per second for full non-recursive synthetic aperture B-mode imaging at roughly 30 high-resolution images/s. Both RF element data and beamformed data can be stored in the system for later storage and processing. The stored data can be transferred in parallel using the system's sixty-four 1-Gbit Ethernet interfaces at a theoretical rate of 3.2 GB/s to a 144-core Linux cluster.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Prevas A/S, BK Medical Aps
Pages: 1838-1852
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Main Research Area: Technical/natural sciences

Publication information
Journal: I E E E Transactions on Ultrasonics, Ferroelectrics and Frequency Control
Saturation-recovery metabolic-exchange rate imaging with hyperpolarized [1-13C] pyruvate using spectral-spatial excitation

Within the last decade hyperpolarized [1-13C] pyruvate chemical-shift imaging has demonstrated impressive potential for metabolic MR imaging for a wide range of applications in oncology, cardiology, and neurology. In this work, a highly efficient pulse sequence is described for time-resolved, multislice chemical shift imaging of the injected substrate and obtained downstream metabolites. Using spectral-spatial excitation in combination with single-shot spiral data acquisition, the overall encoding is evenly distributed between excitation and signal reception, allowing the encoding of one full two-dimensional metabolite image per excitation. The signal-to-noise ratio can be flexibly adjusted and optimized using lower flip angles for the pyruvate substrate and larger ones for the downstream metabolites. Selectively adjusting the excitation of the downstream metabolites to 90° leads to a so-called “saturation-recovery” scheme with the detected signal content being determined by forward conversion of the available pyruvate. In case of repetitive excitations, the polarization is preserved using smaller flip angles for pyruvate. Metabolic exchange rates are determined spatially resolved from the metabolite images using a simplified two-site exchange model. This novel contrast is an important step toward more quantitative metabolic imaging. Goal of this work was to derive, analyze, and implement this “saturation-recovery metabolic exchange rate imaging” and demonstrate its capabilities in four rats bearing subcutaneous tumors. Magn Reson Med, 2013. © 2012 Wiley Periodicals, Inc.
Semi-supervised adaptation in ssvep-based brain-computer interface using tri-training

This paper presents a novel and computationally simple tri-training based semi-supervised steady-state visual evoked potential (SSVEP)-based brain-computer interface (BCI). It is implemented with autocorrelation-based features and a Naïve-Bayes classifier (NBC). The system uses nine characters presented on a 100 Hz CRT-monitor, three scalp electrodes for signal acquisition, a gUSB-amp for preamplification and two PCs for data-processing and stimulus control respectively. Preliminary test results of the system on nine healthy subjects, with and without tri-training, indicates that the accuracy improves as a result of tri-training.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, Copenhagen University Hospital
Authors: Bender, T. (Ekstern), Kjaer, T. W. (Ekstern), Thomsen, C. E. (Intern), Sørensen, H. B. D. (Intern), Puthusserypady, S. (Intern)
Number of pages: 4
Pages: 4279-4282
Sequential Beamforming Synthetic Aperture Imaging

Synthetic aperture sequential beamforming (SASB) is a novel technique which allows to implement synthetic aperture beamforming on a system with a restricted complexity, and without storing RF-data. The objective is to improve lateral resolution and obtain a more depth independent resolution compared to conventional ultrasound imaging. SASB is a two-stage procedure using two separate beamformers. The initial step is to construct and store a set of B-mode image lines using a single focal point in both transmit and receive. The focal points are considered virtual sources and virtual receivers making up a virtual array. The second stage applies the focused image lines from the first stage as input data, and take advantage of the virtual array in the delay and sum beamforming. The size of the virtual array is dynamically expanded and the image is dynamically focused in both transmit and receive and a range independent lateral resolution is obtained. The SASB method has been investigated using simulations in Field II and by off-line processing of data acquired with a commercial scanner. The lateral resolution increases with a decreasing F#. Grating lobes appear if F# ≥ 2 for a linear array with k-pitch. The performance of SASB with the virtual source at 20 mm and F# = 1.5 is compared with conventional dynamic receive focusing (DRF). The axial resolution is the same for the two methods. For the lateral resolution there is improvement in FWHM of at least a factor of 2 and the improvement at 40 dB is at least a factor of 3. With SASB the resolution is almost constant throughout the range. For DRF the FWHM increases almost linearly with range and the resolution at 40 dB is fluctuating with range. The theoretical potential improvement in SNR of SASB over DRF has been estimated. An improvement is attained at the entire range, and at a depth of 80 mm the improvement is 8 dB.
SLEEP phenomena as an early biomarker for Parkinsonism

Idiopathic Rapid-Eye-Movement (REM) sleep Behavior Disorder (iRBD) is one of the most potential biomarkers for Parkinson’s Disease (PD) and some atypical PD (AP). It is characterized by REM sleep with abnormal high surface EMG (sEMG) activity. Some twitching during REM sleep is normal, but no one has defined what normal is, and no well-defined methodology for measuring muscle activity in REM sleep exists. The purpose of this study is to investigate the possibility of detecting abnormal high muscle activity during REM sleep in subjects diagnosed with iRBD. This has been achieved by considering the abnormal high muscle activity during REM sleep in iRBD subjects as an outlier detection problem, while exploiting that iRBD muscle activity is more grouped. It was possible to correctly discriminate all iRBD subjects from healthy elderly control subjects and subjects diagnosed with periodic limb movement (PLM) disorder. However, not all PD subjects were classified as having abnormal muscle activity, which is assumed to support the fact that not all PD subjects develop RBD.
Spectral Velocity Estimation in the Transverse Direction

A method for estimating the velocity spectrum for a fully transverse flow at a beam-to-flow angle of 90° is described. The approach is based on the transverse oscillation (TO) method, where an oscillation across the ultrasound beam is made during receive processing. A fourth-order estimator based on the correlation of the received signal is derived. A Fourier transform of the correlation signal yields the velocity spectrum. Performing the estimation for short data segments gives the velocity spectrum as a function of time as for ordinary spectrograms, and it also works for a beam-to-flow angle of 90°. The approach is validated using Field II simulations. A 3 MHz convex array with lambda pitch is modeled. The transmit focus is at 200 mm and 2 times 32 elements are used in receive. A dual-peak Hamming apodization with a spacing of 96 elements between the peaks is used during receive beamforming for creating the lateral oscillation. Pulsatile flow in a femoral artery placed 40 mm from the transducer is simulated for one cardiac cycle using the Womersly-Evan’s flow model. The bias of the mean estimated frequency is 13.6% compared to the true velocity and the mean relative std is 14.3%. This indicates that the new estimation scheme can reliably find the spectrum at 90°, where a traditional estimator yields zero velocity. Measurements have been conducted with the SARUS experimental scanner and a BK 8820e convex array transducer (BK Medical, Herlev, Denmark). A CompuFlow 1000 (Shelley Automation, Inc, Toronto, Canada) generated the artificial femoral artery flow in the phantom. It is demonstrated that the transverse spectrum can be found from the measured data. The estimated spectra degrade when the angle is different from 90°, but are usable down to 60-70°. Below this angle the traditional spectrum is best and should be used. The conventional approach can automatically be corrected for angles from 0-70° to give a fully quantitative velocity spectrum without operator intervention.

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Authors: Jensen, J. A. (Intern)
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Electronic versions: tirsdag.pdf
DOIs: 10.1109/ULTSYM.2013.0163
Source: dtu
Source-ID: u::8113
Publication: Research - peer-review › Article in proceedings – Annual report year: 2013
Subdural to subgaleal EEG signal transmission: The role of distance, leakage and insulating affectors

Objective
To estimate the area of cortex affecting the extracranial EEG signal.

Methods
The coherence between intra- and extracranial EEG channels were evaluated on at least 10min of spontaneous, awake data from seven patients admitted for epilepsy surgery work up.

Results
Cortical electrodes showed significant extracranial coherent signals in an area of approximately 150cm² although the field of vision was probably only 31cm² based on spatial averaging of intracranial channels taking into account the influence of the craniotomy and the silastic membrane of intracranial grids. Selecting the best cortical channels, it was possible to increase the coherence values compared to the single intracranial channel with highest coherence. The coherence seemed to increase linearly with an accumulation area up to 31cm², where 50% of the maximal coherence was obtained accumulating from only 2cm² (corresponding to one channel), and 75% when accumulating from 16cm².

Conclusion
The skull is an all frequency spatial averager but dominantly high frequency signal attenuator. Significance An empirical assessment of the actual area of cerebral sources generating the extracranial EEG provides better opportunities for clinical electroencephalographers to determine the location of origin of particular patterns in the EEG.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Department of Applied Mathematics and Computer Science, Dynamical Systems, Hypo-Safe A/S, Copenhagen University Hospital, University of Copenhagen
Authors: Duun-Henriksen, J. (Intern), Kjaer, T. W. (Ekstern), Madsen, R. E. (Ekstern), Jespersen, B. (Forskerdatabase), Duun-Henriksen, A. K. (Intern), Remvig, L. S. (Ekstern), Thomsen, C. E. (Ekstern), Sørensen, H. B. D. (Intern)
Pages: 1570-1577
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Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.81 SJR 2.456 SNIP 1.783
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.367 SNIP 1.35 CiteScore 2.72
Web of Science (2015): Indexed yes
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Scopus rating (2014): SJR 0.666 SNIP 0.569 CiteScore 2.61
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.101 SNIP 1.462 CiteScore 3
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.14 SNIP 0.301 CiteScore 3.03
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Support system and method for detecting neurodegenerative disorder

The present invention relates to a system and a method for detection of abnormal motor activity during REM sleep, and further to systems and method for assisting in detecting neurodegenerative disorders such as Parkinson's. One embodiment relates to a method for detection of abnormal motor activity during REM sleep comprising the steps of: performing polysomnographic recordings of a sleeping subject, thereby obtaining one or more electromyography (EMG) derivations, preferably surface EMG recordings, and one or more EEG derivations, and/or one or more electrooculargraphy (EOG) derivations, detecting one or more REM sleep stages, preferably based on the one or more EEG and/or EOG derivations, determining the level of muscle activity during the one or more REM sleep stages based on the one or more EMG derivations, wherein a subject having an increased level of muscle activity during REM sleep compared to one or more normal subjects has abnormal motor activity during REM sleep.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Kempfner, J. (Intern), Jennum, P. J. (Ekstern), Sørensen, H. B. D. (Intern)
Publication date: 2013

Publication information
IPC: A61B5/00; A61B5/0476; A61B5/0488; A61B5/0496
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Main Research Area: Technical/natural sciences
Publication: Research › Patent – Annual report year: 2013
implement in a commercial scanner. This method can generate continuous high frame rate flow images with lower
calculation demands than the full synthetic aperture flow imaging. The performance of the approach was investigated
using Field II simulations and measurements with the experimental scanner SARUS. A laminar flow with a parabolic profile
was generated by a flow rig system. The flow data were acquired by a commercial 7 MHz linear array transducer. Four
emissions were transmitted sequentially and repeated 12 times corresponding to 48 emissions. Flow with a peak velocity
of 0.12 m/s was measured, the relative standard deviation was 6.4%, and the bias was 7.6% (2.1% and 3.2% for the
simulations). A parameter study revealed that emission spacing, number of cross-correlation functions used for averaging,
and the length of the velocity searching range influence the performance. Compared to the full synthetic aperture flow
imaging the total number of beamformed samples are reduced by a factor of 64 times, and the frame rate is much higher
than the conventional method for the same velocity estimation accuracy.
Acoustic signal processing, Array signal processing, Flow visualisation, Laminar flow, Ultrasonic measurement, Ultrasonic transducer arrays

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Source-ID: n:oai:DTIC-ART:inspec/385279054::27913
Publication: Research - peer-review › Journal article – Annual report year: 2013

Tidlig Diagnosticering af Neurodegenerative Sygdomme

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Kempfner, J. (Intern), Sørensen, H. B. D. (Intern)
Publication date: 2013

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Publisher: Technical University of Denmark (DTU)
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Main Research Area: Technical/natural sciences

Relations
Projects:
Tidlig Diagnosticering af Neurodegenerative Sygdomme
Publication: Research › Ph.D. thesis – Annual report year: 2013

Tissue Harmonic Synthetic Aperture Imaging
The main purpose of this PhD project is to develop an ultrasonic method for tissue harmonic synthetic aperture imaging. The motivation is to advance the field of synthetic aperture imaging in ultrasound, which has shown great potentials in the clinic. Suggestions for synthetic aperture tissue harmonic techniques have been made, but none of these methods have so far been applicable for in-vivo imaging. The basis of this project is a synthetic aperture technique known as synthetic aperture sequential beamforming (SASB). The technique utilizes a two step beamforming approach to drastically reduce system complexity compared to conventional synthetic aperture techniques. In this project, SASB is sought combined with a pulse inversion technique for 2nd harmonic tissue harmonic imaging. The advantages in tissue harmonic imaging (THI) are expected to further improve the image quality of SASB. The first part of the scientific contribution investigates an implementation of pulse inversion for THI on the experimental ultrasound system SARUS. The technique is initially implemented for linear array transducers and then expanded for convex array transducers. The technique is evaluated based on spatial resolution. The concept of harmonic energy leakage is investigated and minimized using harmonic matched filters. The second part of the study demonstrates that a combination of SASB with THI is feasible for a linear array transducer on SARUS. The method is expanded for convex array transducer and implemented on a commercial
ultrasound system. An optimization study of the scan settings for SASB with THI is performed. In the final part, a clinical investigation of the clinical relevance of SASB with THI is performed. The clinical relevance is determined by the image quality, sensitivity and specificity of the technique. Clinical scans were conducted in collaboration with medical professionals at Copenhagen University. In a series of double blinded trials, image quality and recognition of pathology using SASB with THI was compared with conventional THI. The results of the clinical trial documented, that SASB with THI provided as good image quality and specificity as conventional THI and provided 6% better sensitivity compared with conventional THI.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Rasmussen, J. (Intern), Jensen, J. A. (Intern)
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Relations
Projects:
Tissue Harmonic Synthetic Aperture Imaging
Publication: Research › Ph.D. thesis – Annual report year: 2014
Vector Volume Flow in Arteriovenous Fistulas

The majority of patients with end stage renal disease are in hemodialysis, and therefore dependent on a well functioning vascular access. The arteriovenous fistula is the recommended access and in order to maintain and keep the fistula patent, regular monitoring of the function is necessary. The Ultrasound Dilution Technique is the reference method for volume flow measurement, but it only works in conjunction with the dialysis machine, and use is therefore restricted to dialysis sessions. Volume flow measurement with conventional Doppler ultrasound provides a non invasive, highly accessible solution, but is very challenging due to the angle dependency of the Doppler technique and the anatomy of the fistula. The angle independent vector ultrasound technique Transverse Oscillation provides a new and more intuitive way to measure volume flow in an arteriovenous fistula. In this paper the Transverse Oscillation has been used to measure volume flow directly on four patients’ arteriovenous fistulas, and the measurements were compared to subsequent measurements with the Ultrasound Dilution Technique. The results obtained with the Transverse Oscillation deviate -35.1 – 14.9 % from the reference method, and indicates potential for the method.
Void-Free Direct Bonding of CMUT Arrays with Single Crystalline Plates and Pull-In Insulation

The implications on direct bonding quality, when using a double oxidation step to fabricate capacitive micromachined ultrasonic transducers (CMUTs), is analyzed. The protrusions along the CMUT cavity edges created during the second oxidation are investigated using simulations, AFM measurements, and a proposed analytical model, which is in good agreement with the simulated results. The results demonstrate protrusion heights in the order of 10 nm to 40 nm, with higher oxidation temperatures giving the highest protrusions. Isotropically wet etched cavities exhibit significantly smaller protrusions than anisotropically plasma etched cavities after the second oxidation. It is demonstrated that the protrusions will prevent good wafer bonding without subsequent polishing or etching steps. A new fabrication process is therefore proposed, allowing protrusion-free bonding surfaces with no alteration of the final structure and no additional fabrication steps compared to the double oxidation process. Two identical CMUT arrays with circular and square cavities having diameter/side lengths of 72 μm/65 μm and a 20 μm interdistance are fabricated with the two processes, demonstrating void-free bonding and 100% yield from the proposed process compared to poor bonding and 7% yield using the double oxidation process.

Harmonic ultrasound imaging using synthetic aperture sequential beamforming

A method includes generating an ultrasound image based on the harmonic components in the received echoes using multi-stage beam forming and data generated therefrom. An ultrasound imaging system (100, 200) includes a transducer array (108) including a plurality of transducer elements configured to emit ultrasound signals and receive echoes generated in response to the emitted ultrasound signals. The ultrasound imaging system further includes transmit circuitry (110) that generates a set of pulses that actuate a set of the plurality of transducer elements to emit ultrasound signals. The ultrasound imaging system further includes receive circuitry (112), including a first beam former (122) configured to...
process the second harmonic signal components extracted from the received echo signals, generating intermediate scan lines. Memory (126) stores the generated intermediate scan lines. The ultrasound imaging system further includes a synthetic aperture processor (128), including a second beam former (130) configured to process the stored intermediate scan lines, based on a synthetic aperture algorithm, generating a focused image.

**General information**

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**Organisations:** Department of Electrical Engineering, Biomedical Engineering, BK Medical Aps

**Authors:** Jensen, J. A. (Intern), Du, Y. (Intern), Jensen, H. (Ekstern)

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**Main Research Area:** Technical/natural sciences

Publication: Research › Patent – Annual report year: 2011

**In Vivo Evaluation of Synthetic Aperture Sequential Beamforming**

Ultrasound in vivo imaging using synthetic aperture sequential beamforming (SASB) is compared with conventional imaging in a double blinded study using side-by-side comparisons. The objective is to evaluate if the image quality in terms of penetration depth, spatial resolution, contrast and unwanted artifacts is comparable to conventional imaging. In vivo data was acquired using a ProFocus ultrasound scanner (BK Medical, Herlev, Denmark) and a 192-element 3.5 MHz convex array transducer (Sound Technology Inc., PA, USA). Data were acquired interleaved, ensuring that the exact same anatomical locations were scanned. Eighteen volunteers were scanned abdominally resulting in 85 image sequence pairs. Evaluation of image quality was performed by five medical doctors. Results show that image quality using SASB was significantly better than conventional imaging (p value: <0.01). There was not a significant difference in penetration depth (p value: 0.55). The study supports that in vivo ultrasound imaging using SASB is feasible for abdominal imaging.

**General information**

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**Organisations:** Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps, Copenhagen University Hospital, University of Copenhagen

**Authors:** Hemmsen, M. C. (Intern), Hansen, P. M. (Ekstern), Lange, T. (Ekstern), Hansen, J. M. (Intern), Lindskov Hansen, K. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)

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**Main Research Area:** Technical/natural sciences

**Publication information**

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- Web of Science (2017): Indexed Yes
The main purpose of this PhD project is to develop an ultrasonic method for 3D vector flow imaging. The motivation is to advance the field of velocity estimation in ultrasound, which plays an important role in the clinic. The velocity of blood has components in all three spatial dimensions, yet conventional methods can estimate only the axial component. Several approaches for 3D vector velocity estimation have been suggested, but none of these methods have so far produced convincing in vivo results nor have they been adopted by commercial manufacturers. The basis for this project is the Transverse Oscillation (TO) method, which estimates both the axial and the lateral velocity components.

The first part of the scientific contribution demonstrates that a commercial implementation of the TO method is feasible. Afterwards, the method is expanded to a phased array geometry, and performance metrics based on the TO fields are suggested. They can be used to optimize the TO method. In the third part, a TO method for 3D vector velocity estimation...
is proposed. It employs a 2D phased array transducer and decouples the velocity estimation into three velocity components, which are estimated simultaneously based on 5:1 parallel receive beamforming. Simulation results demonstrate the feasibility of the method.

In the final part, an experimental investigation of the 3D TO method is presented. Velocity measurements of steady flow were conducted in a flow-rig system, and the data were acquired using an experimental ultrasound scanner and a 2D transducer. The three velocity components along the center line are measured with relative (to the expected values) biases and standard deviations lower than 5% and 12%, respectively. At the center of the vessel, the mean and standard deviation of 100 estimated velocity vectors are \((v_x, v_y, v_z) = (-0.03, 95, 1.0) \pm (9, 6, 1) \text{ cm/s}\). Afterwards, 3D vector flow images from a cross-sectional plane of the vessel are presented. The out-of-plane velocities exhibit the expected 2D circular-symmetric parabolic shape. The experimental results verify that the 3D TO method estimates the complete 3D velocity vectors, and that the method is suitable for 3D vector flow imaging.

**General information**

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**Relations**
Projects:
3D vector flow imaging
Publication: Research › Ph.D. thesis – Annual report year: 2012

**A computerized algorithm for arousal detection in healthy adults and patients with Parkinson disease**

Arousals occur from all sleep stages and can be identified as abrupt electroencephalogram (EEG) and electromyogram (EMG) changes. Manual scoring of arousals is time consuming with low interscore agreement. The aim of this study was to design an arousal detection algorithm capable of detecting arousals from non-rapid eye movement (REM) and REM sleep, independent of the subject’s age and disease. The proposed algorithm uses features from EEG, EMG, and the manual sleep stage scoring as input to a feed-forward artificial neural network (ANN). The performance of the algorithm has been assessed using polysomnographic (PSG) recordings from a total of 24 subjects. Eight of the subjects were diagnosed with Parkinson disease (PD) and the rest (16) were healthy adults in various ages. The performance of the algorithm was validated in 3 settings: testing on the 8 patients with PD using the leave-one-out method, testing on the 16 healthy adults using the leave-one-out method, and finally testing on all 24 subjects using a 4-fold crossvalidation. For these 3 validations, the sensitivities were 89.8%, 90.3%, and 89.4%, and the positive predictive values (PPVs) were 88.8%, 89.4%, and 86.1%. These results are high compared with those of previously presented arousal detection algorithms and especially compared with the high interscore variability of manual scorings.

**General information**

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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen
Authors: Sørensen, G. L. (Intern), Jennum, P. (Forskerdatabase), Kempfner, J. (Intern), Zoetmulder, M. (Ekstern), Sørensen, H. B. D. (Intern)
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Age and gender related differences in aortic blood flow

The abdominal aorta (AA) is predisposed to development of abdominal aneurysms (AAA), a focal dilatation of the artery with fatal consequences if left untreated. The blood flow patterns in the AA is thought to play an important role in the development of AAA. The purpose of this work is to investigate the blood flow patterns within a group of healthy volunteers (4 females, 7 males) aged 23 to 76 years to identify changes and differences related to age and gender. The healthy volunteers were categorized by gender (male/female) and age (below/above 35 years). Subject-specific flow and geometry data were acquired using the research interface on a medical ultrasound scanner and segmentation of 3D magnetic resonance angiography respectively. The largest average diameter was among the elderly males (19.7 (± 1.33) mm) and smallest among the young females (12.4 (± 0.605) mm). The highest peak systolic velocity was in the young female group (1.02 (± 0.336) m/s) and lowest in the elderly male group (0.836 (± 0.127) m/s). A geometrical change with age was observed as the AA becomes more bended with age. This also affects the blood flow velocity patterns, which are markedly different from young to elderly. Thus, changes in blood flow patterns in the AA related to age and gender is observed. Further investigations are needed to determine the relation between changes in blood flow patterns and AAA development.
A Method for Direct Localized Sound Speed Estimates Using Registered Virtual Detectors

Accurate sound speed estimates are desirable in a number of fields. In an effort to increase the spatial resolution of sound speed estimates, a new method is proposed for direct measurement of sound speed between arbitrary spatial locations. The method uses the sound speed estimator developed by Anderson and Trahey. Their least squares fit of the received waveform's curvature provides an estimate of the wave's point of origin. The point of origin and the delay profile calculated from the fit are used to arrive at a spatially registered virtual detector. Between a pair of registered virtual detectors, a spherical wave is propagated. By beamforming the data, the time-of-flight between the two virtual sources can be calculated. From this information, the local sound speed can be estimated. Validation of the estimator is made using phantom and simulation data. The set of test phantoms consisted of both homogeneous and inhomogeneous media. Several different inhomogeneous phantom configurations were used for the physical validation. The simulation validation focused on the limits of target depth and signal-to-noise ratio on virtual detector registration. The simulations also compare the impact of two- and three-layer inhomogeneous media. The phantom results varied based on signal-to-noise ratio and geometry. The results for all cases were generally less than 1% mean error and standard deviation. The simulation results varied somewhat with depth and F/#, but primarily, they varied with signal-to-noise ratio and geometry. With two-layer geometries, the algorithm has a worst-case spatial registration bias of 0.02%. With three-layer geometries, the axial registration error gets worse with a bias magnitude up to 2.1% but is otherwise relatively stable over depth. The stability over depth of the bias in a given medium still allows for accurate sound speed estimates with a mean relative error less than 0.2%. 
An active learning approach to education in MRI technology for the biomedical engineering curriculum

It is challenging to give students an intuitive understanding of the basic magnetic resonance phenomenon and a sample of the many MRI techniques. Whereas compact mathematical descriptions of MRI techniques can be made, students are typically left with no intuitive understanding unless the common sense expressed in the math is in focus. Unfortunately, the nuclear dynamics happen in four dimensions, and are therefore not well suited for illustration on blackboard. 3D movies are more appropriate, but they do not encourage active learning. The typical solution employed by educators is hand waving (literally), since arm motions can to a limited extent be used to illustrate nuclear dynamics. Many students find this confusing, however, and students who do not grasp the meaning during lectures, are left in a bad position. For this reason, educational software was developed over the last decade (the Bloch Simulator). It is freely available and can be run directly from the software homepage that also links to YouTube software presentations aimed at educators and students who have already gotten a first introduction to MRI concepts. The software is mainly
aimed at educators for interactive demonstration of MRI techniques but can also be used for student exercises which may significantly improve the understanding of MRI concepts. The presentation demonstrates software made for the first few minutes of MRI education but focuses mostly on the educational value of the more advanced Bloch Simulator. It is explored how, and to what extent, active learning based on the software may improve student understanding. An interactive teaching session on advanced topics (pulse types, the Fourier relationship, selectivity) was evaluated using pre- and post-lecture anonymous questionnaires. These are challenging and significant subjects, and it was hypothesized that the approach may improve student understanding considerably. Though rigorous testing of the benefit over traditional teaching was not within the scope of the project, indications of improved skills were found, and the student satisfaction was excellent.

**General information**
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Organisations: Department of Electrical Engineering, Biomedical Engineering  
Authors: Hanson, L. G. (Intern)  
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**An Efficient Null Model for Conformational Fluctuations in Proteins**
Protein dynamics play a crucial role in function, catalytic activity, and pathogenesis. Consequently, there is great interest in computational methods that probe the conformational fluctuations of a protein. However, molecular dynamics simulations are computationally costly and therefore are often limited to comparatively short timescales. TYPHON is a probabilistic method to explore the conformational space of proteins under the guidance of a sophisticated probabilistic model of local structure and a given set of restraints that represent nonlocal interactions, such as hydrogen bonds or disulfide bridges. The choice of the restraints themselves is heuristic, but the resulting probabilistic model is well-defined and rigorous. Conceptually, TYPHON constitutes a null model of conformational fluctuations under a given set of restraints. We demonstrate that TYPHON can provide information on conformational fluctuations that is in correspondence with experimental measurements. TYPHON provides a flexible, yet computationally efficient, method to explore possible conformational fluctuations in proteins.

**General information**
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Organisations: Department of Informatics and Mathematical Modeling, Department of Electrical Engineering, Biomedical Engineering, Niels Bohr Institute, University of Copenhagen  
Authors: Harder, T. P. (Forskerdatabase), Borg, M. (Forskerdatabase), Bottaro, S. (Intern), Boomsma, W. (Intern), Olsson, S. (Forskerdatabase), Ferkinghoff-Borg, J. (Intern), Hamelryck, T. W. (Forskerdatabase)  
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Scopus rating (2016): SJR 3.975 SNIP 1.085 CiteScore 4.17  
BFI (2015): BFI-level 2
A novel method for coil efficiency estimation: Validation with a 13C birdcage

Coil efficiency, defined as the B1 magnetic field induced at a given point on the square root of supplied power P, is an important parameter that characterizes both the transmit and receive performance of the radiofrequency (RF) coil. Maximizing coil efficiency will maximize also the signal-to-noise ratio. In this work, we propose a novel method for RF coil efficiency estimation based on the use of a perturbing loop. The proposed method consists of loading the coil with a known resistor by inductive coupling and measuring the quality factor with and without the load. We tested the method by measuring the efficiency of a 13C birdcage coil tuned at 32.13 MHz and verified its accuracy by comparing the results with the nuclear magnetic resonance nutation experiment. The method allows coil performance characterization in a short time and with great accuracy, and it can be used both on the bench and inside the scanner. (c) 2012 Wiley Periodicals, Inc. Concepts Magn Reson Part B (Magn Reson Engineering) 41B: 139-143, 2012

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, National Research Council of Italy, University of Pisa
Authors: Giovannetti, G. (Ekstern), Frijia, F. (Ekstern), Hartwig, V. (Ekstern), Menichetti, L. (Ekstern), De Marchi, D. (Ekstern), Positano, V. (Ekstern), Landini, L. (Ekstern), Lombardi, M. (Ekstern), Santarelli, M. F. (Ekstern), Ardenkjær-Larsen, J. H. (Intern)
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A phantom based validation framework for EEG-fMRI acquisition methods

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark
Authors: Andersen, M. (Ekstern), Hanson, L. G. (Intern)
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Assessment of real-time myocardial uptake and enzymatic conversion of hyperpolarized [1-¹³C]pyruvate in pigs using slice selective magnetic resonance spectroscopy.

Hyperpolarization of ¹³C-labeled energy substrates enables the noninvasive detection and mapping of metabolic activity, in vivo, with magnetic resonance spectroscopy (MRS). Therefore, hyperpolarization and ¹³C MRS can potentially become a
powerful tool to study the physiology of organs such as the heart, through the quantification of kinetic patterns under both normal and pathological conditions. In this study we assessed myocardial uptake and metabolism of hyperpolarized $[1^{-13}C]$pyruvate in anesthetized pigs. Pyruvate metabolism was studied at baseline and during dobutamine-induced stimulation. We applied a numerical approach for spectral analysis and kinetic fitting (LSFIT/KIMOfit), making a comparison with a well-known jMRUI/AMARES analysis and $\gamma$-variante function, and we estimated the apparent conversion rate of hyperpolarized $[1^{-13}C]$pyruvate into its downstream metabolites $[1^{-13}C]$lactate, $[1^{-13}C]$alanine and $[13C]$bicarbonate in a 3 T MR scanner. We detected an increase in the apparent kinetic constants ($k(PX)$) for bicarbonate and lactate of twofold during dobutamine infusion. These data correlate with the double product (rate-pressure product), an indirect parameter of cardiac oxygen consumption: we observed an increase in value by 46 ± 11% during inotropic stress. The proposed approach might be applied to future studies in models of cardiac disease and/or for the assessment of the pharmacokinetic properties of suitable $^{13}$C-enriched tracers for MRS.

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**Attenuated heart rate response in REM sleep behavior disorder and Parkinson's disease**

The objective of this study was to determine whether patients with Parkinson's disease with and without rapid-eye-movement sleep behavior disorder and patients with idiopathic rapid-eye-movement sleep behavior disorder have an attenuated heart rate response to arousals or to leg movements during sleep compared with healthy controls. Fourteen and 16 Parkinson's patients with and without rapid-eye-movement sleep behavior disorder, respectively, 11 idiopathic rapid-eye-movement sleep behavior disorder patients, and 17 control subjects underwent 1 night of polysomnography. The heart rate response associated with arousal or leg movement from all sleep stages was analyzed from 10 heartbeats before the onset of the sleep event to 15 heartbeats following onset of the sleep event. The heart rate response to arousals was significantly lower in both parkinsonian groups compared with the control group and the idiopathic rapid-eye-movement sleep behavior disorder group. The heart rate response to leg movement was significantly lower in both Parkinson's groups and in the idiopathic rapid-eye-movement sleep behavior disorder group compared with the control group. The heart rate response for the idiopathic rapid-eye-movement sleep behavior disorder group was intermediate.
with respect to the control and the parkinsonian groups. The attenuated heart rate response may be a manifestation of the autonomic deficits experienced in Parkinson's disease. The idiopathic rapid-eye-movement sleep behavior disorder patients not only exhibited impaired motor symptoms but also incipient autonomic dysfunction, as revealed by the attenuated heart rate response. © 2012 Movement Disorder Society

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital, University of Copenhagen
Authors: Sorensen, G. L. (Intern), Kempfner, J. (Intern), Zoetmulder, M. (Ekstern), Sorensen, H. B. D. (Intern), Jennum, P. (Forskerdatabase)
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Web of Science (2018): Indexed yes
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Scopus rating (2017): SNIP 1.797 SJR 3.184 CiteScore 5.26
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Scopus rating (2016): SJR 2.78 SNIP 1.857 CiteScore 4.47
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.838 SNIP 1.695 CiteScore 3.79
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.588 SNIP 1.747 CiteScore 3.47
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.812 SNIP 1.804 CiteScore 3.75
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.169 SNIP 1.423 CiteScore 3.39
ISI indexed (2012): ISI indexed yes
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BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.343 SNIP 1.468 CiteScore 3.67
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.257 SNIP 1.505
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.339 SNIP 1.29
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.989 SNIP 1.261
Scopus rating (2007): SJR 1.62 SNIP 1.173
Scopus rating (2006): SJR 1.609 SNIP 1.33
Scopus rating (2005): SJR 1.515 SNIP 1.154
Scopus rating (2004): SJR 1.577 SNIP 1.229
Scopus rating (2003): SJR 1.343 SNIP 1.119
Scopus rating (2002): SJR 1.109 SNIP 1.036
Scopus rating (2001): SJR 1.311 SNIP 1.157
Scopus rating (2000): SJR 0.985 SNIP 1.39
Automated Algorithm for Generalized Tonic–Clonic Epileptic Seizure Onset Detection Based on sEMG Zero-Crossing Rate

Patients are not able to call for help during a generalized tonic–clonic epileptic seizure. Our objective was to develop a robust generic algorithm for automatic detection of tonic–clonic seizures, based on surface electromyography (sEMG) signals suitable for a portable device. Twenty-two seizures were analyzed from 11 consecutive patients. Our method is based on a high-pass filtering with a cutoff at 150 Hz, and monitoring a count of zero crossings with a hysteresis of ±50 μV. Based on data from one sEMG electrode (on the deltoid muscle), we achieved a sensitivity of 100% with a mean detection latency of 13.7 s, while the rate of false detection was limited to 1 false alarm per 24 h. The overall performance of the presented generic algorithm is adequate for clinical implementation.
Automatic Detection of Childhood Absence Epilepsy Seizures: Toward a Monitoring Device

Automatic detections of paroxysms in patients with childhood absence epilepsy have been neglected for several years. We acquire reliable detections using only a single-channel brainwave monitor, allowing for unobtrusive monitoring of antiepileptic drug effects. Ultimately we seek to obtain optimal long-term prognoses, balancing antiepileptic effects and side effects. The electroencephalographic appearance of paroxysms in childhood absence epilepsy is fairly homogeneous, making it feasible to develop patient-independent automatic detection. We implemented a state-of-the-art algorithm to investigate the performance of paroxysm detection. Using only a single scalp electroencephalogram channel from 20 patients with a total of 125 paroxysms >2 seconds, 97.2% of paroxysms could be detected with no false detections. This result leads us to recommend further investigations of tiny, one-channel electroencephalogram systems in an ambulatory setting.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Hypo-Safe A/S, Copenhagen University Hospital, University of Copenhagen
Authors: Duun-Henriksen, J. (Intern), Madsen, R. E. (Ekstern), Remvig, L. S. (Ekstern), Thomsen, C. E. (Ekstern), Sørensen, H. B. D. (Intern), Kjaer, T. W. (Ekstern)
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Scopus rating (2017): SNIP 0.958 SJR 0.83 CiteScore 1.69
Automatic detection of REM sleep in subjects without atonia

Idiopathic Rapid-Rye-Movement (REM) sleep Behavior Disorder (iRBD) is a strong early marker of Parkinson's Disease and is characterized by REM sleep without atonia (RSWA) and increased phasic muscle activity. Current proposed methods for detecting RSWA assume the presence of a manually scored hypnogram. In this study a full automatic REM sleep detector, using the EOG and EEG channels, is proposed. Based on statistical features, combined with subject specific feature scaling and post-processing of the classifier output, it was possible to obtain an mean accuracy of 0.96 with a mean sensitivity and specificity of 0.94 and 0.96 respectively.
Automatic multi-modal intelligent seizure acquisition (MISA) system for detection of motor seizures from electrophysiological data and motion data

The objective is to develop a non-invasive automatic method for detection of epileptic seizures with motor manifestations. Ten healthy subjects who simulated seizures and one patient participated in the study. Surface electromyography (sEMG) and motion sensor features were extracted as energy measures of reconstructed sub-bands from the discrete wavelet transformation (DWT) and the wavelet packet transformation (WPT). Based on the extracted features all data segments were classified using a support vector machine (SVM) algorithm as simulated seizure or normal activity. A case study of the seizure from the patient showed that the simulated seizures were visually similar to the epileptic one. The multi-modal intelligent seizure acquisition (MISA) system showed high sensitivity, short detection latency and low false detection rate. The results showed superiority of the multi-modal detection system compared to the uni-modal one. The presented system has a promising potential for seizure detection based on multi-modal data.

General information

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Danish Epilepsy Center, Copenhagen University Hospital
Authors: Conradsen, I. (Intern), Beniczky, S. (Ekstern), Wolf, P. (Ekstern), Kjaer, T. W. (Ekstern), Sams, T. (Intern), Sørensen, H. B. D. (Intern)
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Scopus rating (2016): SJR 0.639 SNIP 1.456 CiteScore 2.67
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.849 SNIP 1.621 CiteScore 2.65
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.801 SNIP 1.558 CiteScore 2.65
BFI (2013): BFI-level 1
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Web of Science (2013): Indexed yes
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Automatic QRS complex detection algorithm designed for a novel wearable, wireless electrocardiogram recording device

We have designed and optimized an automatic QRS complex detection algorithm for electrocardiogram (ECG) signals recorded with the DELTA ePatch platform. The algorithm is able to automatically switch between single-channel and multi-channel analysis mode. This preliminary study includes data from 11 patients measured with the DELTA ePatch platform and the algorithm achieves an average QRS sensitivity and positive predictivity of 99.57% and 99.57%, respectively. The algorithm was also evaluated on all 48 records from the MIT-BIH Arrhythmia Database (MITDB) with an average sensitivity and positive predictivity of 99.63% and 99.63%, respectively.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Odense University Hospital, Sektion for Bioteknologi
Authors: Saadi, D. B. (Intern), Egstrup, K. (Forskerdatabase), Branebjerg, J. (Intern), Andersen, G. (Forskerdatabase), Sorensen, H. B. (Intern)
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Electronic versions:
Basic MRI Physics - A Visual Introduction for Laymen

Magnetic resonance imaging (MRI) has become one of the most important imaging modalities due to its flexibility and high contrast between soft tissues. It is also known as a conceptually challenging technique. The purpose of the presentation is to demonstrate that MR techniques are maybe not as difficult to understand as often said [1]. In fact, the basic magnetic resonance phenomenon can be understood intuitively and even demonstrated with very simple means, including freely available software running directly in any browser [2]. A wide range of MRI techniques can be visualized [3] and understood in detail, certainly also by people who are not trained in physics [4]. The presentation is aimed at those new to MR, and those who will teach it.

But can simple explanations based on classical mechanics be trusted? The basic magnetic resonance (MR) phenomenon is often said to rely on quantum mechanics which is incomprehensible to most people. In fact, MR is not a quantum phenomenon [5]. Spin and certain kinds of nuclear couplings relevant to MR are indeed of quantum origin. Spin is important for understanding MR, but even though this effect is mind-boggling, most people have little difficulty taking it for granted. Once done, all the remaining MRI theory and typical spectroscopy, follows from the common sense expressed in classical mechanics (for MR in nuclear ensembles, quantum mechanics can be shown rigorously to reduce to classical mechanics). Unfortunately, typical attempts of explaining MR in terms of quantum mechanics contain severe errors [1].
Objective: To investigate the performance of epileptic seizure detection using only a few of the recorded EEG channels and the ability of software to select these channels compared with a neurophysiologist. Methods: Fifty-nine seizures and 1419 h of interictal EEG are used for training and testing of an automatic channel selection method. The characteristics of the seizures are extracted by the use of a wavelet analysis and classified by a support vector machine. The best channel selection method is based upon maximum variance during the seizure. Results: Using only three channels, a seizure detection sensitivity of 96% and a false detection rate of 0.14/h were obtained. This corresponds to the performance obtained when channels are selected through visual inspection by a clinical neurophysiologist, and constitutes a 4% improvement in sensitivity compared to seizure detection using channels recorded directly on the epileptic focus. Conclusions: Based on our dataset, automatic seizure detection can be done using only three EEG channels without loss of performance. These channels should be selected based on maximum variance and not, as often done, using the focal channels. Significance: With this simple automatic channel selection method, we have shown a computational efficient way of making automatic seizure detection.
Clinical evaluation of synthetic aperture sequential beamforming

In this study clinically relevant ultrasound images generated with synthetic aperture sequential beamforming (SASB) is compared to images generated with a conventional technique. The advantage of SASB is the ability to produce high resolution ultrasound images with a high frame rate and at the same time massively reduce the amount of generated data. SASB was implemented in a system consisting of a conventional ultrasound scanner connected to a PC via a research interface. This setup enables simultaneous recording with both SASB and conventional technique. Eighteen volunteers were ultrasound scanned abdominally, and 84 sequence pairs were recorded. Each sequence pair consists of two simultaneous recordings of the same anatomical location with SASB and conventional B-mode imaging. The images were evaluated in terms of spatial resolution, contrast, unwanted artifacts, and penetration depth of the ultrasound beam. Five ultrasound experts (radiologists) evaluated the sequence pairs in a side-by-side comparison, and the results show that image quality using SASB was better than conventional B-mode imaging. 73 % of the evaluations favored SASB, and a probability of 70 % was calculated for a new radiologist to prefer SASB over conventional imaging, if a new sequence was recorded. There was no significant difference in penetration depth.

General information

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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital, University of Copenhagen
Authors: Hansen, P. M. (Intern), Hemmsen, M. C. (Intern), Lange, T. (Ekstern), Hansen, J. M. (Intern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Cluster formation restricts dynamic nuclear polarization of xenon in solid mixtures

During dynamic nuclear polarization (DNP) at 1.5 K and 5 T, Xe-129 nuclear magnetic resonance (NMR) spectra of a homogeneous xenon/1-propanol/trityl-radical solid mixture exhibit a single peak, broadened by H-1 neighbors. A second peak appears upon annealing for several hours at 125 K. Its characteristic width and chemical shift indicate the presence of spontaneously formed pure Xe clusters. Microwave irradiation at the appropriate frequencies can bring both peaks to either positive or negative polarization. The peculiar time evolution of Xe-129 polarization in pure Xe clusters during DNP can be modelled as an interplay of spin diffusion and T-1 relaxation. Our simple spherical-cluster model offers a sensitive tool to evaluate major DNP parameters in situ, revealing a severe spin-diffusion bottleneck at the cluster boundaries and a significant sample overheating due to microwave irradiation. Subsequent DNP system modifications designed to reduce the overheating resulted in four-fold increase of Xe-129 polarization, from 5.3% to 21%. (C) 2012 American Institute of Physics. [http://dx.doi.org/10.1063/1.4751021]
Coil Sensitivity Estimation with Perturbing Sphere Method: Application to 13C Birdcages

Radiofrequency coils in magnetic resonance systems are used to irradiate nuclear spins and to pick up the signals emitted by the nuclei with high signal-to-noise ratio and large sensitivity region. The quality of the obtained images strongly depends upon the coil performance. When used at low frequencies, a number of drawbacks arise that drastically reduce their overall performances. In this work, we describe and verify the accuracy of a coil sensitivity estimation method based on the perturbing sphere theory which permits characterization of coil performance in a short time and that can be useful for periodical coil quality controls. In particular, we describe the application of the method by testing two 13C birdcage coils tuned at 32.13 MHz and verifying its accuracy using theoretical and experimental approaches.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, National Research Council of Italy, University of Pisa
Authors: Giovannetti, G. (Ekstern), Frijia, F. (Ekstern), Menichetti, L. (Ekstern), Ardenkjaer-Larsen, J. H. (Intern), Hartwig, V. (Ekstern), Marchi, D. D. (Ekstern), Positano, V. (Ekstern), Landini, L. (Ekstern), Lombardi, M. (Ekstern), Santarelli, M. F. (Ekstern)
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Comparison of 3D Synthetic Aperture Imaging and Explososcan using Phantom Measurements

In this paper, initial 3D ultrasound measurements from a 1024 channel system are presented. Measurements of 3D Synthetic aperture imaging (SAI) and Explososcan are presented and compared. Explososcan is the ‘gold standard’ for real-time 3D medical ultrasound imaging. SAI is compared to Explososcan by using tissue and wire phantom measurements. The measurements are carried out using a 1024 element 2D transducer and the 1024 channel experimental ultrasound scanner SARUS. To make a fair comparison, the two imaging techniques use the same number of active channels, the same number of emissions per frame, and they emit the same amount of energy per frame. The measurements were performed with parameters similar to standard cardiac imaging, with 256 emissions to image a volume spanning 90×90 and 150mm in depth. This results in a frame rate of 20 Hz. The number of active channels is set to 316 from the design of Explososcan. From wire phantom measurements the point spread functions of both techniques were measured. At 40mm depth Explososcan achieves a main lobe width (FWHM) of 2.5mm while SAI’s FWHM is 2.2 mm. At 80mm the FWHM is 5.2mm for Explososcan and 3.4mm for SAI, which is a difference of...
35 %. Another metric used on the PSF is the cystic resolution, which expresses the ability to detect anechoic cysts in a uniform scattering media. SAI improved the cystic resolution, R20dB, at 40mm depth from 4.5mm to 1.7mm and at 80mm from 8.2mm to 2.8 mm, compared to Explososcan. The speckle pattern looked better for SAI compared to Explososcan’s spatial shift variant speckle pattern.

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Comparison of Real-Time In Vivo Spectral and Vector Velocity Estimation
The purpose of this study is to show whether a newly introduced vector flow method is equal to conventional spectral estimation. Thirty-two common carotid arteries of 16 healthy volunteers were scanned using a BK Medical ProFocus scanner (DK-2730, Herlev, Denmark) and a linear transducer at 5 MHz. A triplex imaging sequence yields both the conventional velocity spectrum and a two-dimensional vector velocity image. Several clinical parameters were estimated and compared for the two methods: Flow angle, peak systole velocity (PS), end diastole velocity (ED) and resistive index (RI). With a paired t-test, the spectral and vector angles did not differ significantly (p = 0.658), whereas PS (p = 0.034), ED (p = 0.004) and RI (p <0.0001) differed significantly. Vector flow can measure the angle for spectral angle correction, thus eliminating the bias from the radiologist performing the angle setting with spectral estimation. The flow angle limitation in velocity estimation is also eliminated, so that flow at any angle can be measured.

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Scopus rating (2014): SJR 1.054 SNIP 1.407 CiteScore 2.65
Compounding in synthetic aperture imaging
A method for obtaining compound images using synthetic aperture data is investigated using a convex array transducer. The new approach allows spatial compounding to be performed for any number of angles without reducing the frame rate or temporal resolution. This important feature is an intrinsic property of how the compound images are constructed using synthetic aperture data and an improvement compared with how spatial compounding is obtained using conventional methods. The synthetic aperture compound images are created by exploiting the linearity of delay-and-sum beamformation for data collected from multiple spherical emissions to synthesize multiple transmit and receive apertures, corresponding to imaging the tissue from multiple directions. The many images are added incoherently, to produce a single compound image. Using a 192-element, 3.5-MHz, \( \lambda \)-pitch transducer, it is demonstrated from tissue-phantom measurements that the speckle is reduced and the contrast resolution improved when applying synthetic aperture compound imaging. At a depth of 4 cm, the size of the synthesized apertures is optimized for lesion detection based on the speckle information density. This is a performance measure for tissue contrast resolution which quantifies the tradeoff between resolution loss and speckle reduction. The speckle information density is improved by 25% when comparing synthetic aperture compounding to a similar setup for compounding using dynamic receive focusing. The cystic resolution and clutter levels are measured using a wire phantom setup and compared with conventional application of the array, as well as to synthetic aperture imaging without compounding. If the full aperture is used for synthetic aperture compounding, the cystic resolution is improved by 41% compared with conventional imaging, and is at least as good as what can be obtained using synthetic aperture imaging without compounding.
Computational fluid dynamics using in vivo ultrasound blood flow measurements

This paper presents a model environment for construction of patient-specific computational fluid dynamic (CFD) models for the abdominal aorta (AA). Realistic pulsatile velocity waveforms are employed by using in vivo ultrasound blood flow measurements. Ultrasound is suitable for acquisition of blood velocity profiles, but these are influenced by noise, which will cause convergence problems in CFD simulations. Therefore, physiological smoothing of the velocity profiles is needed. This paper uses the Womersley-Evans model for physiological smoothing of measured blood velocity profiles in the AA. The geometry for the CFD simulation model was obtained by segmentation of MRI scans using a 3 Tesla scanner (Magnetom Trio, Siemens Healthcare, Erlangen, Germany). Spectral velocity data were obtained from a BK Medical ProFocus scanner using a research interface. All data were obtained from healthy volunteers. The estimated and smoothed velocity profiles were quantitatively compared. The energy contained in the velocity profile after smoothing is 65% larger relative to the noise contaminated estimated profiles. In conclusion, a model environment that produces realistic patient-specific CFD simulation models without convergence issues has been developed. The data processing for the model environment can be performed within six hours which is fast enough to be used in the clinical setting.

Correlation between intra- and extracranial background EEG

Scalp EEG is the most widely used modality to record the electrical signals of the brain. It is well known that the volume conduction of these brain waves through the brain, cerebrospinal fluid, skull and scalp reduces the spatial resolution and the signal amplitude. So far the volume conduction has primarily been investigated by realistic head models or interictal spike analysis. We have set up a novel and more realistic experiment that made it possible to compare the information in the intra- and extracranial EEG. We found that intracranial EEG channels contained correlated patterns when placed less than 30 mm apart, that intra- and extracranial channels were partly correlated when placed less than 40 mm apart, and that extracranial channels probably were correlated over larger distances. The underlying cortical area that influences the extracranial EEG is found to be up to 45 cm². This area is larger than previously reported.
Decreased sleep spindle density in patients with idiopathic REM sleep behaviour disorder and patients with Parkinson's disease

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Danish Center for Sleep Medicine, H. Lundbeck A/S, Copenhagen University Hospital
Authors: Christensen, J. A. E. (Intern), Jennum, P. (Forskerdatabase), Kempfner, J. (Intern), Zoetmulder, M. (Ekstern), Leonthin, H. (Ekstern), Arvastson, L. (Ekstern), Christensen, S. R. (Ekstern), Sørensen, H. B. D. (Intern)
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Diagnosis of heel pad injuries

The biomechanics of in vivo heel pads has been investigated for more than 30 years, but unfortunately numerical results from the many individual investigators cannot be compared due to the different methodologies used, and the sometimes modest number of subjects investigated. The overall aim of the present thesis is to obtain a thorough understanding of the mechanical properties of in vivo human heel pad by studying the anatomical and physiological structure of healthy and diseased tissue, and to develop quantitative methods for diagnosing injuries. A compression device was built in order to record load-displacement curves from in vivo heel pads. To ensure applicability also for pathological feet, the device uses force levels lower than those needed to reproduce the physiological conditions of walking. One hundred twenty seven healthy volunteers were enrolled for compression tests and ultrasound investigation of heel pad thickness, so that three biomechanical parameters could be investigated: Heel Pad Compressibility Index (HPCI), Elastic modulus (E), and Energy Dissipation Ratio (EDR). Statistical analysis, based on linear regression models, showed that intrinsic subject factors such as age, weight, height and gender did influence HPCI, E and EDR, and that there was a significant statistically difference between males and females in E, but not in EDR and HPCI. In order to attempt a verification of the method used above, compression tests and ultrasound investigations on artificial heel pad models were conducted in two additional studies. In vivo experimental tests were used to validate a numerical 3D subject-specific heel pad model subjected to an external compression, and to further investigate the visco-elastic nature of the heel pad. Ultrasound distance measurements were compared with corresponding distance measurements with MRI and true values in order to assess its reliability in heel pad thickness measurements. The latter study confirmed the need to investigate the real speed of sound for the heel pad tissues, in order to obtain realistic measurements when dealing with human heel pad.
Dynamic gadolinium-enhanced magnetic resonance imaging allows accurate assessment of the synovial inflammatory activity in rheumatoid arthritis knee joints: a comparison with synovial histology

Objective: To determine whether dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) evaluated using semi-automatic image processing software can accurately assess synovial inflammation in rheumatoid arthritis (RA) knee joints. Methods: In 17 RA patients undergoing knee surgery, the average grade of histological synovial inflammation was determined from four biopsies obtained during surgery. A preoperative series of T(1)-weighted dynamic fast low-angle shot (FLASH) MR images was obtained. Parameters characterizing contrast uptake dynamics, including the initial rate of enhancement (IRE), were generated by the software in three different areas: (I) the entire slice (Whole slice); (II) a manually outlined region of interest (ROI) drawn quickly around the joint, omitting large artefacts such as blood vessels (Quick ROI); and (III) a manually outlined ROI following the synovial capsule of the knee joint (Precise ROI). Intra- and interreader agreement was assessed using the intra-class correlation coefficient (ICC).

Results: The IRE from the Quick ROI and the Precise ROI revealed high correlations to the grade of histological inflammation (Spearman's correlation coefficient (rho) = 0.70, p = 0.001 and rho = 0.74, p = 0.001, respectively). Intraand inter-reader ICCs were very high (0.93-1.00). No Whole slice parameters were correlated to histology. Conclusion: DCE-MRI provides fast and accurate assessment of synovial inflammation in RA patients. Manual outlining of the joint to omit large artefacts is necessary.
Effects of pyruvate dose on in vivo metabolism and quantification of hyperpolarized 13C spectra

Real-time in vivo measurements of metabolites are performed by signal enhancement of [1-13C]pyruvate using dynamic nuclear polarization, rapid dissolution and intravenous injection, acquisition of free induction decay signals and subsequent quantification of spectra. The commonly injected dose of hyperpolarized pyruvate is larger than typical tracer doses, with measurement before complete dilution of the injected bolus. Pyruvate is in exchange with its downstream metabolites lactate, alanine and bicarbonate. A transient exposure to high pyruvate blood concentrations may cause the saturation of cellular uptake and metabolic conversion. The goal of this study was to examine the effects of a [1-13C]pyruvate bolus on metabolic conversion in vivo. Spectra were quantified by three different methods: frequency-domain fitting with LCModel, time-domain fitting with AMARES and simple linear least-squares fitting in the time domain. Since the simple linear least-squares approach showed bleeding artifacts and LCModel produced noisier time signals, AMARES performed best in the quantification of in vivo hyperpolarized pyruvate spectra. We examined pyruvate doses of 0.1–0.4 mmol/kg (body mass) in male Wistar rats by acquiring slice-selective free induction decay signals in slices dominated by heart, liver and kidney tissue. Dose effects were noted in all cases, except for alanine in the cardiac slice below the dose of 0.2 mmol/kg. Our results indicate unlimited cellular uptake of pyruvate up to this dose and limited enzymatic activity of lactate dehydrogenase. In the cardiac slice above 0.2 mmol/kg and in liver and kidney slices, reflect limited cellular uptake or enzymatic activity, or a combination of both effects. The results indicate that the dose of pyruvate must be recognized as an important determinant for metabolic tissue kinetics, and saturation effects must be taken into account for the quantitative interpretation of the observed results. Copyright © 2011 John Wiley & Sons, Ltd.
Evaluation of novel algorithm embedded in a wearable sEMG device for seizure detection

We implemented a modified version of a previously published algorithm for detection of generalized tonic-clonic seizures into a prototype wireless surface electromyography (sEMG) recording device. The method was modified to require minimum computational load, and two parameters were trained on prior sEMG data recorded with the device. Along with the normal sEMG recording, the device is able to set an alarm whenever the implemented algorithm detects a seizure. These alarms are annotated in the data file along with the signal. The device was tested at the Epilepsy Monitoring Unit (EMU) at the Danish Epilepsy Center. Five patients were included in the study and two of them had generalized tonic-clonic seizures. All patients were monitored for 2–5 days. A double-blind study was made on the five patients. The overall result showed that the device detected four of seven seizures and had a false detection rate of 0.003/h or one in twelve days.

How the signal-to-noise ratio influences hyperpolarized 13C dynamic MRS data fitting and parameter estimation

MRS of hyperpolarized 13C-labeled compounds represents a promising technique for in vivo metabolic studies. However, robust quantification and metabolic modeling are still important areas of investigation. In particular, time and spatial resolution constraints may lead to the analysis of MRS signals with low signal-to-noise ratio (SNR). The relationship between SNR and the precision of quantitative analysis for the evaluation of the in vivo kinetic behavior of metabolites is unknown. In this article, this topic is addressed by Monte Carlo simulations, covering the problem of MRS signal model parameter estimation, with strong emphasis on the peak amplitude and kinetic model parameters. The results of Monte Carlo simulation were confirmed by in vivo experiments on medium-sized animals injected with hyperpolarized [1-13C]pyruvate. The results of this study may be useful for the establishment of experimental planning and for the optimization of kinetic model estimation as a function of the SNR value.

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Hyperpolarized 13C metabolic imaging using dissolution dynamic nuclear polarization
This article describes the basic physics of dissolution dynamic nuclear polarization (dissolution-DNP), and the impact of the resulting highly nonequilibrium spin states, on the physics of magnetic resonance imaging (MRI) detection. The hardware requirements for clinical translation of this technology are also presented. For studies that allow the use of externally administered agents, hyperpolarization offers a way to overcome normal magnetic resonance sensitivity limitations, at least for a brief T1-dependent observation window. A 10,000–100,000-fold signal-to-noise advantage provides an avenue for real-time measurement of perfusion, metabolite transport, exchange, and metabolism. The principles behind these measurements, as well as the choice of agent, and progress toward the application of hyperpolarized 13C metabolic imaging in oncology, cardiology, and neurology are reviewed. J. Magn. Reson. Imaging 2012; 36:1314–1328. © 2012 Wiley Periodicals, Inc.
Hyperpolarized C-13 MRS Cardiac Metabolism Studies in Pigs: Comparison Between Surface and Volume Radiofrequency Coils

Cardiac metabolism assessment with hyperpolarized 13C magnetic resonance spectroscopy in pig models requires the design of dedicated coils capable of providing large field of view with high signal-to-noise ratio (SNR) data. This work presents a comparison between a commercial 13C quadrature birdcage coil and a homebuilt 13C circular coil both designed for hyperpolarized studies of pig heart with a clinical 3T scanner. In particular, the simulation of the two coils is described by developing an SNR model for coil performance prediction and comparison. While coil resistances were calculated from Ohm's law, the magnetic field patterns and sample-induced resistances were calculated using a numerical finite-difference time-domain algorithm. After the numerical simulation of both coils, the results are presented as SNR-versus-depth profiles using experimental SNR extracted from the [1-13C]acetate phantom chemical shift image and with a comparison of metabolic maps acquired by hyperpolarized [1-13C]pyruvate injected in a pig. The accuracy of the developed SNR models was demonstrated by good agreement between the theoretical and experimental coil SNR-versus-depth profiles.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Giovannetti, G. (Ekstern), Hartwig, V. (Ekstern), Frijia, F. (Ekstern), Menichetti, L. (Ekstern), Positano, V. (Ekstern), Ardenkjaer-Larsen, J. H. (Intern), Lionetti, V. (Ekstern), Donato Aquaro, G. (Ekstern), Marchi, D. (Ekstern), Fiori, A. (Intern), Landini, L. (Ekstern), Lombardi, M. (Ekstern), Santarelli, M. F. (Ekstern)
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Hyperpolarized singlet NMR on a small animal imaging system

Nuclear spin hyperpolarization makes a significant advance toward overcoming the sensitivity limitations of in vivo magnetic resonance imaging, particularly in the case of low-gamma nuclei. The sensitivity may be improved further by storing the hyperpolarization in slowly relaxing singlet populations of spin-1/2 pairs. Here, we report hyperpolarized 13C spin order transferred into and retrieved from singlet spin order using a small animal magnetic resonance imaging scanner. For spins in sites with very similar chemical shifts, singlet spin order is sustained in high magnetic field without requiring strong radiofrequency irradiation. The demonstration of robust singlet-to-magnetization conversion, and vice versa, on a small animal scanner, is promising for future in vivo and clinical deployments.
Imaging blood’s velocity using synthetic aperture ultrasound

The blood velocity vector can be estimated using synthetic aperture techniques in medical ultrasound by using short emission sequences. The whole image region is insonified and the flow can be tracked in all directions continuously. This is a major advantage compared to commercial systems, since the separation between blood and tissue is greatly eased by this, and the estimates can be averaged over long time than in traditional systems. Vector velocity imaging can, thus,
be made and attain an order of magnitude higher precision than in current commercial systems and at higher frame rates. It is also possible to visualize very slow moving flow. The paper will present methods for making such imaging.

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Authors: Jensen, J. A. (Intern), Li, Y. (Intern)
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Imaging blood’s velocity using synthetic aperture ultrasound
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Implementation of a versatile research data acquisition system using a commercially available medical ultrasound scanner
This paper describes the design and implementation of a versatile, open-architecture research data acquisition system using a commercially available medical ultrasound scanner. The open architecture will allow researchers and clinicians to rapidly develop applications and move them relatively easy to the clinic. The system consists of a standard PC equipped with a camera link and an ultrasound scanner equipped with a research interface. The ultrasound scanner is an easy-to-use imaging device that is capable of generating high-quality images. In addition to supporting the acquisition of multiple data types, such as B-mode, M-mode, pulsed Doppler, and color flow imaging, the machine provides users with full control over imaging parameters such as transmit level, excitation waveform, beam angle, and focal depth. Beamformed RF data can be acquired from regions of interest throughout the image plane and stored to a file with a simple button press. For clinical trials and investigational purposes, when an identical image plane is desired for both an experimental and a reference data set, interleaved data can be captured. This form of data acquisition allows switching between multiple setups while maintaining identical transducer, scanner, region of interest, and recording time. Data acquisition is controlled through a graphical user interface running on the PC. This program implements an interface for third-party software to interact with the application. A software development toolkit is developed to give researchers and clinicians the ability to utilize third-party software for data analysis and flexible manipulation of control parameters. Because of the advantages of speed of acquisition and clinical benefit, research projects have successfully used the system to test and implement their customized solutions for different applications. Three examples of system use are presented in this paper: evaluation of synthetic aperture sequential beamformation, transverse oscillation for blood velocity estimation, and acquisition of spectral velocity data for evaluating aortic aneurysms.

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Authors: Hemmsen, M. C. (Intern), Nikolov, S. I. (Intern), Pedersen, M. M. (Ekstern), Pihl, M. J. (Intern), Enevoldsen, M. S. (Intern), Hansen, J. M. (Intern), Jensen, J. A. (Intern)
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Implementation of Tissue Harmonic Synthetic Aperture Imaging on a Commercial Ultrasound System

This paper presents an imaging technique for synthetic aperture (SAI) tissue harmonic imaging (THI) on a commercial ultrasound system. Synthetic aperture sequential beamforming (SASB) is combined with a pulse inversion (PI) technique on a commercial BK 2202 UltraView system. An interleaved scan sequence that performs dynamic receive focused (DRF) imaging and SASB, both using PI, is implemented. From each acquisition four images can be created: DRF image, SASB image, tissue harmonic DRF image (DRF-THI), and tissue harmonic SASB image (SASB-THI). For SASB imaging, a fixed transmit and receive focus at 80 mm and an F# of 3 is applied. For DRF imaging, default scanner settings are used, which are a focus at 85 mm and F# of 5.7 in transmit and a dynamic receive aperture with an F# of 0.8. In all cases a 2.14 MHz one-and-a-half cycle excitation transmit waveform is used. A BK 8820e 192 element convex array transducer is used to conduct scans of wire phantoms. The -6 dB and -20 dB lateral resolution is measured for each wire in the phantom. Results show that the -6 dB lateral resolution for SASB-THI is as good as for DRF-THI except at the point of the virtual source. SASB-THI even shows 7% reduction in -6 dB lateral resolution for the deepest wire at 100 mm. The -20 dB resolution for SASB-THI at [25, 50, 75, 100] mm was reduced by [5, 0 -34, 11] % compared to DRF-THI, which shows, that except for the point of the virtual source, the lateral resolution was improved by SASB-THI. A successful implementation of SASB-THI was achieved on a commercial system, which can be used for future pre-clinical trials.

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Investigating tumor perfusion and metabolism using multiple hyperpolarized 13C compounds: HP001, pyruvate and urea

The metabolically inactive hyperpolarized agents HP001 (bis-1,1-(hydroxymethyl)-[1-13C]cyclopropane-d8) and urea enable a new type of perfusion magnetic resonance imaging based on a direct signal source that is background-free. The addition of perfusion information to metabolic information obtained by spectroscopic imaging of hyperpolarized [1-13C]pyruvate would be of great value in exploring the relationship between perfusion and metabolism in cancer. In preclinical normal murine and cancer model studies, we performed both dynamic multislice imaging of the specialized hyperpolarized perfusion compound HP001 (T1=95 s ex vivo, 32 s in vivo at 3 T) using a pulse sequence with balanced steady-state free precession and ramped flip angle over time for efficient utilization of the hyperpolarized magnetization and three-dimensional echo-planar spectroscopic imaging of urea copolarized with [1-13C]pyruvate, with compressed sensing for resolution enhancement. For the dynamic data, peak signal maps and blood flow maps derived from perfusion modeling were generated. The spatial heterogeneity of perfusion was increased 2.9-fold in tumor tissues (P=.05), and slower washout was observed in the dynamic data. The results of separate dynamic HP001 imaging and copolarized pyruvate/urea imaging were compared. A strong and significant correlation (R=0.73, P=.02) detected between the urea and HP001 data confirmed the value of copolarizing urea with pyruvate for simultaneous assessment of perfusion and metabolism.

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Investigations on in vivo human heel pad thickness

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Authors: Matteoli, S. (Intern), Madsen, M. M. (Ekstern), Virga, A. (Ekstern), Wilhjelm, J. E. (Intern), Torp-Pedersen, S. T. (Ekstern)
In vivo color flow mapping using synthetic aperture dual stage beamforming
An in vivo investigation of synthetic aperture flow imaging using a dual stage beamformer is presented in this paper. In the previous work, simulations and Doppler flow phantom experiments showed promising results, which indicated the methods capability of producing fast color flow mapping with a good quality. Due to the continuous data, both high velocity and low velocity can be estimated. Moreover, synthetic aperture flow imaging can be implemented on a commercial platform, because the number of calculations have been reduced. In this work, A commercial ultrasound scanner (Pro Focus equipped with a UA 2227 Research Interface, BK Medical, Herlev, Denmark) was used to transmit signals and record echoes. The data are processed off-line. The method is validated using a pulsatile flow phantom. Volume flow is calculated, and is compared with the volume flow set for the pump. The relative standard deviation is 14.3% and relative bias is 6.4% for the phantom measurements. The blood flow in a common carotid artery of a 35-year-old healthy male is scanned by a medical doctor (PMH). The in vivo data is processed off-line. Fast synthetic aperture color flow mapping with frame rate of 85 Hz is produced and the volume flow is calculated.

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Measuring 3D Velocity Vectors using the Transverse Oscillation Method
Experimentally obtained estimates of threedimensional (3D) velocity vectors using the 3D Transverse Oscillation (TO) method are presented. The method employs a 2D transducer and synthesizes two double-oscillating fields in receive to obtain the axial, transverse, and elevation velocity components simultaneously. Experimental data are acquired using the ultrasound research scanner SARUS. The double-oscillating TO fields are investigated in an experimental scanning tank setup. The results demonstrate that the created fields only oscillate in the axial plus either the transverse or the elevation direction. Velocity measurements are conducted in an experimental flow-rig with steady flow in two different directions (mainly in x or y direction). Velocity estimates are obtained along the z axis. All three velocity components (vx, vy, vz) are measured with relative biases and standard deviations (normalized to expected value) below 5% and 12%, respectively. For an expected velocity magnitude of 25.2 cm/s, the method estimates 24.4±3.1 cm/s and 25.1±1.9 cm/s for the two
directions. Under similar conditions, Field II simulations yield 25.1±1.5 cm/s and 25.4±1.6 cm/s. The experimental results validate the results obtained through simulations and verify that the 3D TO method estimates the full 3D velocity vectors simultaneously as well as the correct velocity magnitudes.

**Mechanical behaviour of the heel pad: experimental and numerical approach**

The aim of the present work was to investigate the stress relaxation phenomena of the heel pad region under different loading conditions. A 31-year-old healthy female was enrolled in this study and her left foot underwent both MRI and experimental compression tests. Experimental results were compared with those obtained from finite element analysis performed on numerical 3D subject-specific heel pad model built on the basis of MRI. The calcaneal fat pad tissue was described with a visco-hyperelastic model, while a fiber-reinforced hyperelastic model was formulated for the skin. The reliability and accuracy of the investigation performed was confirmed by comparing results obtained from experimental data and numerical analysis. Specifically, the mean absolute percentage error was found to be less than 1%. The evaluation of viscous phenomena can be useful for understanding the mechanical response during daily activities.

**Methods and systems for producing compounded ultrasound images**

Disclosed is a method for producing compounded ultrasound images by beamforming a first and a second low-resolution image using data from a first ultrasound emission, beamforming a third and a fourth low-resolution image using data from a second ultrasound emission, summing said first and said third low-resolution image creating a first high-resolution image and said second and said fourth low-resolution image creating a second high-resolution image, wherein the method further comprises computing a first envelope image for said first high-resolution image and a second envelope image for said second high-resolution image, and processing said first envelope image and said second envelope image creating in a first compounded high-resolution image.
Modelling of CMUTs with Anisotropic Plates

Traditionally, CMUTs are modelled using the isotropic plate equation and this leads to deviations between analytical calculations and FEM simulations. In this paper, the deflection profile and material parameters are calculated using the anisotropic plate equation. It is shown that the anisotropic calculations match perfectly with FEM while an isotropic approach causes up to 10% deviations in deflection profile. Furthermore, we show how commonly used analytic modelling methods such as static calculations of the pull-in voltage and dynamic modelling through an equivalent circuit representation can be adjusted to include the correct anisotropic behaviour by using an effective flexural rigidity. The anisotropic calculations are also compared to experimental data from actual CMUTs showing an error of maximum 3%.

Modulation of epileptiform EEG discharges in juvenile myoclonic epilepsy: An investigation of reflex epileptic traits

Purpose: Previous studies have suggested that cognitive tasks modulate (provoke or inhibit) the epileptiform electroencephalography (EEG) discharges (EDs) in patients with juvenile myoclonic epilepsy (JME). Their inhibitory effect was found to be especially frequent (64–90%). These studies arbitrarily defined modulation as a >100% increase or >50% decrease of the EDs compared with baseline, which may not sufficiently distinguish from spontaneous fluctuations. The aim of our study was to assess the modulation of EDs and the precipitation of myoclonic seizures by cognitive tasks and by conventional provocation methods, taking into account also the spontaneous fluctuation of EDs. Method: Thirty patients with JME underwent video-EEG recordings including 50-min baseline, sleep, hyperventilation, intermittent photic stimulation (IPS), and cognitive tasks. To account for spontaneous fluctuations of the EDs we divided the baseline period into 5-min epochs and calculated the 95% confidence interval for the baseline EDs in each patient. Modulation was assumed when the number of EDs during any 5-min test period was outside the 95% confidence interval. Key Findings: Using the arbitrary method, our results were similar to previous publications: Cognitive tasks seemed to inhibit the EDs in
94% of the patients, and to provoke them in 22%. However, when the spontaneous fluctuations were accounted for, inhibition was found in only 29% of the patients and provocation in 18%. A nonspecific effect of any cognitive task seemed to account for the observed significant inhibition in two-thirds of the cases, but was observed in only one of the patients with significant provocation. Photoparoxysmal response was observed in 23% of the patients. When accounting for the spontaneous occurrence of EDs, IPS had provocative effect in 10% of the patients. Hyperventilation and sleep had provocative effect on EDs to an extent similar to the cognitive tasks (hyperventilation: 22%; sleep: 18%). The conventional provocation methods tended to be more efficient in patients who were not seizure free. Myoclonia were recorded most often during the cognitive tasks (10 patients). Significance: Spontaneous fluctuations of EDs account for most of the previously described inhibitory effect of the cognitive tasks. The provocative effect of the cognitive tasks is task-specific, whereas the inhibitory effect seems to be related to cognitive activation in general.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Danish Epilepsy Center, Universidade Federal de São Paulo-Escola Paulista de Medicina, All India Institute of Medical Sciences, University Medical Centre Ljubljana, Institute of Neurology, National Epilepsy Center
Authors: Beniczky, S. (Forskerdatabase), Guaranha, M. S. B. (Ekstern), Conradsen, I. (Intern), Singh, M. B. (Ekstern), Rutar, V. (Ekstern), Lorber, B. (Ekstern), Braga, P. (Ekstern), Fressola, A. B. (Ekstern), Inoue, Y. (Ekstern), Yacubian, E. M. T. (Ekstern), Wolf, P. (Forskerdatabase)
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Scopus rating (2010): SJR 1.697 SNIP 1.626
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Scopus rating (2009): SJR 1.954 SNIP 1.628
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Monte Carlo Methods for Inference in High-Dimensional Systems

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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Ferkinghoff-Borg, J. (Intern)
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MRI safety in practice: The EU directive on work in electromagnetic fields: Practical and clinical aspects

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Authors: Hanson, L. G. (Intern)
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Multilayer piezoelectric transducer models combined with Field II
One-dimensional and three-dimensional axisymmetric transducer model have been compared to determine their feasibility to predict the volt-to-surface impulse response of a circular Pz27 piezoceramic disc. The ceramic is assumed mounted with silver electrodes, bounded at the outer circular boundary with a polymer ring, and submerged into water. The
transducer models are developed to account for any external electrical loading impedance in the driving circuit. The models are adapted to calculate the surface acceleration needed by the Field II software in predicting pressure pulses at any location in front of the transducer. Results show that both models predict the longitudinal resonances with consistency. The one-dimensional model is found to exhibit approximately 2.9 dB peak overshoot at the lowest longitudinal resonance frequencies prediction. These values are decreasing for higher longitudinal modes. If the three-dimensional model is restricted in its radial movement at the circular boundary both models exhibit identical results. The Field II predicted pressure pulses are found to have oscillating consistency with a 2.0 dB overshoot on the maximum amplitude using the one-dimensional compared to the three-dimensional model. This is with no electronic loading. With a 50 Ω loading an amplitude overshoot is found to be 1.5 dB.

**General information**

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Authors: Bæk, D. (Intern), Willatzen, M. (Intern), Jensen, J. A. (Intern)
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- BFI (2009): BFI-level 1
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Optimizing Synthetic Aperture Compound Imaging

Spatial compound images are constructed from synthetic aperture data acquired using a linear phased-array transducer. Compound images of wires, tissue, and cysts are created using a method, which allows both transmit and receive compounding without any loss in temporal resolution. Similarly to conventional imaging, the speckle reduction achieved by spatial compounding comes at the cost of a reduced detail resolution and a compromise must be made. Using a performance indicator, which can be measured from an image of a phantom without cysts, it is demonstrated how a compromise can be made, which is optimal for lesion detection. Synthetic aperture data are acquired from unfocused emissions and 154 compound images are constructed by synthesizing different aperture configurations with more or less compounding, all maintaining a constant resolution across depth corresponding to an f-number of 2.0 for transmit and receive. The same configurations are used for scanning a phantom with cysts, and it is demonstrated how an improved cysts contrast follows from an aperture configuration, which gives a higher value for the performance measure extracted from the phantom without cysts. A correlation value $R = 0.81$ is observed with a p-value less than 0.0001. For the optimal compound image, the contrast is improved by 3 dB for a cyst at a depth of 50 mm compared to an image without compounding.
Patient-Specific Simulation Models of the Abdominal Aorta With and Without Aneurysms

This research study presents computational simulation models for analysis of parameters which are in evidence of development and clinical management of abdominal aortic aneurysms (AAA). The research covers three main areas: interpretation of material parameters, implementation of the constitutive relations for computational analysis, and evaluation of the material model predictability. The constitutive framework applied is the four fiber family (4FF) model. This model assumes that the wall is a constrained mixture of an amorphous isotropic elastin dominated matrix reinforced by collagen fibers. The collagen fibers are grouped in four directions of orientation. The purpose of the first study was to investigate whether significant risk factors related to AAA development can be identified from a specific pattern in the material parameters of the 4FF model. Smoking is a leading self-inflicted risk factor for cardiovascular diseases in general, and AAA in particular. Results suggests that arterial stiffening caused by smoking is reflected by consistent increase in an elastin-associated material parameter, and moreover by marked increase in the collagen-associated material parameters. The arterial stiffening appears to be isotropic, which may allow simpler phenomenological models to capture these effects. There is a pressing need, however, for more detailed histological information coupled with more complete experimental data for the systemic arteries. The second study was aimed at developing computational simulation models incorporating subject-specific geometry of the abdominal aorta (AA) as well as subject-specific blood flow conditions. The geometry was acquired from magnetic resonance imaging, and the blood flow characteristics were acquired from ultrasound. The solid AA wall was modeled as a thick-walled cylinder allowing for inspection of the stress distributions inside the wall. The 4FF model characterizes the mechanical behavior. The blood is assumed to be an incompressible Newtonian fluid. The fluid and solid models were implemented in a commercially available finite element software. The goal of third study was to evaluate the predictability of the 4FF model. This was achieved by combining subject-specific blood flow and age-matched material parameters of the 4FF model in a fluid-structure interaction (FSI) model. The predicted wall dynamics were compared to in vivo wall dynamics obtained with ultrasound. Simulation results indicate that the 4FF model overestimates the displacement of the AA wall in a realistic simulation setup. This is believed to be the first study to evaluate the predictability of the 4FF model using a FSI model environment.

Phased-array vector velocity estimation using transverse oscillations

A method for estimating the 2-D vector velocity of blood using a phased-array transducer is presented. The approach is based on the transverse oscillation (TO) method. The purposes of this work are to expand the TO method to a phased-array geometry and to broaden the potential clinical applicability of the method. A phased-array transducer has a smaller footprint and a larger field of view than a linear array, and is therefore more suited for, e.g., cardiac imaging. The method
relies on suitable TO fields, and a beamforming strategy employing diverging TO beams is proposed. The implementation of the TO method using a phased-array transducer for vector velocity estimation is evaluated through simulation and flow-rig measurements are acquired using an experimental scanner. The vast number of calculations needed to perform flow simulations makes the optimization of the TO fields a cumbersome process. Therefore, three performance metrics are proposed. They are calculated based on the complex TO spectrum of the combined TO fields. It is hypothesized that the performance metrics are related to the performance of the velocity estimates. The simulations show that the squared correlation values range from 0.79 to 0.92, indicating a correlation between the performance metrics of the TO spectrum and the velocity estimates. Because these performance metrics are much more readily computed, the TO fields can be optimized faster for improved velocity estimation of both simulations and measurements. For simulations of a parabolic flow at a depth of 10 cm, a relative (to the peak velocity) bias and standard deviation of 4% and 8%, respectively, are obtained. Overall, the simulations show that the TO method implemented on a phased-array transducer is robust with relative standard deviations around 10% in most cases. The flow-rig measurements show similar results. At a depth of 9.5 cm using 32 emissions per estimate, the relative standard deviation is 9% and the relative bias is 4%-9%. At the center of the vessel, the velocity magnitude is estimated to be 0.25 ± 0.023 m/s, compared with an expected peak velocity magnitude of 0.25 m/s, and the beam-to-flow angle is calculated to be 89.3° ± 0.77°, compared with an expected angle value between 89° and 90°. For steering angles up to ±20° degrees, the relative standard deviation is less than 20%. The results also show that a 64-element transducer implementation is feasible, but with a poorer performance compared with a 128-element transducer. The simulation and experimental results demonstrate that the TO method is suitable for use in conjunction with a phased-array transducer, and that 2-D vector velocity estimation is possible down to a depth of 15 cm.
Planning and Evaluation of Radio-Therapeutic Treatment of Head-and-Neck Cancer Using PET/CT scanning

Radiation therapy relies in great extent on delineations of tumour and organs on medical images. These delineations are essential for the entire treatment. Unfortunately manual delineations are both prone to variation. At the same time the manual delineation process is time-consuming. This thesis represent a work within the automatic definition of organs and tumours. The thesis includes a summary of the prior methods employed for automatic segmentation and 3 articles describing segmentation algorithms of different areas of application for radiation therapy. Variation within and between manual and automatic segmentation methods is documented in the thesis. The last article of the thesis analyses treatment outcome difference due to manual delineation variation.
Preliminary comparison of 3D synthetic aperture imaging with Explososcan

Explososcan is the ‘gold standard’ for real-time 3D medical ultrasound imaging. In this paper, 3D synthetic aperture imaging is compared to Explososcan by simulation of 3D point spread functions. The simulations mimic a 32x32 element prototype transducer. The transducer mimicked is a dense matrix phased array with a pitch of 300 μm, made by Vermon. For both imaging techniques, 289 emissions are used to image a volume spanning 60 in both the azimuth and elevation direction and 150mm in depth. This results for both techniques in a frame rate of 18 Hz. The implemented synthetic aperture technique reduces the number of transmit channels from 1024 to 256, compared to Explososcan. In terms of FWHM performance, was Explososcan and synthetic aperture found to perform similar. At 90mm depth is Explososcan’s FWHM performance 7% better than that of synthetic aperture. Synthetic aperture improved the cystic resolution, which expresses the ability to detect anechoic cysts in a uniform scattering media, at all depths except at Explososcan's focus point. Synthetic aperture reduced the cyst radius, R20dB, at 90mm depth by 48%. Synthetic aperture imaging was shown to reduce the number of transmit channels by four and still, generally, improve the imaging quality.

Quantification of In Vivo 2D Vector Flow Ultrasound

This PhD thesis has investigated the use of a new ultrasound technique that to measure the movement of blood. The technique was developed at the Center for Fast Ultrasound Imaging at the Technical University of Denmark and has previously only been available with experimental ultrasound scanners. Now, the method has been implemented into a commercial ultrasound scanner made for hospital use. In real-time, the technique measures movements in all directions as 2D vector fields, including movements perpendicular to the ultrasound beam. This is not available with conventional ultrasound scanners today. The thesis consists of three studies that uses vector flow ultrasound measurements on healthy volunteers. In study I the common carotid artery of 16 healthy volunteers were scanned simultaneously with the vector technique and the conventional, spectral estimation method. The study compared the clinical parameters: peak systole velocity, end diastole velocity, resistive index, and the flow direction. The results showed significant difference on the velocities and the resistive index. However, no significant difference on the manually defined flow angle and the calculated mean flow angle by the vector technique. With the conventional technique, the manual setting of the angle is operator dependent. With the calculated vector angle, this operator is relieved from the angle setting and the measurement is angle corrected by the identical method every time. With study II the carotid bifurcation including the carotid bulb and the common carotid artery were scanned on 8 healthy volunteers. The flow patterns of the two structures were outlined and presented to each of 5 experienced radiologists. The complexity of the identical areas were calculated by the vector concentration and compared to the visual evaluations. No significant difference was found between the two methods which were equally good at discriminating the laminar flow of the common carotid artery from the complex flow in the carotid bulb. Thus, a new method was presented to quantify complex flow patterns with vector flow. The final study III presented the rotational flow patterns in the cross-sectional plane of three arteries: The common carotid artery, the abdominal aorta, and the common iliac artery. Five healthy volunteers were included in the study and nine datasets visualized the flow patterns during the diastole. The rotational frequency was calculated and the results indicate a constant direction of the rotation for each artery. Extended measurements on the abdominal aorta showed a two-directional rotation
during the cardiac cycle. An observation that corresponds to previous MR and Doppler studies. With the three studies, this thesis presents new methods that quantifies in vivo vector flow obtained in real-time with a new implementation.

**Quantitative pupil analysis in stimulated emission depletion microscopy using phase retrieval.**

The resolution attainable with stimulated emission depletion (STED) microscopy greatly depends on the quality of the STED laser focus. So far, visual inspection of a measured STED focus has been the only convenient means of gauging the source of aberrations. Here we describe a method, requiring no instrument modifications, for obtaining an equivalent to the complex pupil function at the back aperture of the objective and show that it provides quantitative information about aberration sources (including aberrations induced by the objective or sample). We show the accuracy of this field representation to be sufficient for reconstructing the STED focus in three dimensions and determining corrective steps.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Kempfner, J. (Intern), Sørensen, G. L. (Intern), Leonthin, H. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern)
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Separation of Parkinson's patients in early and mature stages from control subjects using one EOG channel

In this study, polysomnographic left side EOG signals from ten control subjects, ten iRBD patients and ten Parkinson's patients were decomposed in time and frequency using wavelet transformation. A total of 28 features were computed as the means and standard deviations in energy measures from different reconstructed detail subbands across all sleep epochs during a whole night of sleep. A subset of features was chosen based on a cross validated Shrunken Centroids Regularized Discriminant Analysis, where the controls were treated as one group and the patients as another. Classification of the subjects was done by a leave-one-out validation approach using same method, and reached a sensitivity of 95%, a specificity of 70% and an accuracy of 86.7%. It was found that in the optimal subset of features, two hold lower frequencies reflecting the rapid eye movements and two hold higher frequencies reflecting EMG activity. This study demonstrates that both analysis of eye movements during sleep as well as EMG activity measured at the EOG channel hold potential of being biomarkers for Parkinson's disease.

Shadow effects in simulated ultrasound images derived from computed tomography images using a focused beam tracing model

Simulation of ultrasound images based on computed tomography (CT) data has previously been performed with different approaches. Shadow effects are normally pronounced in ultrasound images, so they should be included in the simulation. In this study, a method to capture the shadow effects has been developed, which makes the simulated ultrasound images appear more realistic.

The method using a focused beam tracing model gives diffuse shadows that are similar to the ones observed in measurements on real objects. Ultrasound images of a cod (Gadus morhua) were obtained with a BK Medical 2202 ProFocus ultrasound scanner (BK Medical, Herlev, Denmark) equipped with a dedicated research interface giving access to beamformed radio frequency data.

CT images were obtained with an Aquilion ONE Toshiba CT scanner (Toshiba Medical Systems Corp., Tochigi, Japan). CT data were mapped from Hounsfield units to backscatter strength, attenuation coefficients, and characteristic acoustic impedance. The focused beam tracing model was used to create maps of the transmission coefficient and scattering strength maps. FIELD II was then used to simulate an ultrasound image of 38.955.34.5 mm, using 106 point scatterers. As there is no quantitative method to assess quality of a simulated ultrasound image compared to a measured one, visual inspection was used for evaluation.
Spatial impulse response of a rectangular double curved transducer

Calculation of the pressure field from transducers having both a convex and a concave surface geometry is a complicated assignment that often is accomplished by subdividing the transducer surface into smaller flat elements of which the spatial impulse response is known. This method is often seen applied to curved transducers because an analytical solution is unknown. In this work, a semi-analytical algorithm for the exact solution to a first order in diffraction effect of the spatial impulse response of rectangular shaped double curved transducers is presented. The algorithm and an approximation of it are investigated. The approximation reformulates the algorithm to an analytically integrable expression which is computationally efficient to solve. Simulation results are compared with the simulation software Field II. Calculating the response from 200 different points yields a mean error for the different approximations ranging from 0.03 % to 0.8 % relative to a numerical solution for the spatial impulse response. It is shown that the presented algorithm gives consistent results with Field II for a linear flat, a linear focused, and a convex non-focused element. Best solution was found to be 0.01 % with a three-point Taylor expansion.
Although Markov chain Monte Carlo (MC) simulation is a potentially powerful approach for exploring conformational space, it has been unable to compete with molecular dynamics (MD) in the analysis of high density structural states, such as the native state of globular proteins. Here, we introduce a kinetic algorithm, CRISP, that greatly enhances the sampling efficiency in all-atom MC simulations of dense systems. The algorithm is based on an exact analytical solution to the classic chain-closure problem, making it possible to express the interdependencies among degrees of freedom in the molecule as correlations in a multivariate Gaussian distribution. We demonstrate that our method reproduces structural variation in proteins with greater efficiency than current state-of-the-art Monte Carlo methods and has real-time simulation performance on par with molecular dynamics simulations. The presented results suggest our method as a valuable tool in the study of molecules in atomic detail, offering a potential alternative to molecular dynamics for probing long time-scale conformational transitions.

**Subtle Monte Carlo Updates in Dense Molecular Systems**

Although Markov chain Monte Carlo (MC) simulation is a potentially powerful approach for exploring conformational space, it has been unable to compete with molecular dynamics (MD) in the analysis of high density structural states, such as the native state of globular proteins. Here, we introduce a kinetic algorithm, CRISP, that greatly enhances the sampling efficiency in all-atom MC simulations of dense systems. The algorithm is based on an exact analytical solution to the classic chain-closure problem, making it possible to express the interdependencies among degrees of freedom in the molecule as correlations in a multivariate Gaussian distribution. We demonstrate that our method reproduces structural variation in proteins with greater efficiency than current state-of-the-art Monte Carlo methods and has real-time simulation performance on par with molecular dynamics simulations. The presented results suggest our method as a valuable tool in the study of molecules in atomic detail, offering a potential alternative to molecular dynamics for probing long time-scale conformational transitions.

**General information**

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Copenhagen
Authors: Bottaro, S. (Intern), Boomsma, W. (Intern), Johansson, K. E. (Ekstern), Andreetta, C. (Forskerdatabase), Hamelryck, T. (Forskerdatabase), Ferkinghoff-Borg, J. (Intern)

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Synthetic Aperture Compound Imaging

Medical ultrasound imaging is used for many purposes, e.g. for localizing and classifying cysts, lesions, and other processes. Almost any mass is first observed using B-mode imaging and later classified using e.g. color flow, strain, or attenuation imaging. It is therefore important that the B-mode images have high contrast. Like all imaging modalities, ultrasound is subject to a number of inherent artifacts that compromise image quality. The most prominent artifact is the degradation by coherent wave interference, known as “speckle”, which gives a granular appearance to an otherwise homogeneous region of parenchyma. A successful approach to reduce the speckle artifacts is spatial compounding, where images are acquired from a number of directions and combined after envelope-detection. Today, spatial compounding is implemented in all highend ultrasound systems and available when using a low pitch transducer with a
fairly high number of independent channels. A drawback of conventional compounding is a reduction of the frame rate. In this dissertation, a method for obtaining compound images using synthetic aperture data is proposed and investigated. The new approach allows spatial compounding to be performed for any number of angles without reducing the frame rate or temporal resolution. This important feature is an intrinsic property of how the compound images are constructed using synthetic aperture data and an improvement compared to how spatial compounding is obtained using conventional methods. The method is investigated using simulations and through measurements using both phased array and convex array transducers. The images all show an improved contrast compared to images without compounding, and by construction, imaging using an improved frame rate is possible. Using a phased array transducer, it is demonstrated through theoretical considerations that the compound effect achieved is close to a theoretical maximum for the amount of compounding attainable and using a -pitch convex array transducer, the first in-vivo images are created. The computational demands for an implementation are massive and the limiting factor is the amount of memory IO resources available. An equally high demand for memory throughput is found in the computer gaming industry, where a large part of the processing takes place on the graphics processing unit (GPU). Using the GPU, a framework for synthetic aperture imaging is implemented providing proof-of-concept for real-time implementations of synthetic aperture imaging.

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Authors: Hansen, J. M. (Intern), Jensen, J. A. (Intern)
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Synthetic Aperture Flow Imaging Using a Dual Beamformer Approach
Color flow mapping systems have become widely used in clinical applications. It provides an opportunity to visualize the velocity profile over a large region in the vessel, which makes it possible to diagnose, e.g., occlusion of veins, heart valve deficiencies, and other hemodynamic problems. However, while the conventional ultrasound imaging of making color flow mapping provides useful information in many circumstances, the spatial velocity resolution and frame rate are limited. The entire velocity distribution consists of image lines from different directions, and each image line is estimated using multiple emissions. Therefore, it is very difficult to acquire a full volume of data for the blood flow in the heart in real-time. A radical break with this has been the synthetic aperture technique. This technique makes it possible to increase the frame rate, and the reconstruction also makes it possible to improve significantly the focusing and frame rate. However, it requires a large amount of calculations to fulfill the performance because the signal from each channel is stored and processed simultaneously. The implementation of the full synthetic aperture would be very expensive on the current commercial ultrasound scanner. The motivation for this project is to develop a method lowering the amount of calculations and still maintaining beamforming quality sufficient for flow estimation.

Synthetic aperture using a dual beamformer approach is investigated using Field II simulations, phantom measurements and in vivo measurements. Firstly, the method is used to estimate the velocity along the ultrasound beam, which is the axial component. The results all show good quality of color flow mapping in terms of standard deviations and bias. The results of in vivo measurements show the capability of acquiring color flow mapping with a high frame rate. Secondly, the new method is extended to the vector velocity estimation using directional beamforming, which beamforms data in the flow direction. The magnitude of the flow can be obtained and results of simulations and phantom measurements show good agreements with the truth. With directional beamforming, the velocity in the transverse direction can be achieved, which is impossible for the conventional method. Comparing the amount of calculations shows a reduction in number of calculations for the new method compared to full synthetic aperture.

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Synthetic Aperture Sequential Beamformation applied to medical imaging.

Synthetic Aperture Sequential Beamforming (SASB) is applied to medical ultrasound imaging using a multi element convex array transducer. The main motivation for SASB is to apply synthetic aperture techniques without the need for storing RF-data for a number of elements and hereby devise a system with a reduced system complexity. Using a 192 element, 3.5 MHz, λ-pitch transducer, it is demonstrated using tissue-phantom and wire-phantom measurements, how the speckle size and the detail resolution is improved compared to conventional imaging.

Tools and methods for teaching magnetic resonance concepts and techniques

Teaching of MRI methodology can be challenging for teachers as well as students. To support student learning, two graphical simulators for exploration of basic magnetic resonance principles are here introduced. The first implements a simple compass needle analogy implemented for day one of NMR and MRI education. After a few minutes of use, any user with minimal experience of magnetism will be able to explain the basic magnetic resonance principle. A second piece of software, the Bloch Simulator, aims much further, as it can be used to demonstrate and explore a wide range of phenomena including RF interactions, relaxation, weighting, echoes, imaging principles and more. Both simulators run in almost any browser without installation of software, but are also freely available for download. Example uses are documented in a series of short videos available on YouTube.
Towards a General Probabilistic Model of Protein Structure: The Reference Ratio Method

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Leeds, University of Copenhagen
Authors: Frellsen, J. (Forskerdatabase), Mardia, K. V. (Ekstern), Borg, M. (Ekstern), Ferkinghoff-Borg, J. (Intern), Hamelryck, T. W. (Ekstern)
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Transverse Oscillation Vector Velocity Estimation using a Phased Array Transducer

The Transverse Oscillation method has shown its commercial feasibility, providing the user with 2D velocity information. Today's implementation on commercial ultrasound platforms only support linear array transducers and are limited in depth. Extending the implementation to a phased array transducer, vector velocity echocardiography will become possible. This paper describes the general modification made on the BK Medical 2202 Pro Focus UltraView using a 64 element phased array transducer and the simulations and measurements performed. The results show that velocities can be obtained at depths even greater than 100 mm. Tests at depths of 72 mm and 82 mm with a peak velocity of 0.5 m/s, showed a relative mean bias $\sim v_x$ that varied from 0 % and to 21 % and a relative mean standard deviation $\sim v_x$ that varied from 18 % and to 51 %. The investigation showed an increasing bias with respect to depth, which leaves room for optimization. Despite the bias, the method has shown to work and produce reliable results, and 2D velocity estimates are provided within the entire color-box down to a depth of more than 100 mm making vector velocity imaging possible in the entire heart.

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Authors: Marcher, J. (Ekstern), Pihl, M. J. (Intern), Seerup, G. (Ekstern), Haugaard, P. (Ekstern), Nikolov, S. I. (Ekstern), Jensen, J. A. (Intern)
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Ultrasound backscatter from free-swimming fish at 1 MHz for fish identification

In the frequency range well below 1 MHz, the swimbladder is often considered the most important part for acoustic fish detection. In this work a portable system was developed to not only detect but also try to identify free-swimming fish. It has been used to measure the ultrasound backscatter at 1 MHz from fish.

The system consists of a Reson TC3210 1 MHz single-element transducer, a dual-frequency, multi-beam Blueview P900-2250 sonar, and three Oregon ATC9K cameras. The Reson transducer is connected to an Olympus pulser-receiver monitored by a portable computer through a Picoscope 4226 PC oscilloscope. Exsitu experiments were performed at the NorthSea Oceanarium in Hirtshals, Denmark. The positions, orientations, and lengths of fish were estimated by three dimensional image analysis, taking the measured acoustic distance into account, while species were identified manually. These experiments indicate that at 1 MHz the surface areas (also fins and tail) of the fish can give echoes that are much stronger (up to 3 times) than the swimbladder can, therefore important for identification of fish.

Ultrasound pulse-echo measurements on rough surfaces with linear array transducers

The echo from planar surfaces with rms roughness, Rq, in the range from 0-155 μm was measured with a clinical linear array transducer at different angles of incidence at 6 MHz and 12 MHz. The echo-pulse from the surfaces was isolated with an equal sized window and the power of the echo-pulse was calculated. The power of the echo from the smooth surface (Rq = 0) is highly angle-dependent due to a high degree of specular reflection. Within the angular range considered here, -10° to 10°, the variation spans a range of 18 dB at both 6 MHz and 12 MHz. When roughness increases, the angle-dependence decreases, as the echo process gradually changes from pure reflection to being predominantly governed by backscattering. The power of the echoes from the two roughest surfaces (Rq = 115 μm and 155 μm) are largely independent of angle at both 6 MHz and 12 MHz with a variation of 2 dB in the angular range from -10° to 10°. The least rough surfaces (Rq = 32 μm and 89 μm) have responses in between with a higher degree of angle-dependence at 6 MHz than at 12 MHz.
Use of web-based simulators and YouTube for teaching of Magnetic Resonance Imaging

Interactive web-based software for teaching of 3D vector dynamics involved in Magnetic Resonance Imaging (MRI) was developed. The software is briefly discussed along with the background, design, implementation, dissemination and educational value.

Validation of a novel automatic sleep spindle detector with high performance during sleep in middle aged subjects

Many of the automatic sleep spindle detectors currently used to analyze sleep EEG are either validated on young subjects or not validated thoroughly. The purpose of this study is to develop and validate a fast and reliable sleep spindle detector with high performance in middle aged subjects. An automatic sleep spindle detector using a bandpass filtering approach and a time varying threshold was developed. The validation was done on sleep epochs from EEG recordings with manually scored sleep spindles from 13 healthy subjects with a mean age of 57.9 ± 9.7 years. The sleep spindle detector reached a mean sensitivity of 84.6 % and a mean specificity of 95.3 %. The sleep spindle detector can be used to obtain measures of spindle count and density together with quantitative measures such as the mean spindle frequency, mean spindle amplitude, and mean spindle duration.
3D Vector Velocity Estimation using a 2D Phased Array

A method to estimate the three dimensional (3D) velocity vector is presented in this paper. 3D velocity vector techniques are needed to measure the full velocity and characterize the complicated flow patterns in the human body. The Transverse Oscillation (TO) method introduces oscillations transverse to the ultrasound beam, which enables the estimation of the transverse velocity. To expand the method from 2D to 3D, it is proposed to decouple the velocity estimation into separate estimates of vx, vy, and vz in combination with a 2D phased matrix array. Through simulations the feasibility of using the TO method for estimation 3D velocity vectors, and the proposed decoupling is demonstrated. A 64x64 and a 32x32 elements transducer are emulated using Field II. Plug flow with a speed of 1 m/s in a small region is rotated in the XY-plane. A binary flow example with [vx,vy]=[1,0] and [0,1] m/s shows, that the velocity estimation can be decoupled into the transverse and elevation velocity components. This is substantiated by the results for seven different angles, where the mean and the standard deviation of the estimated speed are 0.970.05 m/s and of the angle bias are -0.733.3 for the 64x64 matrix transducer. For the 32x32 transducer, the mean and standard deviation for the speed are 0.94 0.11 m/s and for the angle bias -0.487.7. The simulation study clearly demonstrates, that the new method can be used to estimate the 3D velocity vector using a 2D phased matrix array, and that the velocity vector estimation can be decoupled into separate estimates of vx, vy, and vz.

An Architecture and Implementation of Real-time Synthetic Aperture Compounding with SARUS

Synthetic aperture and compounding are imaging techniques for increasing the resolution and contrast of ultrasound images. Both techniques are computationally intensive, and combined they require approximately two orders of magnitude more lines to be beamformed per second compared to conventional B-mode imaging with similar frame rates. In this paper, an implementation of a system capable of synthetic aperture compound imaging in real-time producing more than 325 million complex beamformed samples per second is presented. This corresponds to synthetic aperture compound imaging at 13 frames per second with 64 emissions and 3 compound angles with 128 lines each. The beamformer is implemented in the SARUS research scanner which consists of 320 Virtex4 FPGAs and has 1024 independent transmit and receive channels. The beamformer is partitioned across 64 FPGAs and runs at 87.5 MHz while consuming 76% of the available logic resources in each FPGA. The beamformed images have resolution similar to offline processed images.
An Asynchronous P300 BCI With SSVEP-Based Control State Detection

In this paper, an asynchronous brain–computer interface (BCI) system combining the P300 and steady-state visually evoked potentials (SSVEPs) paradigms is proposed. The information transfer is accomplished using P300 event-related potential paradigm and the control state (CS) detection is achieved using SSVEP, overlaid on the P300 base system. Offline and online experiments have been performed with ten subjects to validate the proposed system. It is shown to achieve fast and accurate CS detection without significantly compromising the performance. In online experiments, the system is found to be capable of achieving an average data transfer rate of 19.05 bits/min, with CS detection accuracy of about 88%.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, National University of Singapore
Authors: Panicker, R. C. (Ekstern), Puthusserypady, S. (Intern), Sun, Y. (Ekstern)
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An Auditory Go/No-Go Study of Event-Related Potentials in Children with Fetal Alcohol Spectrum Disorders

Abstract—in this study event-related potentials (ERPs) were used to investigate the effects of prenatal alcohol exposure on response inhibition identified during task performance. ERPs were recorded during a auditory Go/No Go task in two groups of children with mean age of 12.8 years (11 years to 14.7 years): one diagnosed with fetal alcohol syndrome (FAS) or partial FAS (FAS/PFAS; n = 12) and a control group of children of same age whose mothers abstained from alcohol or drank minimally during pregnancy (n = 11). The children were instructed to push a button in response to the Go stimulus and not to press the button when the No Go stimulus were heard. Task performance accuracy did not differ between the two groups, however differences were observed in the ERP components: P2, N2, and P3. The P2 amplitude were larger for Go trials in both groups. The FAS/PFAS group showed slower N2 response to Go trials, suggesting a less efficient early classification of the stimulus. P3 showed larger amplitudes to No-Go vs. Go in both groups. The study has provided new evidence for inhibition deficits in FAS/PFAS subjects identified by ERPs.
The paper presents an Angular Spectrum Approach (ASA) for simulating pulsed non-linear ultrasound fields. The source of the ASA is generated by Field II, which can simulate array transducers of any arbitrary geometry and focusing. The non-linear ultrasound simulation program - Abersim, is used as the reference. A linear array transducer with 64 active elements is simulated by both Field II and Abersim. The excitation is a 2-cycle sine wave with a frequency of 5 MHz. The second harmonic field in the time domain is simulated using ASA. Pulse inversion is used in the Abersim simulation to remove the fundamental and keep the second harmonic field, since Abersim simulates non-linear fields with all harmonic components. ASA and Abersim are compared for the pulsed fundamental and second harmonic fields in the time domain at depths of 30 mm, 40 mm (focal depth) and 60 mm. Full widths at -6 dB (FWHM) are 0.97, 0.95 mm at the focal depth for the fundamental fields for ASA and Abersim, and 0.56, 0.55 mm for the second harmonic fields. Full widths at -12 dB are 1.27, 1.26 mm for the fundamental fields for ASA and Abersim, and 0.77, 0.73 mm for the second harmonic fields. The calculation time, for the second harmonic fields, using ASA is 12 minutes and for all harmonic fields using Abersim is 14 hours. Compared to Abersim, the error of ASA for calculating the second harmonic fields is 1.5% at -6 dB and 6.4% at -12 dB, and the calculation time is reduced by a factor of 70.

**Angular spectrum approach for fast simulation of pulsed non-linear ultrasound fields**

Focusing and apodization are an essential part of signal processing in ultrasound imaging. Although the fundamental principles are simple, the dramatic increase in computational power of CPUs, GPUs, and FPGAs motivates the development of software based beamformers, which further improves image quality (and the accuracy of velocity estimation). For developing new imaging methods, it is important to establish proof-of-concept before using resources on real-time implementations. With this in mind, an effective and versatile Matlab toolbox written in C++ has been developed to assist in developing new beam formation strategies. It is a general 3D implementation capable of handling a multitude of
focusing methods, interpolation schemes, and parametric and dynamic apodization. Despite being exible, it is capable of exploiting parallelization on a single computer, on a cluster, or on both. On a single computer, it mimics the parallelization in a scanner containing multiple beam formers. The focusing is determined using the positions of the transducer elements, presence of virtual sources, and the focus points. For interpolation, a number of interpolation schemes can be chosen, e.g. linear, polyno- mial, or cubic splines. Apodization can be specied by a number of window functions of xed size applied on the individual elements as a function of distance to a reference point, or it can be dynamic with an expanding or contracting aperture to obtain a constant F-number, or both. On a standard PC with an Intel Quad-Core Xeon E5520 processor running at 2.26 GHz, the toolbox can beamform 300:000 points using 700:000 data samples in 3 seconds using a transducer with 192 elements, dynamic apodization in transmit and receive, and cubic splines for interpolation. This is 19 times faster than our previous toolbox.

Arterial secondary blood flow patterns visualized with vector flow ultrasound

This study presents the first quantification and visualisation of secondary flow patterns with vector flow ultrasound. The first commercial implementation of the vector flow method Transverse Oscillation was used to obtain in-vivo, 2D vector fields in real-time. The hypothesis of this study was that the rotational direction is constant within each artery. Three data sets of 10 seconds were obtained from three main arteries in healthy volunteers. For each data set the rotational flow patterns were identified during the diastole. Each data set contains a 2D vector field over time and with the vector angles and velocity magnitudes the blood flow patterns were visualised with streamlines in Matlab (Mathworks, Natick, MA, USA). The rotational flow was quantified by the angular frequency for each cardiac cycle, and the mean rotational frequencies and standard deviations were calculated for the abdominal aorta f-1.30.4;-1.00.3;-0.90.2gHz, the common iliac artery f-0.40.1;-1.00.2;-0.40.1gHz, and the common carotid artery f0.80.3;1.40.3;0.40.1gHz. A positive sign indicates an anti-clockwise rotation, and a negative sign indicates clockwise rotation. The sign of the rotational directions within each artery were constant.

Arterial secondary blood flow patterns visualized with vector flow ultrasound

This study presents the first quantification and visualisation of secondary flow patterns with vector flow ultrasound. The first commercial implementation of the vector flow method Transverse Oscillation was used to obtain in-vivo, 2D vector fields in real-time. The hypothesis of this study was that the rotational direction is constant within each artery. Three data sets of 10 seconds were obtained from three main arteries in healthy volunteers. For each data set the rotational flow patterns were identified during the diastole. Each data set contains a 2D vector field over time and with the vector angles and velocity magnitudes the blood flow patterns were visualised with streamlines in Matlab (Mathworks, Natick, MA, USA). The rotational flow was quantified by the angular frequency for each cardiac cycle, and the mean rotational frequencies and standard deviations were calculated for the abdominal aorta f-1.30.4;-1.00.3;-0.90.2gHz, the common iliac artery f-0.40.1;-1.00.2;-0.40.1gHz, and the common carotid artery f0.80.3;1.40.3;0.40.1gHz. A positive sign indicates an anti-clockwise rotation, and a negative sign indicates clockwise rotation. The sign of the rotational directions within each artery were constant.
Articular Cartilage Thickness Measured with US is Not as Easy as It Appears: A Systematic Review of Measurement Techniques and Image Interpretation

Background: Theoretically, the high spatial resolution of US makes it well suited to monitor the decrease in articular cartilage thickness in osteoarthritis. A requirement is, however, that the borders of the cartilage are correctly identified and that the cartilage is measured under orthogonal insonation. If US measurements are compared to measurements with other techniques, they should be corrected for the higher sound speed in cartilage. Purpose: To study whether investigators correctly identify the articular cartilage, whether they insonate orthogonally, and whether they correct for sound speed. Materials and Methods: A literature search limited to the last 10 years of studies applying US to measure cartilage thickness. Results: 15 studies were identified and they referred to another 8 studies describing methods of thickness measurement. 11 of the 15 studies identified the superficial cartilage border incorrectly, and 6 applied oblique insonation. 2 of the 15 studies corrected for sound speed. Of the further 8 studies, one might correctly identify the superficial cartilage border, 4 applied oblique insonation, and none corrected for sound speed. Conclusion: We found that the majority of studies over the last 10 years, evaluating articular cartilage thickness with US, underestimated the cartilage thickness by not including the leading interface as part of the cartilage. Since the cartilage is relatively thin, this error is substantial. Some investigators also overestimated cartilage thickness by using oblique insonation of the cartilage. By not correcting for the high sound speed in cartilage, most investigators underestimated the cartilage thickness.
A Spiral And Discipline-Oriented Curriculum In Medical Imaging

This contribution describes and evaluates an experimental combination of a spiral and discipline-oriented curriculum implemented in the bachelor's and master's program in Medicine and Technology. The implementation in the master's program is in the form of a study line in Medical Imaging and Radiation Physics containing three disciplines: Imaging modalities, Radiation therapy and Image processing. The two imaging courses in the bachelor's program and the first imaging course in the master's program follow a spiral curriculum in which most disciplines are encountered in all courses, but in a gradually more advanced manner. The remaining courses in the master's program follow a discipline-oriented curriculum. From a practical point of view, the spiral course portfolio works well in an undergraduate environment, where the courses involved are to be taken by all students and in the order planned. However, in the master's program, such a tight schedule is impractical since students are likely to seek specialization. From a pedagogical point of view, the spiral curriculum is advantageous to use in the initial semesters where the teaching can be conducted so that the students can build on their intuitive understanding of the subject. The program was evaluated in terms of the progression in scientific demands in exam from course to course and in terms of the pattern of course selection by the students. The analysis was based on 96 students. The pattern of course selection was found to follow the intentions of the program, thus demonstrating high fulfillment of the learning outcomes.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Image Analysis and Computer Graphics, Department of Informatics and Mathematical Modeling, Copenhagen University Hospital
Authors: Wilhjelm, J. E. (Intern), Hanson, L. G. (Intern), Henneberg, K. (Intern), Jensen, J. A. (Intern), Larsen, R. (Intern), Lilseth, H. (Ekstern)
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Automatic REM Sleep Detection Associated with Idiopathic REM Sleep Behavior Disorder

Rapid eye movement sleep Behavior Disorder (RBD) is a strong early marker of later development of Parkinsonism. Currently there are no objective methods to identify and discriminate abnormal from normal motor activity during REM sleep. Therefore, a REM sleep detection without the use of chin electromyography (EMG) is useful. This is addressed by analyzing the classification performance when implementing two automatic REM sleep detectors. The first detector uses the electroencephalography (EEG), electrooculography (EOG) and EMG to detect REM sleep, while the second detector only uses the EEG and EOG. Method: Ten normal controls and ten age matched patients diagnosed with RBD were enrolled. All subjects underwent one polysomnographic (PSG) recording, which was manual scored according to the new sleep-scoring standard from the American Academy of Sleep Medicine. Based on the manual scoring, an automatic computerized REM detection algorithm has been implemented, using wavelet packet combined with artificial neural network. Results: When using the EEG, EOG and EMG modalities, it was possible to correctly classify REM sleep with an average Area Under Curve (AUC) equal to 0.900.03 for normal subjects and AUC = 0.810.05 for RBD subjects. The performance difference between the two groups was significant (p<0.05) in performance was observed when only using the EEG and EOG in neither of the groups. Conclusion: The overall result indicates that the EMG does not play an important role when classifying REM sleep.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Copenhagen University Hospital
Authors: Kempfner, J. (Intern), Sørensen, G. L. (Intern), Sørensen, H. B. D. (Intern), Jennum, P. (Ekstern)
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A visual, interactive introduction to basic and advanced magnetic resonance techniques

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Authors: Hanson, L. G. (Intern)
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Blood velocity estimation using ultrasound and spectral iterative adaptive approaches
This paper proposes two novel iterative data-adaptive spectral estimation techniques for blood velocity estimation using medical ultrasound scanners. The techniques make no assumption on the sampling pattern of the emissions or the depth samples, allowing for duplex mode transmissions where B-mode images are interleaved with the Doppler emissions. Furthermore, the techniques are shown, using both simplified and more realistic Field II simulations as well as in vivo data, to outperform current state-of-the-art techniques, allowing for accurate estimation of the blood velocity spectrum using only 30% of the transmissions, thereby allowing for the examination of two separate vessel regions while retaining an adequate updating rate of the B-mode images. In addition, the proposed methods also allow for more flexible transmission patterns,
as well as exhibit fewer spectral artifacts as compared to earlier techniques.

**General information**
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Lund University, Uppsala University
Authors: Gudmundson, E. (Ekstern), Jakobsson, A. (Ekstern), Jensen, J. A. (Intern), Stoica, P. (Ekstern)
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Scopus rating (2003): SJR 0.499 SNIP 0.966
Scopus rating (2002): SJR 0.615 SNIP 1.041
Scopus rating (2001): SJR 0.784 SNIP 1.216
Scopus rating (2000): SJR 0.527 SNIP 0.975
Comparison of Simulated and Measured Non-linear Ultrasound Fields

In this paper results from a non-linear AS (angular spectrum) based ultrasound simulation program are compared to water-tank measurements. A circular concave transducer with a diameter of 1 inch (25.4 mm) is used as the emitting source. The measured pulses are first compared with the linear simulation program Field II, which will be used to generate the source for the AS simulation. The generated non-linear ultrasound field is measured by a hydrophone in the focal plane. The second harmonic component from the measurement is compared with the AS simulation, which is used to calculate both fundamental and second harmonic fields. The focused piston transducer with a center frequency of 5 MHz is excited by a waveform generator emitting a 6-cycle sine wave. The hydrophone is mounted in the focal plane 118 mm from the transducer. The point spread functions at the focal depth from Field II and measurements are illustrated. The FWHM (full width at half maximum) values are 1.96 mm for the measurement and 1.84 mm for the Field II simulation. The fundamental and second harmonic components of the experimental results are plotted compared with the AS simulations. The RMS (root mean square) errors of the AS simulations are 7.19% and 10.3% compared with the fundamental and second harmonic components of the measurements.
Compound Imaging using Synthetic Aperture Sequential Beamforming

Synthetic Aperture Sequential Beamforming (SASB) is a technique with low complexity and the ability to yield a more uniform lateral resolution with range. However, the presence of speckle artifacts in ultrasound images degrades the contrast. In conventional imaging speckle is reduced by using spatial compounding at the cost of a reduced frame rate. The objective is to apply spatial compounding to SASB and evaluate if the images have a reduced speckle appearance and thereby an improved image quality in terms of contrast compared to ordinary SASB. Using the simulation software Field II, RF data are acquired for a phantom with cysts at different sizes and scattering levels. 192 scanlines are recorded for five steering angles (0, 2, 4 degrees) using a 192 element linear array transducer. SASB is performed for each angle using a rectangular grid in the second stage beamformation. After envelope detection the five second stage images are added to form the compounded image. Using a ProFocus scanner and the 8804 linear array transducer (BK Medical, Herlev, Denmark) measurements of a phantom containing water filled cysts are obtained to validate the simulation results. The setup is the same as in the simulations and SASB second stage beamformation data are processed offline for each of the five angles. Contrast-to-noise ratio (CNR) and speckle-to-noise ratio (SNR) are extracted for the compounded image and the reference image (ordinary SASB). CNR was calculated for the simulated cysts at depths of 40, 50, 60, 70 and 80 mm. On average the CNR was improved by 33.2% compared to the values obtained from the reference image. For regions of increasing depth SNR was on average increased by 9.3%. Results from the simulation were confirmed by calculations on the measured data. CNR of cysts at depths from 18 to 78 mm with a separation of 10 mm was on average improved by 45.9%. On average an improvement of 16.6% in SNR was obtained. The calculations along with visual inspection revealed larger improvements in deeper regions, and the compounded image for the measured phantom showed a 3 mm diameter cyst not detectable in the reference image. Compounding applied to SASB improves CNR and SNR results in images with a reduced speckle appearance. This was shown for simulations and confirmed on measured data.
Demonstration of a Vector Velocity Technique

With conventional Doppler ultrasound it is not possible to estimate direction and velocity of blood flow, when the angle of insonation exceeds 60–70°. Transverse oscillation is an angle independent vector velocity technique which is now implemented on a conventional ultrasound scanner. In this paper a few of the possibilities with transverse oscillation are demonstrated.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Hansen, P. M. (Ekstern), Pedersen, M. M. (Ekstern), Hansen, K. L. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
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Detection of arousals in Parkinson’s disease patients

Arousals from sleep are short awakenings, which can be identified in the EEG as an abrupt change in frequency. Arousals can occur in all sleep stages and the number and frequency increase with age. Frequent arousals during sleep result in sleep fragmentation and are associated with daytime sleepiness. Manual scoring of arousals is time-consuming and the inter-score agreement is highly varying especially for patients with sleep related disorders. The aim of this study was to design an arousal detection algorithm capable of detecting arousals from sleep, in both non-REM and REM sleep in patients suffering from Parkinson’s disease (PD). The proposed algorithm uses features from EEG, EMG and the manual sleep stage scoring as input to a feed-forward artificial neural network (ANN). The performance of the algorithm has been assessed using polysomnographic (PSG) recordings from a total of 8 patients diagnosed with PD. The performance of the algorithm was validated using the leave-one-out method resulting in a sensitivity of 89.8 % and a positive predictive value (PPV) of 88.8 %. This result is high compared to previous presented arousal detection algorithms.

Directional synthetic aperture flow imaging using a dual stage beamformer approach

A new method for directional synthetic aperture flow imaging using a dual stage beamformer approach is presented. The velocity estimation is angle independent and the amount of calculations is reduced compared to full synthetic aperture, but still maintains all the advantages at the same time. The new method has been studied using the Field II simulations and experimental flow rig measurements. A linear array transducer with 7 MHz center frequency is used, and 64 elements are active to transmit and receive signals. The data is processed in two stages. The first stage has a fixed focus point. In the second stage, focal points are considered as virtual sources and data is beamformed along the flow direction. Then the velocities are estimated by finding the spatial shift between two signals. In the experimental measurements the angle between the transmit beam and flow vessel was 70 and a laminar flow with a parabolic profile was generated by a flow rig. The flow with a peak velocity of 0.1 m/s was sampled at a pulse repetition frequency of 4 kHz. The signals were transmitted and received by the experimental scanner SARUS (Synthetic Aperture Realtime Ultrasound System). A relative standard deviation of 2.3% and bias of 6.4% at 65 were achieved in the simulations, and 4.3% and 4.2% for the experimental measurements. A color flow map image was made in 48 emissions corresponding to a frame rate of 83 frames/s.
Dopplerultryldskanning af abdomen

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Hansen, K. L. (Intern), Pedersen, M. M. (Intern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
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Examples of Vector Velocity Imaging

To measure blood flow velocity in vessels with conventional ultrasound, the velocity is estimated along the direction of the emitted ultrasound wave. It is therefore impossible to obtain accurate information on blood flow velocity and direction, when the angle between blood flow and ultrasound wave approaches 90°. The majority of the vessels in the human body is parallel to the surface and therefore positioned in a way that prevents proper placement and angulation of the transducer, when the velocity and direction of blood flow is to be estimated. Different techniques to circumvent this problem have been tried including Transverse Oscillation. This method has been tested in computer simulations, on flow phantoms and in-vivo, and subsequently validated against MRI angiography. Transverse Oscillation is now implemented in a commercial ultrasound scanner from BK Medical (UltraView). In this article UltraView is demonstrated on the carotid artery, jugular vein and femoral vein that all runs almost parallel to the skin and thus is angled near 90° to the ultrasound waves. Arterial and venous simple and complex flow with formation of vortices is demonstrated by scanning on the longitudinal axis with a 90° angle on the vessel. Moreover secondary flow in the abdominal aorta is illustrated by scanning on the transversal axis.

Finite Element Implementation of a Structurally-Motivated Constitutive Relation for the Human Abdominal Aortic Wall with and without Aneurysms

The structural integrity of the abdominal aorta is maintained by elastin, collagen, and vascular smooth muscle cells. Changes with age in the structure can lead to development of aneurysms. This paper presents initial work to capture these changes in a finite element model (FEM) of a structural-ly-motivated anisotropic constitutive relation for the “four
fiber family” arterial model. First a 2D implementation is used for benchmarking the FEM implementation to fitted biaxial stress-strain data obtained experimentally from four different groups of persons; 19-29 years, 30-60 years, 61-79 years and abdominal aortic aneurysm (AAA) patients. Next the constitutive model is implemented in an anisotropic 3D FEM formulation for future simulation of intact aortic geometries. The 2D simulations of the biaxial test experiment show good agreement with experimental data with a standard deviation below 0.5% in all cases. The maximum axial and hoop stress in the group of AAA patients was 94.9 kPa (±0.283 kPa) and 94.3 kPa (±0.224 kPa) at maximum stretch ratios of 1.043 and 1.037, respectively. In the 3D simulations, the maximum stress is also found to occur in the AAA patient group, with the highest stress in the circumferential direction (275 kPa). Comparison with an already published isotropic model indicates that the latter underestimates the peak stress significantly. Based on these results it is concluded that the four fiber family model has been successfully implemented into a 3D anisotropic finite element model and that this model can provide more accurate insight into the stress conditions in aortic aneurysms.

**Generative probabilistic models extend the scope of inferential structure determination**

Conventional methods for protein structure determination from NMR data rely on the ad hoc combination of physical forcefields and experimental data, along with heuristic determination of free parameters such as weight of experimental data relative to a physical forcefield. Recently, a theoretically rigorous approach was developed which treats structure determination as a problem of Bayesian inference. In this case, the forcefields are brought in as a prior distribution in the form of a Boltzmann factor. Due to high computational cost, the approach has been only sparsely applied in practice. Here, we demonstrate that the use of generative probabilistic models instead of physical forcefields in the Bayesian formalism is not only conceptually attractive, but also improves precision and efficiency. Our results open new vistas for the use of sophisticated probabilistic models of biomolecular structure in structure determination from experimental data.
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Scopus rating (2013): SJR 1.103 SNIP 0.937 CiteScore 2.41
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Scopus rating (2012): SJR 1.117 SNIP 1.046 CiteScore 2.28
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Generic Single-Channel Detection of Absence Seizures

A long-term EEG-monitoring system, which automatically marks seizure events, is useful for diagnosing and treating epilepsy. A generic method utilizing the low interand intra-patient variabilities in EEG-characteristics during absence seizures is proposed. This paper investigates if the spike-and-wave behaviour during absence seizures is so distinct that a single-channel implementation is possible. 18 channels of scalp electroencephalography (EEG), from 19 patients suffering from childhood absence epilepsy, are analysed individually. The characteristics of the seizures are captured using the energy content of wavelet transform subbands and classified using a support vector machine. To ease the evaluation of the method, we present a new graphical visualization of the performance based on the topographical distribution on the scalp. The presented seizure detection method shows that the best result is obtained for the derivation F7-FP1. Using this channel a sensitivity of 99.1 %, positive predictive value of 94.8 %, mean detection latency of 3.7 s, and false detection rate value of 0.5/h was obtained. The topographical visualization of the results clearly shows that the frontal, midline, and parietal channels outperform detection based on the channels in the occipital region.

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Organisations: Biomedical Engineering, Department of Electrical Engineering, Department of Informatics and Mathematical Modeling, Technical University of Denmark, Copenhagen University Hospital, University of Copenhagen
Authors: Petersen, E. B. (Ekstern), Duun-Henriksen, J. (Intern), Mazzaretto, A. (Intern), Kjær, T. W. (Ekstern), Thomsen, C. E. (Ekstern), Sørensen, H. B. D. (Intern)
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Image processing in medical ultrasound
This Ph.D project addresses image processing in medical ultrasound and seeks to achieve two major scientific goals: First to develop an understanding of the most significant factors influencing image quality in medical ultrasound, and secondly to use this knowledge to develop image processing methods for enhancing the diagnostic value of medical ultrasound. The project is an industrial Ph.D project co-sponsored by BK Medical ApS., with the commercial goal to improve the image quality of BK Medicals scanners. Currently BK Medical employ a simple conventional delay-and-sum beamformer to generate B-mode images. This is a simple and well understood method that allows dynamic receive focusing for an improved resolution, the drawback is that only optimal focus is achieved in the transmit focus point. Synthetic aperture techniques can overcome this drawback, but at a cost of increased system complexity and computational demands. The development goal of this project is to implement, Synthetic Aperture Sequential Beamforming (SASB), a new synthetic aperture (SA) beamforming method. The benefit of SASB is an improved image quality compared to conventional beamforming and a reduced system complexity compared to conventional synthetic aperture techniques. The implementation is evaluated using both simulations and measurements for technical and clinical evaluations. During the course of the project three sub-projects were conducted. The first project were development and implementation of a real-time data acquisition system. The system were implemented using the commercial available 2202 ProFocus BK Medical ultrasound scanner equipped with a research interface and a standard PC. The main feature of the system is the possibility to acquire several seconds of interleaved data, switching between multiple imaging setups. This makes the system well suited for development of new processing methods and for clinical evaluations, where acquisition of the exact same scan location for multiple methods is important. The second project addressed implementation, development and evaluation of SASB using a convex array transducer. The evaluation were performed as a three phased clinical trial. In the first phase, the prototype phase, the technical performance of SASB were evaluated using the ultrasound simulation software Field II and Beamformation toolbox III (BFT3) and subsequently evaluated using phantom and in-vivo measurements. The technical performance were compared to conventional beamforming and gave motivation to continue to phase two. The second phase evaluated the clinical performance of abdominal imaging in a pre-clinical trial in
comparison with conventional imaging, and were conducted as a double blinded study. The result of the pre-clinical trial motivated for a larger scale clinical trial. Each of the two clinical trials were performed in collaboration with Copenhagen University Hospital, Rigshospitalet, and Copenhagen University, Department of Biostatistic. Evaluations were performed by medical doctors and experts in ultrasound, using the developed Image Quality assessment program (IQap). The study concludes that the image quality in terms of spatial resolution, contrast and unwanted artifacts is statistically better using SASB imaging than conventional imaging. The third and final project concerned simulation of the acoustic field for high quality imaging systems. During the simulation study of SASB, it was noted that the simulated results did not predict the measured responses with an appropriate confidence for simulated system performance evaluation. Closer inspection of the measured transducer characteristics showed a sever time-offlight phase error, sensitivity deviations, and deviating frequency responses between elements. Simulations combined with experimentally determined element pulse echo wavelets, showed that conventional simulation using identical pulse echo wavelets for all elements is too simplistic to capture the true performance of the imaging system, and that the simulations can be improved by including individual pulse echo wavelets for each element. Using the improved model the accuracy of the simulated response is improved significantly and is useful for simulated system evaluation. It was further shown that conventional imaging is less sensitive to phase and sensitivity errors than SASB imaging. This shows that for simulated performance evaluation a realistic simulation model is important for a reliable evaluation of new high quality imaging systems.

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Authors: Hemmsen, M. C. (Intern), Jensen, J. A. (Intern), Kortbæk, J. (Ekstern), Martins, B. (Ekstern)
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Initial studies on the variations of load-displacement curves of in vivo human healthy heel pads
The aim of this study was to quantify on the measurement variation of in vivo load-displacement curves by using a group of human healthy heel pads. The recordings were done with a compression device measuring force and displacement. Twenty three heel pads, one from each of 23 subjects aged 20-35 years, were tested. The load-displacement curves showed the hysteresis, typical for a visco-elastic tissue. Seven load-displacement curves were measured for each subject. Each hysteresis was approximated by a 3rd degree polynomial, which in turn was described by two parameters: the slope and the average curvature. No statistically significant tendency (increasing or decreasing) were found for the seven polynomials (chi² test, P-values of 0.81 and 0.17 for the two parameters, respectively). The study revealed no systematic error in the recorded load-displacement curves. The mean slope and the average curvature for the 23 subjects were found to be 6.02±1.54 N/mm and 0.02±0.01, respectively. The new apparatus shows its reliability for further clinical investigations.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, University of Florence, Copenhagen University Hospital
Authors: Matteoli, S. (Intern), Wilhjelm, J. E. (Intern), Virga, A. (Ekstern), Corvi, A. (Ekstern), Torp-Perdersen, S. T. (Ekstern)
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In-vivo studies of new vector velocity and adaptive spectral estimators in medical ultrasound

In this PhD project new ultrasound techniques for blood flow measurements have been investigated in-vivo. The focus has mainly been on vector velocity techniques and four different approaches have been examined: Transverse Oscillation, Synthetic Transmit Aperture, Directional Beamforming and Plane Wave Excitation. Furthermore two different adaptive spectral estimators have been investigated: Blood spectral Power Capon method (BPC) and Blood Amplitude and Phase Estimation method (BAPES). The novel techniques investigated in this thesis are developed to circumvent some of the main limitations in conventional Doppler ultrasound. That is angle dependency, reduced temporal resolution and low frame rate. Transverse Oscillation, Synthetic Transmit Aperture and Directional Beamforming can estimate the blood velocity angle independently. The three methods were validated in-vivo against magnetic resonance phase contrast angiography when measuring stroke volumes in simple vessel geometry on 11 volunteers. Using linear regression and Bland-Altman analyses good agreements were found, indicating that vector velocity methods can be used for quantitative blood flow measurements. Plane Wave Excitation can estimate blood velocities angle independently with a high frame rate. Complex vessel geometries in the cardiovascular system were explored in-vivo on four volunteers using the technique. Flow patterns previously visualized with magnetic resonance angiography and predicted by models of computational fluid dynamics, were shown for the first time with ultrasound. Additionally, new information on complex flow patterns in bifurcations and around venous valves was discovered. BPC and BAPES are adaptive spectral estimators which can produce spectrograms with a high temporal resolution. Spectrograms obtained in-vivo with the two techniques on ten volunteers were evaluated quantitatively and qualitatively and compared to the conventional spectral Doppler method. Descriptive statistics, kappa statistics and multiple t-tests were performed and it was shown that BAPES and BPC can produce useful spectrograms with a narrower observation window compared to the conventional spectral Doppler method. The thesis shows, that novel information can be obtained with vector velocity methods providing quantitative estimates of blood flow and insight in to the complexity of fluid dynamics. This could give the clinician a new tool in assessment and treatment of cardiovascular diseases. Also solutions to produce spectrograms with fewer emissions per estimate were given. This could potentially bring improvements to spectral blood estimation as an increase of the temporal resolution of the spectrogram or as an increase of the frame rate for the interleaved B-mode images.

Measurements of the persistent singlet state of N2O in blood and other solvents—Potential as a magnetic tracer

The development of hyperpolarized tracers has been limited by short nuclear polarization lifetimes. The dominant relaxation mechanism for many hyperpolarized agents in solution arises from intramolecular nuclear dipole–dipole coupling modulated by molecular motion. It has been previously demonstrated that nuclear spin relaxation due to this mechanism can be removed by storing the nuclear polarization in long-lived, singlet-like states. In the case of N2O, storing the polarization of the nitrogen nuclei has been shown to substantially increase the polarization lifetime. The feasibility of utilizing N2O as a tracer is investigated by measuring the singlet-state lifetime of the N2O when dissolved in a variety of solvents including whole blood. Comparison of the singlet lifetime to longitudinal relaxation and between protonated and
Measuring the effect of demagnetization in stacks of gadolinium plates using the magnetocaloric effect

The effect of demagnetization in a stack of gadolinium plates is determined experimentally by using spatially resolved measurements of the adiabatic temperature change due to the magnetocaloric effect. The number of plates in the stack, the spacing between them and the position of the plate on which the temperature is measured are varied. The orientation of the magnetic field is also varied. The measurements are compared to a magnetostatic model previously described. The results show that the magnetocaloric effect, due to the change in the internal field, is sensitive to the stack configuration and the orientation of the applied field. This may have significant implications for the construction of a magnetic cooling device.

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Motion tracking from gradient induced signals in electrode recordings

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Authors: Vestergaard, M. B. (Ekstern), Schulz, J. (Ekstern), Turner, R. (Ekstern), Hanson, L. G. (Intern)
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Neural mechanism of activity spread in the cat motor cortex and its relation to the intrinsic connectivity

NON TECHNICAL SUMMARY: The motor cortex (MCx) is an important brain region that initiates and controls voluntary movements. Neurons in MCx are anatomically connected by recurrent (feedback) networks. This connectivity pattern allows neurons to communicate reciprocally with each other potentially over distances of 6–7 mm. However, how far such neural activity is actually communicated was not known. We found that the activity of a small cortical point, about 0.4 mm in radius, activates a surrounding territory of approximately 7.22 mm² in area. This is smaller than the area covered by the anatomical connections, indicating the existence of mechanisms that limit the spread of activity. Nonetheless, such an area contains the representations of a variety of muscles spanning several joints, from digits to shoulder. These results support the hypothesis that the MCx controls the forelimb musculature in small synergistic groups, rather than singly and separately. Understanding motor cortical physiology is important for the design of neuro-prostheses to interface the brain to paralysed muscles.

ABSTRACT: Motor cortical points are linked by intrinsic horizontal connections having a recurrent network topology. However, it is not known whether neural activity can propagate over the area covered by these intrinsic connections and whether there are spatial anisotropies of synaptic strength, as opposed to synaptic density. Moreover, the mechanisms by which activity spreads have yet to be determined. To address these issues, an 8 x 8 microelectrode array was inserted in the forelimb area of the cat motor cortex (MCx). The centre of the array had a laser etched hole ∼500 μm in diameter. A microiontophoretic pipette, with a tip diameter of 2–3 μm, containing bicuculline methiodide (BIC) was inserted in the hole and driven to a depth of 1200–1400 μm from the cortical surface. BIC was ejected for ∼2 min from the tip of the micropipette with positive direct current ranging between 20 and 40 nA in different experiments. This produced spontaneous nearly periodic bursts (0.2–1.0 Hz) of multi-unit activity in a radius of about 400 μm from the tip of the micropipette. The bursts of neural activity spread at a velocity of 0.11–0.24 m s⁻¹ (mean = 0.14 mm ms⁻¹, SD = 0.05) with decreasing amplitude. The area activated was on average 7.22 mm² (SD = 0.91 mm²), or ∼92% of the area covered by the recording array. The mode of propagation was determined to occur by progressive recruitment of cortical territory, driven by a central locus of activity of some 400 μm in radius. Thus, activity did not propagate as a wave. Transection of the connections between the thalamus and MCx did not significantly alter the propagation velocity or the size of the recruited area, demonstrating that the bursts spread along the routes of intrinsic cortical connectivity. These experiments demonstrate that neural activity initiated within a small motor cortical locus (400 μm in radius) can recruit a relatively large neighbourhood in which a variety of muscles acting at several forelimb joints are represented. These results support the hypothesis that the MCx controls the forelimb musculature in an integrated and anticipatory manner based on a recurrent network topology.
New interpretation of arterial stiffening due to cigarette smoking using a structurally motivated constitutive model

Cigarette smoking is the leading self-inflicted risk factor for cardiovascular diseases; it causes arterial stiffening with serious sequelae including atherosclerosis and abdominal aortic aneurysms. This work presents a new interpretation of arterial stiffening caused by smoking based on data published for rat pulmonary arteries. A structurally motivated "four fiber family" constitutive relation was used to fit the available biaxial data and associated best-fit values of material parameters were estimated using multivariate nonlinear regression. Results suggested that arterial stiffening caused by smoking was reflected by consistent increase in an elastin-associated parameter and moreover by marked increase in the collagen-associated parameters. That is, we suggest that arterial stiffening due to cigarette smoking appears to be isotropic, which may allow simpler phenomenological models to capture these effects using a single stiffening parameter similar to the approach in isotropic continuum damage mechanics. There is a pressing need, however, for more detailed histological information coupled with more complete biaxial mechanical data for a broader range of systemic arteries.

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Authors: Enevoldsen, M. S. (Intern), Henneberg, K. (Intern), Jensen, J. A. (Intern), Lönn, L. (Ekstern), Humphrey, J. (Ekstern)
Non-linear Imaging using an Experimental Synthetic Aperture Real Time Ultrasound Scanner

This paper presents the first non-linear B-mode image of a wire phantom using pulse inversion attained via an experimental synthetic aperture real-time ultrasound scanner (SARUS). The purpose of this study is to implement and validate non-linear imaging on SARUS for the further development of new non-linear techniques. This study presents non-linear and linear B-mode images attained via SARUS and an existing ultrasound system as well as a Field II simulation. The non-linear image shows an improved spatial resolution and lower full width half max and -20 dB resolution values compared to linear B-mode imaging on the other systems. For the second scatterer at 47 mm depth the -20 dB resolution value for the non-linear SARUS image is 0.9907 mm and 1.1970 mm for the linear image from SARUS.

Non-linear Ultrasound Imaging

The theory for modeling non-linear acoustic propagation is addressed in the dissertation. The solutions to both the linear and non-linear wave equations have been found by an angular spectrum approach (ASA), in which an analytical expression can be derived. This makes the calculation complete without iteration steps. The ASA is implemented in combination with Field II and extended to simulate the pulsed ultrasound fields. The simulated results from a linear array transducer are made by the ASA based on Field II, and by a released non-linear simulation program - Abersim, respectively. The calculation speed of the ASA is increased approximately by a factor of 140. For the second harmonic point spread function the error of the full width is 1.5% at -6 dB and 6.4% at -12 dB compared to Abersim. To further investigate the linear and non-linear ultrasound fields, hydrophone measurements are performed under water by two geometrical focused piston transducers. It can be seen that the time pulses measured from a 0.5 inch diameter transducer and linearly simulated using the ASA are fairly comparable. The root mean square (RMS) error for the second harmonic field simulated by the ASA is 10.3% relative to the measurement from a 1 inch diameter transducer. A preliminary study for harmonic imaging using synthetic aperture sequential beamforming (SASB) has been demonstrated. A wire phantom underwater measurement is made by an experimental synthetic aperture real-time ultrasound scanner (SARUS) with a linear array transducer. The second harmonic imaging is obtained by a pulse inversion technique. The received data is beamformed by the SASB using a Beamformation Toolbox. In the measurements the lateral resolution at -6 dB is improved by 66% compared to the conventional imaging algorithm. There is also a 35% improvement for the lateral resolution at -6 dB compared with the sole harmonic imaging and a 46% improvement compared with merely using the SASB.
On the comparison between MRI and US imaging for human heel pad thickness measurements.
The human heel pad thickness, defined as the shortest distance between the calcaneus and heel skin, is one of the intrinsic factors which must be taken into account when investigating the biomechanics of the heel pad. US and MRI are the preferable imaging modalities used to measure the heel pad thickness as they are both ionizing-free radiations. The aim of this paper is to measure the bone-to-skin distance of nine heel pad phantoms from MRI and US images, and to compare the results with a true value (TV) in order to find the errors. Paired sample t-test was used to compare the measurements. Results showed a statistically significant difference between MRI and US1540 (P-value=0.005), and between TV and US1540 (P-value=0.013). Furthermore, results showed no statistically significant difference between US1530 or MRI and TV (P-value=0.103 and P-value=0.358, respectively), and between MRI and US1530 (P-value=0.402). Results confirm the necessity to investigate on the real speed of sound for the heel pad tissues, in order to have realistic measurements when dealing with human heel pads.

On the mechanical behavior of healthy and aneurysmal abdominal aorta

Pathophysiology of tonic muscle activation during epileptic seizures: Abstract of paper SC223
Tonic seizures and the tonic phase of tonic-clonic epileptic seizures are defined as a “sustained tonic” muscle contraction. Visual inspection of the surface electromyograms (sEMG) during seizures significantly contributed to a better understanding and diagnosis of several seizure types. However, quantitative analysis of the sEMG during the epileptic seizures has received surprisingly little attention. The aim of our study was to elucidate the pathophysiology of the tonic muscle activation during seizures. SEMG was recorded from the deltoid muscles, during 58 seizures from 18 patients (9 with generalised tonic and 9 with tonic-clonic seizures). 18 age and gender matched normal controls simulated 90 generalised tonic seizures. We calculated the root mean square (RMS) of the amplitudes, the median frequency (MF), the relative power (RP) and the coherence. During the epileptic seizures (especially the tonic ones) there was a significant
shift towards higher frequencies, expressed by increase in the MF and RP 100-500Hz. The amplitude characteristic (RMS) was significantly higher during the tonic phase of the tonic-clonic seizures as compared to the simulated ones, while the RMS of the tonic seizures was significantly lower than the simulated ones. The coherence was significantly higher during the epileptic seizures. The mechanism of muscle activation during epileptic seizures is different from the physiological one. Furthermore the sustained muscle activation during the tonic phase of tonic-clonic seizures is different from that during tonic seizures suggesting that distinct efferent neural pathways are involved in the generation of the sustained muscle contraction during tonic and tonic-clonic seizures.
Patterns of muscle activation during generalized tonic and tonic–clonic epileptic seizures

Purpose: Tonic seizures and the tonic phase of tonic–clonic epileptic seizures are defined as “sustained tonic” muscle contraction lasting a few seconds to minutes. Visual inspection of the surface electromyogram (EMG) during seizures contributed considerably to a better understanding and accurate diagnosis of several seizure types. However, quantitative analysis of the surface EMG during the epileptic seizures has received surprisingly little attention until now. The aim of our study was to elucidate the pathomechanism of the tonic muscle activation during epileptic seizures. Methods: Surface EMG was recorded from the deltoid muscles, on both sides, during 63 seizures from 20 patients with epilepsy (10 with generalized tonic and 10 with tonic–clonic seizures). Twenty age- and gender-matched normal controls simulated 100 generalized tonic seizures. To characterize the signal properties we calculated the root mean square (RMS) of the amplitudes, the median frequency (MF), and the coherence. Based on the spectrograms of both epileptic and simulated seizures, we chose to determine the relative spectral power (RP) in the higher (100–500 Hz) frequency domain. Key Findings: During the tonic seizures there was a significant shift toward higher frequencies, expressed by an increase in the MF and the RP (100–500 Hz). The amplitude characteristic of the signal (RMS) was significantly higher during the tonic phase of the tonic–clonic seizures as compared to the simulated ones, whereas the RMS of the tonic seizures was significantly lower than the simulated ones. The EMG–EMG coherence was significantly higher during the epileptic seizures (both types) as compared to the simulated ones. Significance: Our results indicate that the mechanism of muscle activation during epileptic seizures is different from the physiologic one. Furthermore the sustained muscle activation during the tonic phase of tonic–clonic seizures is different from that during tonic seizures: The tonic phase of tonic–clonic seizures is characterized by increased amplitude of the signal, whereas tonic seizures are produced by a significant increase in the frequency of the signal.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Danish Epilepsy Center
Authors: Conradsen, I. (Intern), Wolf, P. (Ekstern), Sams, T. (Intern), Sørensen, H. B. D. (Intern), Beniczky, S. (Ekstern)
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.646 SNIP 2 CiteScore 4.52
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.66 SNIP 1.878 CiteScore 4.7
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.525 SNIP 2.008 CiteScore 4.52
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Performance Evaluation of a Synthetic Aperture Real-Time Ultrasound System

This paper evaluates the signal-to-noise ratio, the time stability, and the phase difference of the sampling in the experimental ultrasound scanner SARUS: A synthetic aperture, real-time ultrasound system. SARUS has 1024 independent transmit and receive channels and is capable of handling 2D probes for 3D ultrasound imaging. It samples at 12 bits per sample and has a sampling rate of 70 MHz with the possibility of decimating the sampling frequency at the input. SARUS is capable of advanced real-time computations such as synthetic aperture imaging. The system is built using fieldprogrammable gate arrays (FPGAs) making it very flexible and allowing implementation of other real-time ultrasound processing methods in the future. For conventional B-mode imaging, a penetration depth around 7 cm for a 7 MHz transducer is obtained (signal-to-noise ratio of 0 dB), which is comparable to commercial ultrasound scanners. Furthermore, the jitter between successive acquisitions for flow estimation is around 1.41 ps with a standard deviation of 48.3 ps. This has a negligible impact (0.03%) on the flow measurement. Additionally, for the phase of the sampling, it is shown that the small differences between different channels (on average 111 ps for a 70 MHz sampling clock) are deterministic and can therefore be compensated for.
Performance of Synthetic Aperture Compounding for in-vivo imaging

A method for synthetic aperture compounding (SAC) is applied to data from water tank measurements, data from a tissue-mimicking phantom, and clinical data from the abdomen of a healthy 27 year old male. Further, using this method compounding can be obtained without any loss in temporal resolution. The water tank measurements reveal an improved detail resolution of 45% when comparing SAC to conventional compounding and an improvement of 22%, when comparing synthetic aperture (SA) imaging. The cystic resolution at 12 dB is improved by 50% and 12% when comparing SAC to conventional compounding and SA imaging respectively. The tissue phantom measurements show a 3.2 dB improvement of the normalized information density (NID) when comparing images formed using SAC to conventional compound images and an improvement of 2 dB for a comparison between SAC imaging and SA imaging. For the clinical images, contrast ratios (CR) are computed between regions in the portal and hepatic veins and the surrounding tissue. An average improvement of 15% is obtained when comparing SAC images to SA images without compounding.

Preliminary comparison between real-time in-vivo spectral and transverse oscillation velocity estimates

Spectral velocity estimation is considered the gold standard in medical ultrasound. Peak systole (PS), end diastole (ED), and resistive index (RI) are used clinically. Angle correction is performed using a flow angle set manually. With Transverse Oscillation (TO) velocity estimates the flow angle, peak systole (PSTO), end diastole (EDTO), and resistive index (RITO) are estimated. This study investigates if these clinical parameters are estimated equally good using spectral and TO data. The right common carotid arteries of three healthy volunteers were scanned longitudinally. Average TO flow angles and std were calculated (52±18 ; 55±23 ; 60±16)°. Spectral angles (52 ; 56 ; 52)° were obtained from the B-mode images. Obtained values are: PSTO (76±15 ; 89±28 ; 77±7) cm/s, spectral PS (77 ; 110 ; 76) cm/s, EDTO (10±3 ; 14±8 ; 15±3) cm/s, spectral ED (18 ; 13 ; 20) cm/s, RITO (0.87±0.05 ; 0.79±0.21 ; 0.79±0.06), and spectral RI (0.77 ; 0.88 ; 0.73). Vector angles are within ±two std of the spectral angle. TO velocity estimates are within ±three std of the spectral estimates. RITO are within ±two std of the spectral estimates. Preliminary data indicates that the TO and spectral velocity estimates are equally good. With TO there is no manual angle setting and no flow angle limitation. TO velocity estimation can also automatically handle situations where the angle varies over the cardiac cycle. More detailed temporal and spatial vector estimates with diagnostic potential are available with the TO velocity estimation.
Preliminary Experimental Verification of Synthetic Aperture Flow Imaging Using a Dual Stage Beamformer Approach

A dual stage beamformer method for synthetic aperture flow imaging has been developed. The motivation is to increase the frame rate and still maintain a beamforming quality sufficient for flow estimation that is possible to implement in a commercial scanner. With the new method high resolution images can be obtained continuously, which will highly increase the frame rate. The flow velocity is estimated by using a time-domain cross-correlation technique. The approach is investigated through experiments with the SARUS scanner (Synthetic Aperture Real-time Ultrasound System). A flow rig generates a parabolic laminar flow, and the SARUS scanner is used for acquiring the data from individual channels of the transducer. The experimental results showed that increasing the number of imaging lines used for the estimation from 4 to 24 reduces the standard deviation from 21% to 7.6%. The parameter study showed that the number of crosscorrelation functions for averaging and length of the search range influence the performance.

Preliminary In-Vivo evaluation of Synthetic Aperture Sequential Beamformation using a multielement convex array

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps, Copenhagen University Hospital, University of Copenhagen
Authors: Hemmsen, M. C. (Intern), Hansen, P. M. (Ekstern), Lange, T. (Ekstern), Hansen, J. M. (Intern), Nikolov, S. I. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
Recent advances in blood flow vector velocity imaging

A number of methods for ultrasound vector velocity imaging are presented in the paper. The transverse oscillation (TO) method can estimate the velocity transverse to the ultrasound beam by introducing a lateral oscillation in the received ultrasound field. The approach has been thoroughly investigated using both simulations, flow rig measurements, and in-vivo validation against MR scans. The TO method obtains a relative accuracy of 10% for a fully transverse flow in both simulations and flow rig experiments. In-vivo studies performed on 11 healthy volunteers comparing the TO method with magnetic resonance phase contrast angiography (MRA) revealed a correlation between the stroke volume estimated by TO and MRA of 0.91 (p<0.01) with an equation for the line of regression given as: MRA = 1.1 · TO - 0.4 ml. Several clinical examples of complex flow in e.g. bifurcations and around valves have been acquired using a commercial implementation of the method (BK Medical ProFocus Ultraview scanner). A range of other methods are also presented. This includes synthetic aperture imaging using either spherical or plane waves with velocity estimation performed with directional beamforming or speckle tracking. The key advantages of these techniques are very fast imaging that can attain an order of magnitude higher precision than conventional methods. SA flow imaging was implemented on the experimental scanner RASMUS using an 8-emission spherical emission sequence and reception of 64 channels on a BK Medical 8804 transducer. This resulted in a relative standard deviation of 1.2% for a fully transverse flow. Plane wave imaging was also implemented on the RASMUS scanner and a 100 Hz frame rate was attained. Several vector velocity image sequences of complex flow were acquired, which demonstrates the benefits of fast vector flow imaging. A method for extending the 2D TO method to 3D vector velocity estimation is presented and the implications for future vector velocity imaging is indicated.
Scalable Intersample Interpolation Architecture for High-channel-count Beamformers

Modern ultrasound scanners utilize digital beamformers that operate on sampled and quantized echo signals. Timing precision is of essence for achieving good focusing. The direct way to achieve it is through the use of high sampling rates, but that is not economical, so interpolation between echo samples is used. This paper presents a beamformer architecture that combines a band-pass filter-based interpolation algorithm with the dynamic delay-and-sum focusing of a digital beamformer. The reduction in the number of multiplications relative to a linear perchannel interpolation and band-pass per-channel interpolation architecture is respectively 58% and 75% beamformer for a 256-channel beamformer using 4-tap filters. The approach allows building high channel count beamformers while maintaining high image quality due to the use of sophisticated intersample interpolation.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps
Authors: Tomov, B. G. (Intern), Nikolov, S. I. (Ekstern), Jensen, J. A. (Intern)
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Focusing, Beamforming, Interpolation

Second harmonic imaging using synthetic aperture sequential beamforming
The paper investigates Second Harmonic Imaging (SHI) using Synthetic Aperture Sequential Beamforming (SASB). The investigation is made by an experimental Synthetic Aperture Real-time Ultrasound System (SARUS). A linear array transducer is used to scan 4 wires at the image depths of 22.5, 47.5, 72.5, 97.5 mm, respectively. Three different experiments are made using three different transmit foci at 10 mm, 25 mm and 50 mm. A 2-cycle sine wave with a center frequency of 5 MHz is used as the excitation. The SHI is achieved by using Pulse Inversion (PI) technique. The data received with and without PI from SARUS are beamformed using Dynamic Receive Focusing (DRF) and SASB by a Beamformation Toolbox. The Full Widths at Half Maximum (FWHM) in both the lateral and axial directions for these four wire targets using different imaging algorithms (DRF, DRF+SHI, SASB and SASB+SHI) are calculated and shown in the paper. The Full Width at One Tenth Maximum (FWOTM) is also investigated. By combining SASB and SHI, the lateral resolution is improved by 66%, 35% and 46% for FWHM, and 52%, 20% and 29% for FWOTM, compared to DRF, DRF+SHI and SASB, respectively. The axial resolution is improved 24% on average by SHI.

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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps
Authors: Du, Y. (Intern), Rasmussen, J. (Intern), Jensen, H. (Ekstern), Jensen, J. A. (Intern)
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Main Research Area: Technical/natural sciences
Seizure Onset Detection based on one sEMG channel

We present a new method to detect seizure onsets of tonic-clonic epileptic seizures based on surface electromyography (sEMG) data. The proposed method is generic and based on a single channel making it ideal for a small detection or monitoring device. The sEMG signal is high-pass filtered with a Butterworth filter with a cut-off frequency of 150 Hz. The number of zero-crossings with a hysteresis of ±50μV is the only feature extracted. The number of counts in a window of 1 second and the number of windows to make a detection is tested with a leave-one-out method. On 6 patients the method performs with a sensitivity of 100%, a median latency of 7.6 seconds and a median false detection rate of 0.04/h.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, University of Southern Denmark, DELTA, Danish Epilepsy Center
Authors: Conradsen, I. (Intern), Beniczky, S. (Ekstern), Hoppe, K. (Ekstern), Wolf, P. (Ekstern), Sams, T. (Intern), Sørensen, H. B. D. (Intern)
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Simulation of shadowing effects in ultrasound imaging from computed tomography images

General information
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Organisations: Section for Management Systems, National Institute of Aquatic Resources, Section for Vessels, Biomedical Engineering, Department of Electrical Engineering
Authors: Pham, A. H. (Intern), Stage, B. (Intern), Hemmsen, M. C. (Intern), Lundgren, B. (Intern), Pedersen, M. M. (Intern), Jensen, J. A. (Intern)
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Simulation of ultrasound backscatter images from fish

The objective of this work is to investigate ultrasound (US) backscatter in the MHz range from fish to develop a realistic and reliable simulation model. The long term objective of the work is to develop the needed signal processing for fish species differentiation using US. In in-vitro experiments, a cod (Gadus morhua) was scanned with both a BK Medical ProFocus 2202 ultrasound scanner and a Toshiba Aquilion ONE computed tomography (CT) scanner. The US images of the fish were compared with US images created using the ultrasound simulation program Field II. The center frequency of the transducer is 10 MHz and the Full Width at Half Maximum (FWHM) at the focus point is 0.54 mm in the lateral direction. The transducer model in Field II was calibrated using a wire phantom to validate the simulated point spread function. The inputs to the simulation were the CT image data of the fish converted to simulated scatter maps. The positions of the point scatterers were assumed to be uniformly distributed. The scatter amplitudes were generated with a new method based on the segmented CT data in Hounsfield Units and backscatter data for the different types of tissues from the literature. The simulated US images reproduce most of the important characteristics of the measured US image.

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Organisations: Section for Management Systems, National Institute of Aquatic Resources, Section for Vessels, Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging
Authors: Pham, A. H. (Intern), Stage, B. (Intern), Hemmsen, M. C. (Intern), Lundgren, B. (Intern), Pedersen, M. M. (Intern), Pedersen, T. B. (Ekstern), Jensen, J. A. (Intern)
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Series: Proceedings of S P I E - International Society for Optical Engineering
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Main Research Area: Technical/natural sciences
Ultrasound, Simulation, Acoustical properties, Small animal experiment, CT
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10.1117/12.878012
Source: orbit
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Publication: Research - peer-review Article in proceedings – Annual report year: 2011

Special Edition on Neurodegenerative Diseases

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering
Authors: Sørensen, H. B. D. (Intern)
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Main Research Area: Technical/natural sciences

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Original language: English
Synthetic Aperture Beamformation using the GPU
A synthetic aperture ultrasound beamformer is implemented for a GPU using the OpenCL framework. The implementation supports beamformation of either RF signals or complex baseband signals. Transmit and receive apodization can be either parametric or dynamic using a fixed F-number, a reference, and a direction. Images can be formed using an arbitrary number of emissions and receive channels. Data can be read from Matlab or directly from memory and the setup can be configured using Matlab. A large number of different setups has been investigated and the frame rate measured. A frame rate of 40 frames per second is obtained for full synthetic aperture imaging using 16 emissions and 64 receive channels for an image size of 512x512 pixels and 4000 complex 32-bit samples recorded at 40 MHz. This amounts to a speed up of more than a factor of 6 compared to a highly optimized beamformer running on a powerful workstation with 2 quad-core Xeon-processors.

Synthetic Aperture Focusing for a Single Element Transducer undergoing Helix Motion
This paper describes the application of 3D synthetic aperture focusing (SAF) to a single element trans-rectal ultrasound transducer. The transducer samples a 3D volume by simultaneous rotation and translation giving a helix motion. Two different 3D SAF methods are investigated, a direct and a two-step approach. Both methods perform almost identical for simulated scatterers and give a significant improvement in azimuth resolution and a constant resolution in elevation. Sidelobes below -60 dB is achievable for both methods. Validation of the method is achieved by scanning a simple wire phantom and a complex phantom containing wires in azimuth and elevation. The simple wire phantom shows the same results as that found through simulation. The complex phantom shows simultaneous focusing in azimuth and elevation for the wire scatterers. Considerations on processing requirements for both 3D SAF methods show that the two-step approach can give equivalent performance using an order of magnitude lower calculations. This reduction requires a temporary storage of 9.1 GB of data for the investigated setup.
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 2.94 SJR 1.183 SNIP 1.447
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.73 SJR 0.986 SNIP 1.402
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.814 SNIP 1.494 CiteScore 2.43
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.088 SNIP 1.627 CiteScore 2.18
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.872 SNIP 1.496 CiteScore 2.18
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.733 SNIP 1.325 CiteScore 1.95
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.928 SNIP 1.562
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.296 SNIP 1.775
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 1.324 SNIP 1.567
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.328 SNIP 1.924
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.197 SNIP 2.162
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.104 SNIP 1.768
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.114 SNIP 1.918
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 1.437 SNIP 1.742
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 1.525 SNIP 1.916
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 1.703 SNIP 1.6
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.749 SNIP 2.005
The Bloch Simulator: Interactive MR physics directly in a browser

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Organisations: Biomedical Engineering, Department of Electrical Engineering
Authors: Hanson, L. G. (Intern)
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The ReNoC Reconfigurable Network-on-Chip: Architecture, Configuration Algorithms, and Evaluation
This article presents a reconfigurable network-on-chip architecture called ReNoC, which is intended for use in general-purpose multiprocessor system-on-chip platforms, and which enables application-specific logical NoC topologies to be configured, thus providing both efficiency and flexibility. The article presents three novel algorithms that synthesize an application-specific NoC topology, map it onto the physical ReNoC architecture, and create deadlock-free, application-specific routing algorithms. We apply our algorithms to a mixture of real and synthetic applications and target three different physical architectures. Compared to a conventional NoC, ReNoC reduces power consumption by up to 58% on average.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Department of Informatics and Mathematical Modeling, Computer Science and Engineering
Authors: Stuart, M. B. (Intern), Stensgaard, M. B. (Intern), Sparsø, J. (Intern)
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.017 SJR 0.32 CiteScore 1.59
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.362 SNIP 1.223 CiteScore 1.69
BFI (2015): BFI-level 1
Third Harmonic Imaging using a Pulse Inversion

The pulse inversion (PI) technique can be utilized to separate and enhance harmonic components of a waveform for tissue harmonic imaging. While most ultrasound systems can perform pulse inversion, only few image the 3rd harmonic component. PI pulse subtraction can isolate and enhance the 3rd harmonic component for imaging on any ultrasound system capable of PI. PI was used to perform 3rd harmonic B-mode scans of a water-filled wire phantom on an experimental ultrasound system. The 3rd harmonic scans were compared to fundamental and 2nd harmonic scans on the same system. The 3rd harmonic image showed a 46% improvement in the lateral FWHM resolution compared to fundamental B-mode imaging. The axial FWHM resolution was improved by 35% and 30% for 3rd harmonic imaging compared to fundamental and 2nd harmonic imaging respectively. The improvements in spatial resolution and the fact that PI can isolate the 3rd harmonic suggest that it is advantageous to implement 3rd harmonic imaging on ultrasound systems capable of PI.

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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging
Authors: Rasmussen, J. (Intern), Du, Y. (Intern), Jensen, J. A. (Intern)
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Ultrasonic colour Doppler imaging

Ultrasonic colour Doppler imaging is an imaging technique that combines anatomical information derived using ultrasonic pulse-echo techniques with velocity information derived using ultrasonic Doppler techniques to generate colour-coded maps of tissue velocity superimposed on grey-scale images of tissue anatomy. The most common use of the technique is to image the movement of blood through the heart, arteries and veins, but it may also be used to image the motion of solid tissues such as the heart walls. Colour Doppler imaging is now provided on almost all commercial ultrasound machines, and has been found to be of great value in assessing blood flow in many clinical conditions. Although the method for obtaining the velocity information is in many ways similar to the method for obtaining the anatomical information, it is technically more demanding for a number of reasons. It also has a number of weaknesses, perhaps the greatest being that in conventional systems, the velocities measured and thus displayed are the components of the flow velocity directly towards or away from the transducer, while ideally the method would give information about the magnitude and direction of the three-dimensional flow vectors. This review briefly introduces the principles behind colour Doppler imaging and describes some clinical applications. It then describes the basic components of conventional colour Doppler systems and the methods used to derive velocity information from the ultrasound signal. Next, a number of new techniques that seek to overcome the vector problem mentioned above are described. Finally, some examples of vector velocity images are presented.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, University of Leicester, Copenhagen University Hospital
Authors: Evans, D. H. (Ekstern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
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Web of Science (2018): Indexed yes
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Web of Science (2017): Indexed Yes
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Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 1.096 SNIP 0.909 CiteScore 2.46
Web of Science (2015): Indexed yes
Scopus rating (2014): SJR 1.24 SNIP 1.5 CiteScore 3.23
Web of Science (2014): Indexed yes
Scopus rating (2013): SJR 1.093 SNIP 1.677 CiteScore 3.19
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Scopus rating (2012): SJR 0.655 SNIP 1.058 CiteScore 2.06
ISI indexed (2012): ISI indexed no
Web of Science (2012): Indexed yes
Ultrasonography Fused with PET-CT Hybrid Imaging

We present a method with fusion of images of three modalities 18F-FDG PET, CT, and 3-D ultrasound (US) applied to imaging of the anal canal and the rectum. To obtain comparable geometries in the three imaging modalities, a plexiglas rod, with the same dimensions as the US transducer, is placed in the anal canal prior to the PET-CT examination. The method is based on manual co-registration of PET-CT images and 3-D US images. The three-modality imaging of the rectum-rectum canal may become useful as a supplement to conventional imaging in the external radiation therapy in the treatment of anal cancer, where the precise delineation of a tumor is crucial to avoid damage from radiation therapy to the healthy tissue surrounding it. The technique is still in a phase of development, and the demands for integration different company software systems are significant before commercial application. Three-modality imaging may also be used in certain other diagnostic or therapeutic fields.
What is Magnetic Resonance?

Automatic Sleep Scoring in Normals and in Individuals with Neurodegenerative Disorders According to New International Sleep Scoring Criteria

The aim of this study was to develop a fully automatic sleep scoring algorithm on the basis of a reproduction of new international sleep scoring criteria from the American Academy of Sleep Medicine. A biomedical signal processing algorithm was developed, allowing for automatic sleep depth quantification of routine polysomnographic recordings through feature extraction, supervised probabilistic Bayesian classification, and heuristic rule-based smoothing. The performance of the algorithm was tested using 28 manually classified day-night polysomnograms from 18 normal subjects and 10 patients with Parkinson disease or multiple system atrophy. This led to quantification of automatic versus manual epoch-by-epoch agreement rates for both normals and abnormals. Resulting average agreement rates were 87.7% (Cohen's Kappa: 0.79) and 68.2% (Cohen's Kappa: 0.26) in the normal and abnormal group, respectively. Based on an observed reliability of the manual scorer of 92.5% (Cohen's Kappa: 0.87) in the normal group and 85.3% (Cohen's Kappa: 0.73) in the abnormal group, this study concluded that although the developed algorithm was capable of scoring normal sleep with an accuracy around the manual interscorer reliability, it failed in accurately scoring abnormal sleep as encountered for the Parkinson disease/multiple system atrophy patients.
Modelling, Synthesis, and Configuration of Networks-on-Chips
This thesis presents three contributions in two different areas of network-on-chip and system-on-chip research: Application modelling and identifying and solving different optimization problems related to two specific network-on-chip architectures. The contribution related to application modelling is an analytical method for deriving the worst-case traffic pattern caused by an application and the cache-coherence protocol in a cache-coherent shared-memory system. The contributions related to network-on-chip optimization problems consist of two parts: The development and evaluation of six heuristics for solving the network synthesis problem in the MANGO network-on-chip, and the identification and formalization of the ReNoC configuration problem together with three heuristics for solving it.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Embedded Systems Engineering, Department of Informatics and Mathematical Modeling
Authors: Stuart, M. B. (Intern), Sparsø, J. (Intern), Nannarelli, A. (Intern)
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Corrections in clinical Magnetic Resonance Spectroscopy and SPECT: Motion correction in MR spectroscopy Downscatter correction in SPECT

The quality of medical scanner data is often compromised by several mechanisms. This can be caused by both the subject to be measured and the scanning principles themselves. In this PhD project the problem of subject motion was addressed for Single Voxel MR Spectroscopy in a cohort study of preterm infants. In Iodine-123 SPECT the problem of downscatter was addressed. This thesis is based on two papers. Paper I deals with the problem of motion in Single Voxel Spectroscopy. Two novel methods for the identification of outliers in the set of repeated measurements were implemented and compared to the known mean and median filtering. The data comes from non-anesthetized preterm infants, where motion during scanning is a common problem. Both the novel outlier identification and the independent component analysis (ICA) perform satisfactorily and better than the common mean and median filtering. ICA performed best in the sense that it recovered most of the lost peak height in the spectra. The ICA motion correction algorithm described in paper I and in this thesis was applied to a quantitative analysis of the Single Voxel Spectroscopy data from the cohort study of preterm infants. This analysis revealed that differences between term and preterm infants are not to be found in the concentrations of Lactate (caused by inflammation or hypoxia-ischemia) and/or NAA (caused by hypoxia-ischemia) as hypothesized before the cohort study. Instead choline levels were decreased in the preterm infants, which might indicate a detrimental effect of the extra-uterine environment on brain development. Paper II describes a method to correct for downscatter in low count Iodine-123 SPECT with a broad energy window above the normal imaging window. Both spatial dependency and weight factors were measured. As expected, the implicitly assumed weight factor of one for energy windows with equal width is slightly too low, due the presence of a backscatter peak in the energy spectrum coming from high-energy photons. The effect on the contrast was tested in 10 subjects and revealed a 20% increase in the specific binding ratio of the striatum due to downscatter correction. This makes the difference between healthy subjects and patients more profound. Downscatter in Iodine-123 SPECT is not the only deteriorating mechanism. Normal scatter compromises the images quality as well. Since scatter correction of SPECT-images also can be performed by the subtraction of an energy window, a method was developed to perform scatter and downscatter correction simultaneously. A phantom study has been performed, where the in paper II described downscatter correction was extended with scatter correction. This new combined correction was compared to the known Triple Energy Window (TEW) correction method. Results were satisfying and indicate that TEW is more correct from the physics point of view, while the in paper II described method extended with scatter correction gives reasonable results, but is far less noise sensitive than TEW.

General information
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Organisations: Cognitive Systems, Department of Informatics and Mathematical Modeling, Biomedical Engineering, Department of Electrical Engineering
Authors: de Nijs, R. (Intern), Hansen, L. K. (Intern), Hanson, L. G. (Intern)
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A comparative study between a simplified Kalman filter and Sliding Window Averaging for single trial dynamical estimation of event-related potentials

The classical approach for extracting event-related potentials (ERPs) from the brain is ensemble averaging. For long latency ERPs this is not optimal, partly due to the time-delay in obtaining a response and partly because the latency and amplitude for the ERP components, like the P300, are variable and depend on cognitive function. This study compares the performance of a simplified Kalman filter with Sliding Window Averaging in tracking dynamical changes in single trial P300. The comparison is performed on simulated P300 data with added background noise consisting of both simulated and real background EEG in various input signal to noise ratios. While both methods can be applied to track dynamical changes, the simplified Kalman filter has an advantage over the Sliding Window Averaging, most notable in a better noise suppression when both are optimized for faster changing latency and amplitude in the P300 component and in a considerably higher robustness towards suboptimal settings. The latter is of great importance in a clinical setting where the optimal setting cannot be determined.
Adaptation in P300 braincomputer interfaces: A two-classifier cotraining approach

A cotraining-based approach is introduced for constructing high-performance classifiers for P300-based braincomputer interfaces (BCIs), which were trained from very little data. It uses two classifiers: Fishers linear discriminant analysis and Bayesian linear discriminant analysis progressively teaching each other to build a final classifier, which is robust and able to learn effectively from unlabeled data. Detailed analysis of the performance is carried out through extensive cross-validations, and it is shown that the proposed approach is able to build high-performance classifiers from just a few minutes of labeled data and by making efficient use of unlabeled data. An average bit rate of more than 37 bits/min was achieved with just one and a half minutes of training, achieving an increase of about 17 bits/min compared to the fully supervised classification in one of the configurations. This performance improvement is shown to be even more significant in cases where the training data as well as the number of trials that are averaged for detection of a character is low, both of which are desired operational characteristics of a practical BCI system. Moreover, the proposed method outperforms the self-training-based approaches where the confident predictions of a classifier is used to retrain itself. © 2010 IEEE.
Adaptive Beamforming for Medical Ultrasound Imaging

This dissertation investigates the application of adaptive beamforming for medical ultrasound imaging. The investigations have been concentrated primarily on the Minimum Variance (MV) beamformer. A broadband implementation of the MV beamformer is described, and simulated data have been used to demonstrate the performance. The MV beamformer has been applied to different sets of ultrasound imaging sequences; synthetic aperture ultrasound imaging and plane wave ultrasound imaging. And an approach for applying MV optimized apodization weights on both the transmitting and the receiving apertures is suggested. These investigations show that the MV beamformer provides a significantly reduced main-lobe width compared to the conventional delay and sum beamformer. The effects of near-field propagation and a comparison between a subband and a temporal implementation are considered. And an investigation of the influence of sound speed errors on the adaptive beamformers; MV and the Amplitude and Phase Estimation (APES) beamformer. Furthermore, the investigations of previously suggested adaptive spectral Doppler techniques are continued by additional in-vivo measurements. These investigations show that the adaptive spectral Doppler techniques are indeed capable of providing spectrograms with increased resolution and contrast compared to the conventional methods, based on Welch's spectral estimator. The investigation includes measurements of both arterial and venous flow patterns, located at different depths within the human body.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Holfort, I. K. (Intern), Gran, F. (Intern), Jensen, J. A. (Intern)
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Original language: English
A Method for Synthetic Aperture Compounding

An approach to perform ultrasound spatial compounding using synthetic aperture data is proposed. The approach allows compounding to be performed for any number of directions without reducing the frame rate or temporal resolution. It is demonstrated how the contrast is improved by compounding and the effect is quantized by speckle statistics and by computing contrast-to-noise ratios (CNR) from the resulting images. The method is validated using Field II simulations for a 7 MHz, 3°-pitch transducer with 192 elements with 64 elements active for each scan line. Circular regions (cysts) with a diameter of 5 mm and scattering levels ranging from -3 to -12 dB relative to the background are imaged at 2 depths. Compound images composed of 1-5 images with an angular separation of 2 degrees are constructed and for the cysts at -3, -6, -9, and -12 dB, a CNR of -0.43, -1.11, -1.44, and -1.91 dB are obtained when using 5 images. Using the same RF data, a synthetic aperture image without compounding reveals a CNR of -0.36, -0.93, -1.23, and -1.61 dB for the four cysts, respectively.

A Movable Phantom Design for Quantitative Evaluation of Motion Correction Studies on High Resolution PET Scanners

Head movements during brain imaging using high resolution positron emission tomography (PET) impair the image quality which, along with the improvement of the spatial resolution of PET scanners, in general, raises the importance of motion correction. Here, we present a new design for an automatic, movable, mechanical PET phantom to simulate patients' head movements while being scanned. This can be used for evaluating motion correction methods. A low-cost phantom controlled by a rotary stage motor was built and tested for axial rotations of 1 degrees - 10 degrees with the multiple acquisition frame method. The phantom is able to perform stepwise and continuous axial rotations with submillimeter accuracy, and the movements are repeatable. The scans were acquired on the high resolution research tomograph dedicated brain scanner. The scans were reconstructed with the new 3-D ordered subset expectation maximization algorithm with modeling of the point spread function (3DOSEM-PSF), and they were corrected for motions based on external tracking information using the Polaris Vicra real-time stereo motion-tracking system. The new automatic, movable phantom has a robust design and is a potential quality assessment tool for the development and evaluation of future motion correction methods.
An Iterative Adaptive Approach for Blood Velocity Estimation Using Ultrasound

This paper proposes a novel iterative data-adaptive spectral estimation technique for blood velocity estimation using medical ultrasound scanners. The technique makes no assumption on the sampling pattern of the slow-time or the fast-time samples, allowing for duplex mode transmissions where B-mode images are interleaved with the Doppler emissions. Furthermore, the technique is shown, using both simplified and more realistic Field II simulations, to outperform current state-of-the-art techniques, allowing for accurate estimation of the blood velocity spectrum using only 30% of the transmissions, thereby allowing for the examination of two separate vessel regions while retaining an adequate updating rate of the B-mode images. In addition, the proposed method also allows for more flexible transmission patterns, as well as exhibits fewer spectral artifacts as compared to earlier techniques.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Lund University, Uppsala University
Authors: Gudmundson, E. (Ekstern), Jakobsson, A. (Ekstern), Jensen, J. A. (Intern), Stoica, P. (Ekstern)
Pages: 348-352
Publication date: 2010

Asynchronous P300 BCI: SSVEP based control state detection

An asynchronous hybrid brain-computer interface (BCI) system combining the P300 and steady-state visually evoked potentials (SSVEP) paradigms is introduced. A P300 base system is used for information transfer, and is augmented to include SSVEP for control state detection. The proposed system has been validated through off-line and online experiments. It is shown to achieve fast and accurate control state detection without significantly compromising the performance. For the two subjects who participated in the online experiments, the system achieved an average data transfer rate of 20.13 bits/min, with control state classification accuracy of more than 97%.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, National University of Singapore
Authors: Panicker, R. (Ekstern), Puthusserypady, S. (Intern), Sun, Y. (Ekstern)
Pages: 934-938
Publication date: 2010
Automatic Epileptic Seizure Onset Detection Using Matching Pursuit: A case Study

An automatic alarm system for detecting epileptic seizure onsets could be of great assistance to patients and medical staff. A novel approach is proposed using the Matching Pursuit algorithm as a feature extractor combined with the Support Vector Machine (SVM) as a classifier for this purpose. The combination of Matching Pursuit and SVM for automatic seizure detection has never been tested before, making this a pilot study. Data from red different patients with 6 to 49 seizures are used to test our model. Three patients are recorded with scalp electroencephalography (sEEG) and three with intracranial electroencephalography (iEEG). A sensitivity of 78-100% and a detection latency of 5-18s has been achieved, while holding the false detection at 0.16-5.31/h. Our results show the potential of Matching Pursuit as a feature extractor for detection of epileptic seizures.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, Copenhagen University Hospital, University of Copenhagen
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Automatic seizure detection: going from sEEG to iEEG

Several different algorithms have been proposed for automatic detection of epileptic seizures based on both scalp and intracranial electroencephalography (sEEG and iEEG). Which modality that renders the best result is hard to assess though. From 16 patients with focal epilepsy, at least 24 hours of ictal and non-ictal iEEG were obtained. Characteristics of the seizures are represented by use of wavelet transformation (WT) features and classified by a support vector machine. When implementing a method used for sEEG on iEEG data, a great improvement in performance was obtained when the high frequency containing lower levels in the WT were included in the analysis. We were able to obtain a sensitivity of 96.4% and a false detection rate (FDR) of 0.20/h. In general, when implementing an automatic seizure detection algorithm made for sEEG on iEEG, great improvement can be obtained if a frequency band widening of the feature extraction is performed. This means that algorithms for sEEG should not be discarded for use on iEEG - they should be properly adjusted as exemplified in this paper.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Hypo-Safe A/S, Copenhagen University Hospital, Dentist School
Authors: Henriksen, J. (Intern), Remvig, L. S. (Ekstern), Madsen, R. E. (Ekstern), Conradsen, I. (Intern), Kjær, T. W. (Ekstern), Thomsen, C. E. (Ekstern), Sørensen, H. B. D. (Intern)
Publication date: 2010
Automatic sleep scoring in normals and in individuals with neurodegenerative disorders according to new international sleep scoring criteria

Introduction: Reliable polysomnographic classification is the basis for evaluation of sleep disorders in neurological diseases. Aim: To develop a fully automatic sleep scoring algorithm on the basis of a reproduction of new international sleep scoring criteria from the American Academy of Sleep Medicine (AASM). Methods: A biomedical signal processing algorithm was developed, allowing for automatic sleep depth quantification of routine polysomnographic (PSG) recordings through feature extraction, supervised probabilistic Bayesian classification, and heuristic rule-based smoothing. The performance of the algorithm was tested using 28 manually classified day-night PSGs from 18 normal subjects and 10 patients with Parkinson's disease (PD) or multiple system atrophy (MSA). This led to quantification of automatic versus-manual epoch-by-epoch agreement rates for both normal and abnormal recordings. Results: Resulting average agreement rates were 87.7% (Cohen's Kappa: 0.79) and 68.2% (Cohen's Kappa: 0.26) in the normal and abnormal group, respectively. Based on an observed reliability of the manual scorer of 92.5% (Cohen's Kappa: 0.87) in the normal group and 85.3% (Cohen's Kappa: 0.73) in the abnormal group. Conclusion: The developed algorithm was capable of scoring normal sleep with an accuracy around the manual inter-scorer reliability, it failed in accurately scoring abnormal sleep as encountered for the PD/MSA patients, which is due to the abnormal micro- and macrostructure pattern in these patients.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark, Copenhagen University Hospital
Authors: Jensen, P. S. (Ekstern), Sørensen, H. B. D. (Intern), Jennum, P. J. (Ekstern)
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Scopus rating (2015): SJR 1.749 SNIP 1.519 CiteScore 3.34
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.461 SNIP 1.461 CiteScore 2.99
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.694 SNIP 1.811 CiteScore 3.58
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.547 SNIP 1.639 CiteScore 3.29
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Web of Science (2012): Indexed yes
Auto-Segmentation of Head and Neck Cancer using Textural features

Purpose: The conventional treatment for non-metastatic Head & Neck squamous cell carcinoma (HNSCC) is radiation therapy. Despite technological advances and improved efficacy radiation therapy still relies on manual delineation of gross tumour volume which is both time consuming and prone to inter- and intra observer variability. Several automatic segmentation methods have been developed using positron emission tomography (PET) and/or computerised tomography (CT). The aim of the present study is to develop a model for 3-dimensional auto-segmentation, the level set method, to contour gross tumour volumes (GTV) in a training set of 20 HNSCC patients and evaluate its performance in an independent test set of 25 patients. Materials and Methods: 100 PET/CT textural features were extracted from manual contours of GTV on a training set. The training set consisted of PET and CT scans from 20 patients randomly selected among 45 cases with hypopharyngeal carcinoma treated with radiotherapy. All contours had been performed by experienced radiologists for treatment planning. The Jeffreyx-Matusita (JM) distance, a measure of similarity between distributions, was calculated for combinations of features inside and outside the GTV respectively to choose an appropriate feature combination for segmentation giving a distance of 1.1 out of 1.4. For the level set segmentation the DICE coefficient and sensitivity were 0.48±0.18 (mean ± standard deviation) and 0.57±0.24 respectively. Mean DICE coefficient for the 3 SUV and 20% intensity threshold segmentation were respectively 0.41±0.22and 0.40±0.22, giving p-values of 0.04 and 0.02 for a higher DICE coefficient from the level set segmentation. For sensitivity the threshold segmentation yielded 0.52±0.24 and 0.51±0.26 for 3SUV and 20% intensity respectively yielding p-values of 0.01 and 0.03. Conclusion: The level set method provides a more robust and stable method for segmentation of HNSCC at hypopharynx than threshold segmentation. But it should be improved in order to resemble the manual contours of radiologist. The segmentation could serve as an initial GTV estimate for manual corrections reducing both time and variance in the process of GTV contouring.
Beyond rotamers: a generative, probabilistic model of side chains in proteins

Background: Accurately covering the conformational space of amino acid side chains is essential for important applications such as protein design, docking and high resolution structure prediction. Today, the most common way to capture this conformational space is through rotamer libraries discrete collections of side chain conformations derived from experimentally determined protein structures. The discretization can be exploited to efficiently search the conformational space. However, discretizing this naturally continuous space comes at the cost of losing detailed information that is crucial for certain applications. For example, rigorously combining rotamers with physical force fields is associated with numerous problems. Results: In this work we present BASILISK: a generative, probabilistic model of the conformational space of side chains that makes it possible to sample in continuous space. In addition, sampling can be conditional upon the protein's detailed backbone conformation, again in continuous space without involving discretization. Conclusions: A careful analysis of the model and a comparison with various rotamer libraries indicates that the model forms an excellent, fully continuous model of side chain conformational space. We also illustrate how the model can be used for rigorous, unbiased sampling with a physical force field, and how it improves side chain prediction when used as a pseudo-energy term. In conclusion, BASILISK is an important step forward on the way to a rigorous probabilistic description of protein structure in continuous space and in atomic detail.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, University of Copenhagen
Authors: Harder, T. (Ekstern), Boomsma, W. (Intern), Paluszewski, M. (Ekstern), Frellsen, J. (Ekstern), Johansson, K. E. (Intern), Hamelryck, T. (Ekstern)
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Brain N-acetylaspartate levels correlate with motor function in metachromatic leukodystrophy

Background: Late infantile metachromatic leukodystrophy (MLD) is an autosomal recessive lysosomal storage disorder that causes severe demyelination of the nervous system. The neuronal metabolite N-acetylaspartate (NAA) serves as a source of acetyl groups for myelin lipid synthesis in oligodendrocytes and is known as a marker for neuronal and axonal loss. NAA and other metabolite levels measured by proton magnetic resonance spectroscopy (MRS) correlate with performance of the brain in normal children. There is a need for sensitive measures of disease progression in patients with MLD to enable development of future treatments. Methods: A cross-section of 13 children with late infantile MLD were examined by proton MRS. Signals from NAA, total choline, and total creatine in the deep white matter were measured and correlated with the results of cognitive and motor function tests. Results: The NAA signal decreased as the disease process advanced. Motor function, measured by the Gross Motor Function Measure–88, varied from 13 (only head movement in the supine position) to 180 (able to walk) across the study cohort, demonstrating a wide range in functional status. Similarly, varied decreases were observed in cognitive function. We report strong positive correlations between standardized measures of motor and cognitive function and NAA levels in the deep white matter. Conclusions: We suggest that NAA levels could serve as a sensitive biomarker in children with MLD. Proton MRS may provide a valuable tool for measuring the effects of treatment interventions in this disorder.
Calculation of accurate small angle X-ray scattering curves from coarse-grained protein models

Background: Genome sequencing projects have expanded the gap between the amount of known protein sequences and structures. The limitations of current high resolution structure determination methods make it unlikely that this gap will disappear in the near future. Small angle X-ray scattering (SAXS) is an established low resolution method for routinely determining the structure of proteins in solution. The purpose of this study is to develop a method for the efficient calculation of accurate SAXS curves from coarse-grained protein models. Such a method can for example be used to construct a likelihood function, which is paramount for structure determination based on statistical inference. Results: We present a method for the efficient calculation of accurate SAXS curves based on the Debye formula and a set of scattering form factors for dummy atom representations of amino acids. Such a method avoids the computationally costly iteration over all atoms. We estimated the form factors using generated data from a set of high quality protein structures. No ad hoc scaling or correction factors are applied in the calculation of the curves. Two coarse-grained representations of protein structure were investigated; two scattering bodies per amino acid led to significantly better results than a single scattering body. Conclusion: We show that the obtained point estimates allow the calculation of accurate SAXS curves from coarse-grained protein models. The resulting curves are on par with the current state-of-the-art program CRYSOL, which requires full atomic detail. Our method was also comparable to CRYSOL in recognizing native structures among native-like decoys. As a proof-of-concept, we combined the coarse-grained Debye calculation with a previously described probabilistic model of protein structure, TorusDBN. This resulted in a significant improvement in the decoy recognition performance. In conclusion, the presented method shows great promise for use in statistical inference of protein structures from SAXS data.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, The Bioinformatics Centre, Department of Biology
Authors: Stovgaard, K. (Ekstern), Andreetta, C. (Ekstern), Ferkinghoff-Borg, J. (Intern), Hamelryck, T. (Ekstern)
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Web of Science (2013): Indexed yes
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BFI (2011): BFI-level 1
Calibration of Field II using a Convex Ultrasound Transducer

Field II is an ultrasound simulation program capable of simulating the pressure scattering from inhomogeneous tissue. The simulations are based on a convolution between spatial impulse responses from the field in front of the transducer and the volt-to-surface acceleration impulse response of the transducer. For such simulations to reflect actual measured intensities and pressure levels, the transducer impulse response is to be known. This work presents the results of combining a modified form of a 1D linear transducer model originally suggested by Willatzen with the Field II program to calibrate the pressure simulations of a 128 element convex medical transducer with elevation focus at 70mm. The simulations are compared to pressure measurements from an automatic water bath needle hydrophone setup. The transducer was driven at 4.0 MHz using a research scanner with a commercial transducer amplifier from BK-Medical (Herlev, Denmark). As input waveform for the Field model we measured the output voltage of the research amplifier, which peak voltage was limited to 31 V to avoid too high non linear effects. We measured the hydrophone output from three transducer front elements by averaging 40 shoot sequences on each element using a remotely controlled Agilent MSO6014A oscilloscope. The pressure along the elevation line in 32 mm, 70 mm (elevation focus) and 112 mm for each element are measured.

General information

State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Bæk, D. (Intern), Jensen, J. A. (Intern), Willatzen, M. (Intern)
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Complex blood flow quantification using real-time in vivo vector flow ultrasound

A new method to define and quantify complex blood flow is presented. The standard deviations of real-time in vivo vector flow angle estimates are used. Using vector flow ultrasound imaging both carotid bifurcations of two healthy volunteers were scanned. Scanning was performed with a 7.6 MHz linear transducer (8670, B-K Medical, Denmark) and a commercial vector flow ultrasound scanner (ProFocus 2202, B-K Medical). Eight video sequences of one cardiac cycle were obtained. In every frame boxes were placed to define the common carotid artery(box1) and the carotid bulb(box2).

The standard deviation for the vector angle estimates was calculated for each box in every frame. For comparison three ultrasound experts evaluated the presence of complex flow in every box. The trial was blinded. For every sequence the mean standard deviation of the vector angle estimates were calculated for box1 [39;32;35;41;38;39;32;27] and box2 [22;12;11;13;15;22;17;21]. Mean values and standard deviations of the visual evaluations were calculated for the two boxes in every each sequence.

From regression analysis a standard deviation above 30 corresponds to complex flow according to the evaluation given by three experts. Complex flow patterns can be visualised and quantified with real-time in vivo vector flow. Good agreement between visual evaluation and the quantitative method has been shown. A standard deviation of vector angle estimates above 30 is proposed to define complex blood flow.

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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps, Copenhagen University Hospital
Authors: Pedersen, M. M. (Intern), Pihl, M. J. (Intern), Per, H. (Ekstern), Hansen, K. L. (Intern), Bachmann, M. (Ekstern), Jensen, J. A. (Intern)
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Event: Poster session presented at 10th EUROSON 2010, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences

Effect of cigarette smoking on arterial stiffness re-interpreted using a structurally-based model

Cigarette smoking constitutes a major risk factor for diverse cardiovascular diseases (CVD). Many physiological and pathophysiological parameters affect arterial stiffness. While underlying mechanisms remain unclear, smoking increases arterial stiffness, which contributes to many disease processes. The goal of this work was to use a structurally motivated nonlinear constitutive relation to quantify increased arterial stiffness based on available data. Specifically, we used a “four-fiber family model” that includes dominant effects of axial, circumferential, and symmetric-diagonal families of collagen fibers embedded within an isotropic, elastin-dominated matrix. Published data, i.e. biaxial responses during pressure-diameter and axial force-length tests on pulmonary arteries from rats subjected to 2 or 3 months of smoking, were used to determine the associated best-fit values of the material parameters. The primary finding was that cigarette smoking induces significant increases in the material parameters describing the micromechanical properties of all four families of collagen fibers with increased duration of smoking. Additionally, there was a moderate increase in the material parameter describing the behaviour of the elastic fibers. These findings suggest that arterial stiffening in response to smoking is isotropic due to the changes in the material parameters seen in all fiber directions. Although changes are manifested in both elastic and collagen fibers, the predominant stiffening appeared to be due mainly to changes in collagen fiber structure (e.g., cross-linking).

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Texas A&M University, Copenhagen University Hospital
Authors: Enevoldsen, M. S. (Intern), Humphrey, J. D. (Ekstern), Lönn, L. (Ekstern), Jensen, J. A. (Intern), Henneberg, K. (Intern)
Publication date: 2010
Event: Abstract from Annual Meeting of the Biomedical Engineering Society, Austin, Texas, USA.
Main Research Area: Technical/natural sciences
Electronic versions:
Abstract_vers6.pdf
Source: orbit
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Publication: Research › Conference abstract for conference – Annual report year: 2010
Evaluation of automatic time gain compensated in-vivo ultrasound sequences

Ultrasound imaging is increasingly being used in applications such as surgery, anesthesia and urology, where the users are not trained radiologists. User studies indicate that these users rarely adjust the controls of the ultrasound scanner. This project presents a preliminary evaluation of a new algorithm for automatic time gain compensation (TGC) on in-vivo ultrasound sequences. Forty ultrasound sequences were recorded from the abdomen of two healthy volunteers. Each sequence of 5 sec was recorded with 40 frames/sec. Post processing each frame, a mask is created wherein anechoic and hyper echoic regions are mapped. Near field hyper intensity and deep areas with low signal strength are also included in the mask. The algorithm uses this mask to create a parallel image where anechoic and hyper echoic regions are eliminated. From this, the mean power is calculated as a function of depth. The power is then used as an estimate of the attenuation, and from this, the needed compensation is found. The measurements were performed by an experienced sonographer using an ultrasound scanner (2202 ProFocus, BK Medical, Denmark) with a 192 elements concave transducer (8820e BK Medical). A research interface was used to retrieve unprocessed data from the scanner with no preset TGC, using a standard abdominal setup. Five experts in medical ultrasound evaluated the unprocessed and processed video sequences in a double-blinded randomized trial on image quality and penetration depth. In the evaluation of image quality, the unprocessed and processed sequences were displayed in pairs side-by-side in random order and with random left right placement. Each pair was displayed and scored twice, with different permutations. The sequences were evaluated on their relative clinical value. P-values on the order of 10-8 - 10-14 indicate that the image quality of the processed sequences are clinically better than the unprocessed. In the evaluation of penetration depth, all the processed and unprocessed sequences were displayed in random order. Each sequence was evaluated on the basis of; at what depth the image quality had decreased so much that it was of no clinical value. The pooled results show a mean increase in penetration depth of 1.91 cm with a p-value of 1.19 - 10-18. In conclusion a new algorithm has been developed and evaluated. It is capable of compensating for the depth attenuation on abdominal in-vivo ultrasound images.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Technical University of Denmark, BK Medical Aps, Copenhagen University Hospital
Authors: Axelsen, M. C. (Ekstern), Røeboe, K. F. (Ekstern), Hemmsen, M. C. (Intern), Nikolov, S. I. (Ekstern), Pedersen, M. M. (Ekstern), Nielsen, M. B. (Ekstern), Jensen, J. A. (Intern)
Pages: 1640-1643
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Extended seizure detection algorithm for intracranial EEG recordings
Objective: We implemented and tested an existing seizure detection algorithm for scalp EEG (sEEG) with the purpose of improving it to intracranial EEG (iEEG) recordings. Method: iEEG was obtained from 16 patients with focal epilepsy undergoing work up for resective epilepsy surgery. Each patient had 4 or 5 recorded seizures and 24 hours of non-ictal data were used for evaluation. Data from three electrodes placed at the ictal focus were used for the analysis. A wavelet based feature extraction algorithm delivered input to a support vector machine (SVM) classifier for distinction between ictal and non-ictal iEEG. We compare our results to a method published by Shoeb in 2004. While the original method on sEEG was optimal with the use of only four subbands in the wavelet analysis, we found that better seizure detection could be made if all subbands were used for iEEG. Results: When using the original implementation a sensitivity of 92.8% and a false positive ratio (FPR) of 0.93/h were obtained. Our extension of the algorithm rendered a 95.9% sensitivity and only 0.65 false detections per hour. Conclusion: Better seizure detection can be performed when the higher frequencies in the iEEG were included in the feature extraction. Our future work will concentrate on development of a method for identification of the most prominent nodes in the wavelet packets analysis for optimization of an automatic seizure detection algorithm.
Impact of acoustic pressure on ambient pressure estimation using ultrasound contrast agent

Local blood pressure measurements provide important information on the state of health of organs in the body and can be used to diagnose diseases in the heart, lungs, and kidneys. This paper presents an approach for investigating the ambient pressure sensitivity of a contrast agent using diagnostic ultrasound. The experimental setup resembles a realistic clinical setup utilizing a single array transducer for transmit and receive. The ambient pressure sensitivity of SonoVue (Bracco, Milano, Italy) was measured twice using two different acoustic driving pressures, which were selected based on a preliminary experiment. To compensate for variations in bubble response and to make the estimates more robust, the relation between the energy of the subharmonic and the fundamental component was chosen as a measure over the subharmonic peak amplitude. The preliminary study revealed the growth stage of the subharmonic component to occur at acoustic driving pressures between 300 and 500 kPa. Based on this, the pressure sensitivity was investigated using a driving pressure of 485 and 500 kPa. At 485 kPa, a linear pressure sensitivity of 0.42 dB/kPa was found having a linear correlation coefficient of 0.94. The second measurement series at 485 kPa showed a sensitivity of 0.41 dB/kPa with a correlation coefficient of 0.89. Based on the measurements at 500 kPa, this acoustic driving pressure was concluded to be too high causing the bubbles to be destroyed. The pressure sensitivity for these two measurement series were 0.42 and 0.25 dB/kPa with linear correlation coefficients of 0.98 and 0.93, respectively.
Implementation of Synthetic Aperture Imaging in Medical Ultrasound: The Dual Stage Beamformer Approach

The main advantage of medical ultrasound imaging is its real-time capability, which makes it possible to visualize dynamic structures in the human body. Real-time synthetic aperture imaging puts very high demands on the hardware, which currently cannot be met. A method for reducing the number of calculations and still retain the many advantages of SA imaging is described. It consists of a dual stage beamformer, where the first can be a simple fixed focus analog beamformer and the second an ordinary digital ultrasound beamformer. The performance and constrictions of the approach is described.

General information
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Organisations: Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Biomedical Engineering
Authors: Jensen, J. A. (Intern), Kortbek, J. (Intern), Nikolov, S. (Intern), Hemmsen, M. C. (Intern), Tomov, B. G. (Intern)
Number of pages: 4
Publication date: 2010

Introduction to vector velocity imaging
Current ultrasound scanners can only estimate the velocity along the ultrasound beam and this gives rise to the cos() factor on all velocity estimates. This is a major limitation as most vessels are close to perpendicular to the beam. Also the angle varies as a function of space and time making it virtually impossible to compensate for the factor and obtain correct velocity estimates for either CFM or spectral velocity estimation. This talk will describe methods for finding the correct velocity by estimating both the axial and lateral component of the velocity vector. The transverse oscillation method introduces an ultrasound field that oscillation not only along the ultrasound beam but also transverse to it to estimate both the lateral and axial velocity for the full velocity vector. The correct velocity magnitude can be found from this as well as the instantaneous angle. This can be obtained over the full region of interest and a real-time image at a frame rate of 20 Hz can be displayed. Real-time videos have been obtained from both our research systems and from commercial BK Medical scanners. The vector velocity images reveal the full complexity of the human blood flow. It is easy to see direction and the correct velocity magnitude for any orientation of the vessels. At complex geometries like bifurcations, branching and for valves the approach reveals how the velocity changes magnitude and direction over the cardiac cycle. Vector velocity reveals a wealth of new information that now is accessible to the ultrasound community. The displaying and studying of this information is challenging as complex flow changes rapidly over the cardiac cycle.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Jensen, J. A. (Intern), Udesen, J. (Intern), Hansen, K. L. (Intern), Nielsen, M. B. (Ekstern)
Publication date: 2010
Event: Abstract from 8th European Conference on Synthetic Aperture Radar, Aachen, Germany.
Main Research Area: Technical/natural sciences
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Modeling of ultrasound transducers
This Ph.D. dissertation addresses ultrasound transducer modeling for medical ultrasound imaging and combines the modeling with the ultrasound simulation program Field II. The project firstly presents two new models for spatial impulse responses (SIRs) to a rectangular elevation focused transducer (REFT) and to a convex rectangular elevation focused transducer (CREFT). These models are solvable on an analog time scale and give exact smooth solutions to the Rayleigh integral. The REFT model exhibits a root mean square (RMS) error relative to Field II predictions of 0.41 % at 3400 MHz, and 1.37 % at 100 MHz. The CREFT model exhibits a RMS deviation of 0.01 % relative to the exact numerical solution on a CREFT transducer. A convex non-elevation focused, a REFT, and a linear flat transducer are shown to be covered with the CREFT model as well. Pressure pulses calculated with a one-dimensional transducer model in combination with Field II are calculated on a circular piezoceramic transducer and a convex 128 element commercial transducer. The pulses are shown to be predictable within ±2 dB of the amplitude which is excellent for this modeling. Intensity profiles are shown to be predicted with a RMS deviation of 5.5 % to 11.0 %. Finite element modeling of piezoceramics in combination with Field II is addressed and reveals the influence of restricting the modeling of transducers to the one-dimensional case. An investigation on modeling capacitive micromachined ultrasonic transducers (CMUTs) with Field II is addressed. It is shown how a single circular CMUT cell can be well approximated with a simple square transducer encapsulating the cell, and how this influence the modeling of full array elements. An optimal cell discretization with Field II’s mathematical elements is addressed as well. The error in modeling CMUT cells as squares or flat circular plates instead of curved circular plates is also addressed.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, University of Southern Denmark
Authors: Bæk, D. (Intern), Jensen, J. A. (Intern), Willatzen, M. (Ekstern)
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Modeling the human heel pad
General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Università degli Studi di Firenze
Authors: Matteoli, S. (Intern), Corvi, A. (Ekstern), Wilhjelm, J. E. (Intern)
Publication date: 2010
Event: Abstract from Simpleware's Users Meeting, Solihull, UK, .
Main Research Area: Technical/natural sciences
Electronic versions:
Modeling the human heel pad_abstract.pdf
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Modeling transducer impulse responses for predicting calibrated pressure pulses with the ultrasound simulation program Field II
FIELD II is a simulation software capable of predicting the field pressure in front of transducers having any complicated geometry. A calibrated prediction with this program is, however, dependent on an exact voltage-to-surface acceleration impulse response of the transducer. Such impulse response is not calculated by FIELD II. This work investigates the
usability of combining a one-dimensional multilayer transducer modeling principle with the FIELD II software. Multilayer here refers to a transducer composed of several material layers. Measurements of pressure and current from Pz27 piezoceramic disks as well as pressure and intensity measurements in front of a 128 element commercial convex medical transducer are compared to the simulations. Results show that the models can predict the pressure from the piezoceramic disks with a root mean square (rms) error of 11.2% to 36.2% with a 2 dB amplitude decrease. The current through the external driving circuits are predicted within 8.6% to 36% rms error. Prediction errors of 30% and in the range of 5.8%-19.9% for the pressure and the intensity, respectively, are found when simulating the commercial transducer. It is concluded that the multilayer transducer model and the FIELD II software in combination give good agreement with measurements.

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Authors: Bæk, D. (Intern), Jensen, J. A. (Intern), Willatzen, M. (Intern)
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Web of Science (2017): Indexed yes
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Scopus rating (2016): CiteScore 1.83 SJR 0.819 SNIP 1.271
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Scopus rating (2010): SJR 0.734 SNIP 1.511
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Scopus rating (2009): SJR 0.778 SNIP 1.692
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Scopus rating (2008): SJR 0.83 SNIP 1.657
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.838 SNIP 1.635
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.739 SNIP 1.678
Web of Science (2006): Indexed yes
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Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.77 SNIP 1.761
Web of Science (2004): Indexed yes
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Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.785 SNIP 1.572
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Scopus rating (2001): SJR 0.727 SNIP 1.483
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.639 SNIP 1.404
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MR.-skanning ved 7 tesla feltstyrke etableres i Danmark: Nordens første humane 7T skanner giver væsentligt løft til dansk MR-forskning og -diagnostik

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State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering
Authors: Hanson, L. G. (Intern)
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Volume: 4
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On heel pad elasticity modeling

General information
Ordered Incremental Multiobjective Problem Solving Based on Genetic Algorithms

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, IBM, Xian Jiaotong-Liverpool University
Authors: Wenting, M. (Ekstern), Sheng-Uei, G. (Ekstern), Puthusserypady, S. (Intern)
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Main Research Area: Technical/natural sciences

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Journal: International Journal of Applied Evolutionary Computation
Volume: 1
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Performance of SARUS: A Synthetic Aperture Real-time Ultrasound System
The SARUS scanner (Synthetic Aperture Real-time Ultrasound System) for research purposes is described. It can acquire individual channel data for multi-element transducers for a couple of heart beats, and is capable of transmitting any kind of excitation. It houses generous and flexible processing resources that can be reprogrammed and tailored to many kinds of algorithms. The 64 boards in the system house 16 transmit and 16 receive channels each, where data can be stored in 2 GB of RAM and processed using four Virtex 4FX100 and one FX60 FPGAs. The VHDL code can acquire data for 16 channels and perform real-time processing for four channels per board. The receive processing chain consists of three FPGAs. The beamformer FPGA houses 24 focusing units (6 x 4-way) each working in parallel at 220 MHz for parallel four-channel beamforming. The fully parametric focusing unit calculates delays and apodization values in real time in 3D space and can produce 630 million complex samples per second. The processing can, thus, beamform 192 image lines consisting of 1024 complex samples for each emission at a rate of 3200 frames a second yielding full nonrecursive synthetic aperture B-mode imaging at more than 30 high resolution images a second.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Prevas A/S, BK Medical Aps
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Practical Applications of Synthetic Aperture Imaging

Synthetic aperture imaging has been a focus of research for almost 3 decades. The research carried out at the Center for Fast Ultrasound Imaging has demonstrated that synthetic aperture focusing not only can be used in vivo, but that it also yields superior B-mode and blood flow images. In the last years synthetic aperture focusing has moved from the lab to commercial products. The implementations vary in their scope and purpose. Some scanners use synthetic aperture imaging to improve the detail and contrast resolution of the system. Others to increase the image uniformity. Yet others use synthetic aperture acquisition to achieve high frame rates and superior flow estimations. On the other end of the scale are the systems that utilize synthetic aperture techniques to reduce the data rate and take advantage of modern computer hardware. Retrospective transmit beamformation, zone sonography, and multiple angle flash imaging are just a few of the names used to describe the commercial implementations of synthetic aperture focusing. Although they sound like different algorithms, they are the same in their core, as revealed in this paper.

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State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Nikolov, S. I. (Intern), Kortbek, J. (Intern), Jensen, J. A. (Intern)
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Preliminary evaluation of vector flow and spectral velocity estimation.
Spectral estimation is considered as the golden standard in ultrasound velocity estimation. For spectral velocity estimation the blood flow angle is set by the ultrasound operator. Vector flow provides temporal and spatial estimates of the blood flow angle and velocity. A comparison of vector flow estimation and spectral estimates is presented. The variation of the blood flow angle and the effect on the velocity estimate is investigated. The right common carotid arteries of three healthy volunteers were scanned. Real-time spectral and vector flow data were obtained simultaneously from one range gate line covering the vessel diameter. A commercial ultrasound scanner (ProFocus 2202, BK Medical, Denmark) and a 7.6 MHz linear transducer was used (8670, BK Medical). The mean vector blood flow angle estimations were calculated (52(18);55(23);60(16))°. For comparison the fixed angles for spectral estimation were obtained (52;56;52)°. The mean
vector velocity estimates at PS \(76(15);95(17);77(16)\) cm/s and at end diastole (ED) \(17(6);18(6);24(6)\) cm/s were calculated. For comparison spectral velocity estimates at PS \(77;110;76\) cm/s and ED \(18;18;20\) cm/s were obtained. The mean vector angle estimates agrees with the spectral flow angle. The vector velocity estimates agrees with the spectral estimates at PS and ED. From preliminary data it is concluded that vector flow angle estimation can replace the operator-dependent angle correction used for spectral velocity estimation.

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State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps, Copenhagen University Hospital
Authors: Pedersen, M. M. (Intern), Pihl, M. J. (Intern), Haugaard, P. (Ekstern), Hansen, J. M. (Intern), Hansen, K. L. (Intern), Bachmann, M. (Ekstern), Jensen, J. A. (Intern)
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Event: Poster session presented at 10th EUROSON 2010, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Source: orbit
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Publication: Research - peer-review › Poster – Annual report year: 2010

Principle and performance of the transverse oscillation vector velocity technique in medical ultrasound
Medical ultrasound systems measure the blood velocity by tracking the blood cells motion along the ultrasound field. The is done by pulsing in the same direction a number of times and then find e.q. the shift in phase between consecutive pulses. Properly normalized this is directly proportional to the axial blood velocity. A major drawback is that only the axial velocity component is found. Often the lateral component is most important as blood vessels run parallel to the skin surface. The talk presents the transverse oscillation approach, which also can find the lateral velocity component by using a double oscillating field. A special estimator is then used for finding both the axial and lateral velocity component, so that both magnitude and phase can be calculated. The method for generating double oscillating ultrasound fields and the special estimator are described and its performance revealed for a flow rig setup. Several examples from clinical use of the approach are shown. From these it is seen that both velocity magnitude and angle varies temporally and spatially across the cardiac cycle, and it is, thus, important to estimate both continuously over the image region and time.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, GN ReSound A/S, Copenhagen University Hospital
Authors: Jensen, J. A. (Intern), Pihl, M. J. (Intern), Udesen, J. (Ekstern), Pedersen, M. M. (Ekstern), Hansen, K. L. (Ekstern)
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Source-ID: 274019
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2010

Quantification of complex blood flow using real-time in vivo vector flow ultrasound
A quantitative method for distinguishing complex from non-complex flow patterns in ultrasound is presented. A new commercial BK Medical ultrasound scanner uses the Transverse Oscillation vector flow technique for visualising flow patterns in real-time. In vivo vector flow data of the blood flow patterns of the common carotid artery and the carotid bulb were obtained simultaneously as the basis for quantifying complex flow. The carotid bifurcation of two healthy volunteers were scanned. The presence of complex flow patterns from eight cardiac cycles were evaluated by three experts in medical ultrasound. From the same data the mean standard deviation of the flow angles (MSTDA) were calculated and compared to the expert evaluations. Comparison between the combined experts evaluations and the MSTDA was performed. Using linear regression analysis, a correlation coefficient of 0.925 was found. The upper and lower bounds for a 95% confidence interval of 0.974 and 0.792 respectively, were calculated. The MSTDA was below 25 for the common carotid artery and above 25 for the carotid bulb. Thus, the MSTDA value can distinguishing complex flow from non-complex flow and can be used as the basis for automatic detection of complex flow patterns.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, BK Medical Aps, Copenhagen University Hospital
Quorum Sensing Regulation in Aeromonas hydrophila
We present detailed results on the C4-HSL-mediated quorum sensing (QS) regulatory system of the opportunistic Gram-negative bacterium Aeromonas hydrophila. This bacterium contains a particularly simple QS system that allows for a detailed modeling of kinetics. In a model system (i.e., the Escherichia coli monitor strain MH205), the C4-HSL production of A. hydrophila is interrupted by fusion of gfp(ASV). In the present in vitro study, we measure the response of the QS regulatory ahyRI locus in the monitor strain to predetermined concentrations of C4-HSL signal molecules. A minimal kinetic model describes the data well. It can be solved analytically, providing substantial insight into the QS mechanism: at high concentrations of signal molecules, a slow decay of the activated regulator sets the timescale for the QS regulation loop. Slow saturation ensures that, in an A. hydrophila cell, the QS system is activated only by signal molecules produced by other A. hydrophila cells. Separate information on the ahyR and ahyI loci can be extracted, thus allowing the probe to be used in identifying the target when testing QS inhibitors.

General information
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Organisations: Department of Systems Biology, Department of Electrical Engineering, Biomedical Engineering, Panum Institute, University of Copenhagen
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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.13 SJR 3.377 SNIP 1.162
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.005 SNIP 1.099 CiteScore 3.97
Web of Science (2015): Indexed yes
REM Behaviour Disorder Detection Associated with Neurodegerative Diseases

Abnormal skeleton muscle activity during REM sleep is characterized as REM Behaviour Disorder (RBD), and may be an early marker for different neurodegenerative diseases. Early detection of RBD is therefore highly important, and in this ongoing study a semi-automatic method for RBD detection is proposed by analyzing the motor activity during sleep.

Method: A total number of twelve patients have been involved in this study, six normal controls and six patients diagnosed with Parkinson’s Disease (PD) with RBD. All subjects underwent at least one ambulant polysomnographic (PSG) recording. The sleep recordings were scored, according to the new sleep-scoring standard from the American Academy of Sleep Medicine, by two independent sleep specialists. A follow-up analysis of the scoring consensus between the two specialists has been conducted. Based on the agreement of the two manual scorings, a computerized algorithm has been attempted implemented. By analysing the REM and non-REM EMG activity, using advanced signal processing tools combined with a statistical classifier, it is possible to discriminate normal and abnormal EMG activity. Due to the small number of patients, the overall performance of the algorithm was calculated using the leave-one-out approach and
benchmark against a previously published computerized/visual method. Results: Based on the available data and using optimal settings, it was possible to correctly classify PD subjects with RBD with 100% sensitivity, 100% specificity, which is an improvement compared to previous published studies. Conclusion: The overall result indicates the usefulness of a computerized scoring algorithm and may be a feasible way of reducing scoring time. Further enhancement on additional data, i.e. subjects with idiopathic RBD (iRBD) and PD without RBD, is needed to validate its robustness and the overall result.

Robust Estimation of HDR in fMRI using H-Infinity Filters
Estimation and detection of the hemodynamic response (HDR) are of great importance in functional MRI (fMRI) data analysis. In this paper, we propose the use of three H-infinity adaptive filters (finite memory, exponentially weighted, and timevarying) for accurate estimation and detection of the HDR. The H8 approach is used because it safeguards against the worst case disturbances and makes no assumptions on the (statistical) nature of the signals [B. Hassibi and T. Kailath, in Proc. ICASSP, 1995, vol. 2, pp. 949-952; T. Ratnarajah and S. Puthusserypady, in Proc. 8th IEEEWorkshopDSP, 1998, pp. 1483-1487]. Performances of the proposed techniques are compared to the conventional t-test method as well as the well-known LMSs and recursive least squares algorithms. Extensive numerical simulations show that the proposed methods result in better HDR estimations and activation detections.
Segmenting the Parotid Gland using Registration and Level Set Methods

The bilateral parotid glands were segmented using a registration scheme followed by level set segmentation. A training set consisting of computerized tomography from 10 patients with segmentation of the bilateral glands were used to optimize the parameters of registration and level set segmentation. The method was evaluated on a test set consisting of 8 corresponding data sets. The attained total volume Dice coefficient and mean Hausdorff distance were 0.61 ± 0.20 and 15.6 ± 7.4 mm respectively. The method has improvement potential which could be exploited in order for clinical
Seizure Onset Detection based on a Uni- or Multi-modal Intelligent Seizure Acquisition (UISA/MISA) System

An automatic Uni- or Multi-modal Intelligent Seizure Acquisition (UISA/MISA) system is highly applicable for onset detection of epileptic seizures based on motion data. The modalities used are surface electromyography (sEMG), acceleration (ACC) and angular velocity (ANG). The new proposed automatic algorithm on motion data is extracting features as "log-sum" measures of discrete wavelet components. Classification into the two groups "seizure" versus "nonseizure" is made based on the support vector machine (SVM) algorithm. The algorithm performs with a sensitivity of 91-100%, a median latency of 1 second and a specificity of 100% on multi-modal data from five healthy subjects simulating seizures. The uni-modal algorithm based on sEMG data from the subjects and patients performs satisfactorily in some cases. As expected, our results clearly show superiority of the multimodal approach, as compared with the unimodal one.

Simulating Capacitive Micromachined Ultrasonic Transducers (CMUTs) using Field II

Field II has been a recognized simulation tool for piezoceramic medical transducer arrays for more than a decade. The program has its strength in doing fast computations of the spatial impulse response (SIR) from array elements by dividing the elements into smaller mathematical elements (ME)s from which it calculates the SIR responses. The program features
predefined models for classical transducer geometries, but currently none for the fast advancing CMUTs. This work addresses the assumptions required for modeling CMUTs with Field II. It is shown that rectangular array elements, populated with cells, can be well approximated by neglecting the cells. Further, it is demonstrated that scaling of the SIR translates into better computational efficiency.

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Simulation of high quality ultrasound imaging
In this paper the influence using an idealized transducer model (ITM) and a realistic transducer model (RTM) is investigated in a comparative study between Synthetic Aperture Sequential Beamformation (SASB) and Dynamic Receive Focus (DRF).

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Authors: Hemmsen, M. C. (Intern), Nikolov, S. (Intern), Jensen, J. A. (Intern)
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Simulation of High Quality Ultrasound Imaging
This paper investigates if the influence on image quality using physical transducers can be simulated with an sufficient accuracy to reveal system performance. The influence is investigated in a comparative study between Synthetic Aperture Sequential Beamformation (SASB) and Dynamic Receive Focus (DRF). The study is performed as a series of simulations and validated by measurements. The influence from individual element impulse response, phase, and amplitude deviations are quantized by the lateral resolution (LR) at Full Width at Half Maximum (FWHM), Full Width at One-Tenth Maximum (FWOTM), and at Full Width at One-Hundredth Maximum (FWOHM) of 9 points spread functions resulting from evenly distributed point targets at depths ranging from 10 mm to 90 mm. The results are documented for a 64 channel system, using a 192 element linear array transducer model. A physical BK Medical 8804 transducer is modeled by incorporating measured element pulse echo responses into the simulation software. Validation is performed through measurements on a water phantom with three metal wires, each with a diameter of 0.07 mm. Results show that when comparing measurement and simulation, the lateral beam profile using SASB can be estimated with a correlation coefficient of 0.97. Further, it is shown that SASB successfully maintains a constant LR though depth at FWHM, and is a
factor of 2.3 better than DRF at 80 mm. However, when using SASB the LR at FWOHM is affected by non-ideal element responses. Introducing amplitude and phase compensation, the LR at FWOHM improves from 6.3 mm to 4.7 mm and is a factor of 2.2 better than DRF. This study has shown that individual element impulse response, phase, and amplitude deviations are important to include in simulated system performance evaluations. Furthermore, it is shown that SASB provides a constant LR through depth and has improved resolution and contrast compared to DRF.

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Simulation of Second Harmonic Ultrasound Fields
A non-linear ultrasound imaging simulation software should be capable of simulating the non-linear fields for any kind of transducer, focusing, apodization, and attenuation. At present, a major issue is the overlong simulation time of the non-linear software. An Angular Spectrum Approach (ASA) using a quasi-linear approximation for solving the Westervelt equation can simulate the second harmonic pressure at any distance. Therefore, it shortens the execution time compared with the operator splitting method. The purpose of this paper is to implement the monochromatic solution for the second harmonic component based on ASA and Field II, and to compare with results from the simulation program Abersim. A linear array transducer with a center frequency of 4 MHz and 64 active elements is used as the transmitting source. The initial plane is 5 mm away from the transducer surface, and the fundamental pressure is calculated by Field II. The second harmonic pressure in k-space along the propagating direction is calculated as an auto-convolution of the fundamental pressure multiplied by an exponential propagating coefficient. In this case, the second harmonic pressure can be calculated using ASA for any plane parallel to the initial plane. In the focal plane (elevation-lateral) at 60 mm from the transducer surface, calculated by ASA, the RMS errors for the fundamental component are 2.66% referred to Field II and 4.28% referred to Abersim. For the second harmonic component, the RMS error is 0.91% referred to Abersim.

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Stop-and-go kinetics in amyloid fibrillation

Many human diseases are associated with protein aggregation and fibrillation. We present experiments on in vitro glucagon fibrillation using total internal reflection fluorescence microscopy, providing real-time measurements of single-fibril growth. We find that amyloid fibrils grow in an intermittent fashion, with periods of growth followed by long pauses. The observed exponential distributions of stop and growth times support a Markovian model, in which fibrils shift between the two states with specific rates. Even if the individual rates vary considerably, we observe that the probability of being in the growing (STOPPING) state is very close to 1/4 (3/4) in all experiments.
Synthetic aperture flow imaging using a dual beamformer approach

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Synthetic Aperture Flow Imaging Using a Dual Stage Beamformer Approach

Synthetic aperture flow estimation has several advantages compared to the conventional flow estimation however this requires a high number of calculations. A dual beamformer approach is proposed to lower the number of calculations and maintain a beamforming quality sufficient for flow estimation. This approach contains a two-stage procedure using two different beamformers. The first stage beamformer has a single focal point in both transmit and receive. The fully dynamic second beamformer uses the data from the first stage to beamform the image. Focal points in the first beamformer are considered as virtual sources in the second beamformation algorithm. High resolution image lines are generated by the second stage beamformation. Four emissions in each emission sequence repeat over time. The velocity is estimated by cross correlating high resolution lines which is a function of depth. The cross correlation functions are averaged over 16 high resolution image pairs to improve the better estimates. Varying interspaces [2, 6, 10, 14] resulted in the standard deviation and the bias B of the axial velocity were [1.92, 2.0, 2.07, 2.21] % and [0.61, 1.07, 1.29, 1.5] % compared to the peak velocity respectively. The parameter study showed that larger interspaces gave an increased standard deviation and the bias. Furthermore more emissions in averaging gave better performance. The performance of the simulation indicates that this dual beamformer approach is able to estimate the flow velocity. Interspaces between emissions and number of emission sets in averaging have an influence on the estimation.
Testing of a spatial impulse response algorithm for double curved transducers

The spatial impulse response (SIR) method for solving the Rayleigh integral is a well-known method for fast time response simulation of acoustic waves. Several analytical expressions have been found for simple transducer geometries such as rectangles and discs. However, no analytical solution is known for double curved transducers (DCT), i.e., transducers with both concave and convex radius. To calculate the SIR from such transducers Field II uses a far-field approximation by dividing the surface into smaller flat elements and then performs a summation of the response from all the elements using Huygen's principle. This calculation method involves several summations, and it relies on exact phase calculation to avoid numerical noise in the response. A stable analytical expression for the SIR would thus be beneficial to the Field II software as an alternative solver. A semi-analytic algorithm (SAA) has been developed, and it is the objective of this work to validate an analytical approximation of the algorithm as an alternative solver for Field II. Two approximations of a SAA that efficiently finds the SIR for DCT have been implemented into a MATLAB and a C-code environment. The root mean square (RMS) error of calculating the SIR using Field II and the C-implemented approximation are calculated relative to a high resolution solution obtained with MATLAB on a DCT, a linear concave, and a flat transducer. The computation time for solving 400 times is also found. Calculations are performed at sampling frequencies ranging from 100 MHz to 15 GHz in steps of 100 MHz. The transducer width is 250 μm and the height is 10 mm. The C-implementation exhibits errors ranging from 4.9.10-4 % to 0.91 % and Field II 0.0117 % to 0.94 %. A slight trade-off between accuracy and computation time is found. Field II outperforms the SAA in computation time if high accuracy is not needed. However, if a higher accuracy is required, the SAA is the best model choice. © 2010 IEEE.
Three-Dimensional Synthetic Aperture Focusing Using a Rocking Convex Array Transducer

Volumetric imaging can be performed using 1-D arrays in combination with mechanical motion. Outside the elevation focus of the array, the resolution and contrast quickly degrade compared with the lateral plane, because of the fixed transducer focus. This paper shows the feasibility of using synthetic aperture focusing for enhancing the elevation focus for a convex rocking array. The method uses a virtual source (VS) for defocused multi-element transmit, and another VS in the elevation focus point. This allows a direct time-of-flight to be calculated for a given 3-D point. To avoid artifacts and increase SNR at the elevation VS, a plane-wave VS approach has been implemented. Simulations and measurements using an experimental scanner with a convex rocking array show an average improvement in resolution of 26% and 33%, respectively. This improvement is also seen in in vivo measurements. An evaluation of how a change in transducer design will affect the resolution improvement shows a potential for using a modified transducer for 3-D imaging with improved elevation focusing and contrast.

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Scopus rating (2015): SJR 0.814 SNIP 1.494 CiteScore 2.43
Web of Science (2015): Indexed yes
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Scopus rating (2014): SJR 1.088 SNIP 1.627 CiteScore 2.18
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Transducer models in the ultrasound simulation program FIELD II and their accuracy

The FIELD II simulation program can be used for simulating any kind of linear ultrasound fields. The program is capable of describing multi-element transducers used with any kind of excitation, apodization, and focusing. The program has been widely used in both academia and by commercial ultrasound companies for investigating novel transducer geometries and advanced linear imaging schemes. The program models transducer geometries using a division of the transducer elements into either rectangles, triangles, or bounding lines. The precision of the simulation and the simulation time is intimately linked through the choice of the fundamental elements. The rectangular elements use a far-field approximation, whereas the two other methods use the full analytic solution, leading to a higher precision at the price of a slower simulation time. The talk will describe the different compromises and solutions to obtain a fast simulation and still attain a high precision including a newly developed semi-analytic solution for a convex surface elements.

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Transverse Oscillations for Phased Array Vector Velocity Imaging

Medical ultrasound imaging is widely used to visualize blood flow in the human circulatory system. However, conventional methods are angle dependent. The Transverse Oscillation (TO) method is able to measure the lateral velocity component, and it has been demonstrated in in vivo measurements of superficial blood vessels. To broaden the usability of the method, it should be expanded to a phased array geometry enabling vector velocity imaging of the heart. Therefore, the scan depth has to be increased to 10-15 cm. This paper presents suitable pulse echo fields (PEF). Two lines are beamformed in receive to obtain lateral spatial in-phase and quadrature components. The relative mean bias and standard deviation of the lateral velocity component are computed as performance measures. For the PEF, the coefficient of variance, CV, of the spectral frequencies, and the energy ratio, ER, of leakage into negative frequencies are used as metrics to assess estimator performance. At 10 cm's depth for an initial setup, the relative mean bias and standard deviation are 9.1% and 9.5%, respectively. At a depth of 15 cm, the values are 20% and 13%, respectively. The PEF metric ER can be used to assess the bias (correlation coefficient, R: -0.76), and therefore predict estimator performance. CV is correlated with the standard deviation (R=0.74). The results demonstrate the potential for using a phased array for vector velocity imaging at larger depths, and potentially for imaging the heart.
Ultrasound Image Quality Assessment: A framework for evaluation of clinical image quality

Improvement of ultrasound images should be guided by their diagnostic value. Evaluation of clinical image quality is generally performed subjectively, because objective criteria have not yet been fully developed and accepted for the evaluation of clinical image quality. Based on recommendation 500 from the International Telecommunication Union - Radiocommunication (ITU-R) for such subjective quality assessment, this work presents equipment and a methodology for clinical image quality evaluation for guiding the development of new and improved imaging. The system is based on a BK-Medical 2202 ProFocus scanner equipped with a UA2227 research interface, connected to a PC through X64-CL Express camera link. Data acquisition features subject data recording, loading/saving of exact scanner settings (for later experiment reproducibility), free access to all system parameters for beamformation and is applicable for clinical use. The free access to all system parameters enables the ability to capture standardized images as found in the clinic and experimental data from new processing or beamformation methods. The length of the data sequences is only restricted by the memory of the external PC. Data may be captured interleaved, switching between multiple setups, to maintain identical transducer, scanner, region of interest and recording time on both the experimental- and standardized images. Data storage is approximately 15.1 seconds pr. 3 sec sequence including complete scanner settings and patient information, which is fast enough to get sufficient number of scans under realistic operating conditions, so that statistical evaluation is valid and reliable.

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Authors: Hemmsen, M. C. (Intern), Pedersen, M. M. (Ekstern), Nikolov, S. I. (Ekstern), Backmann Nielsen, M. (Ekstern), Jensen, J. A. (Intern)
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Using Phased Array for Transverse Oscillation Vector Velocity Imaging

Objective Previous in vivo measurements of superficial blood vessels using linear arrays have demonstrated that the Transverse Oscillation (TO) method is able to measure the lateral velocity component contrary to conventional velocity estimators. To broaden its usability, the method should be expanded to phased arrays enabling vector velocity imaging of the heart. Therefore, the performance of the TO estimator has to be evaluated for depths up to 10-15 cm. Methods The TO method is based on creating a double oscillating field. Flow phantoms were simulated with a transverse (90°) parabolic flow profile (peak = 1 m/s) and a vessel radius of 5 mm, and 'scanned' orthogonal to the flow with a 3.5 MHz phased array transducer. The performance of the lateral velocity estimates were evaluated by calculating the relative mean bias, Br, and relative mean standard deviation, σr, inside the vessel of N=20 realizations. Results With a F-number of 10 in transmit and
receive peaks (spaced 96 elements apart) shaped as Hanning functions, parabolic velocity profiles were be observed for all cases. At depths of 10, 12, and 15 cm, the following results were obtained in pairs of $\sigma_r$ & $B_r$: 6.5% & 2.6%, 7.5% & 3.8%, and 8.5% & 4.2%, respectively. Conclusions The results show that the TO estimator performs comparably with a standard axial estimator at depths of 10-15 cm. This demonstrates the potential of the TO method for scanning the heart using a phased array.

**Non-invasive ambient pressure estimation using non-linear ultrasound contrast agents**

Many attempts to find a non-invasive procedure to measure the blood pressure locally in the body have been made. This dissertation focuses on the approaches which utilize highly compressible ultrasound contrast agents as ambient pressure sensors. The literature within the topic has been reviewed. From this, the appropriate pressure dependent acoustic properties of the microbubbles can be summarized to be the resonance frequency, the disappearance time, and the subharmonic response. During this thesis, the ambient pressure sensitivity of the subharmonic response has been investigated through simulations and initial experimental measurements. By simulations, a parameter study has investigated what mechanisms of the driving pulse are important to optimize the ambient pressure sensitivity when utilizing the subharmonic component. Investigating two different types of microbubbles clearly showed that two factors are important when striving for an optimum sensitivity. First, the amount of subharmonic energy reduction, when increasing the ambient pressure, is very sensitive to the acoustic excitation pressure. Second, the study also indicated that the amount of reduction in subharmonic energy is increased as the length of the excitation pulse is extended. To carry out measurements in the laboratory, an experimental setup has been established. As the focus has been on preparations for future in vivo measurements, the setup was designed to match a clinical situation. Under the current measurement conditions, this setup showed that the subharmonic component by itself cannot be used as an ambient sensitivity measure. Instead, a new technique looking at the ratio of the subharmonic energy to the energy of the fundamental component was used. Doing so, an ambient pressure dependent behavior of the microbubbles was observed, indicating this to be a more robust measure. When increasing the ambient pressure, the relation decreases linearly. Likewise, decreasing the ambient pressure makes the relation increase linearly. Although the approach seems to reduce factors like time dependency, a high standard deviation was still observed. This could be caused by several reasons and more measurements are needed to investigate it further.
Synthetic Aperture Beamforming in Ultrasound using Moving Arrays.
Medical ultrasound (US) is widely used because it allows cheap real-time imaging of soft tissue with no known side-effects or hazards to either patients or operating personnel. US has existed since the 1960s and was originally adapted from the concept of radar and sonar. The development in ultrasound has allowed the technology to evolve from a showing a simple echo along a line to fully visualize entire organs. The image changes significantly depending on the orientation of the transducer, making it more difficult to see exact features. This poses challenges since anatomy is three-dimensional and the limited view makes diagnosis of pathology difficult [1]. A full 3D volume acquisition makes it possible to capture larger areas at once, and also allows complete freedom in choosing the slice to view after the scan has been completed. This removes the need for doing additional scans if a significant slice was missed and allows a more precise measurement of organ dimensions [2, 3, 4]. Conventional 3D ultrasound imaging is basically faced with two limitations. It is only able to have a single transmit focus point and each line in a 3D volume has to be created independently. This reduces image quality outside the focus point and reduces temporal resolution. For better image quality it is desirable to achieve a good resolution at a large range of depths, and achieving a volume-rate fast enough to visualize the dynamics of the investigated organ. A method showing the possibility of meeting both these challenges is synthetic aperture focusing (SAF). A full dynamic focusing is possible in both transmit and receive as well as the possibility of imaging an entire volume with only a few emission. The resolution of the resulting volume can be improved by using more emissions, giving a trade-off between temporal and spatial resolution. A challenge with SAF is a large increase in processing requirements, especially for 3D systems. Ideally the method is able to achieve a good image quality for all depths in the volume with a time-resolution fast enough for cardiac images. This will allow better diagnoses with fewer scans, making each investigation less user-dependent. In the end this has the potential of reducing costs for each investigation, as both time required to scan, and the expertise needed to do so successfully can be reduced.
A Combined Mathematical-Physical Model of Laser-Induced Thermotherapy (LITT)

Laser-induced thermo therapy (LITT) is an alternative, gentle therapy of cancer. In this work a new computa- tional model (3D space and time) of LITT is presented. Using an arbitrary small number (<20) of optical bers, multiple low energy laser light sources are applied internal to an arbitrary shaped tumor in the human liver. The power and position of each source can be chosen arbitrary. Each source is a spherical point source emitting light isotropically. The model consists of two, semi-coupled partial differential equations (PDEs) describing the light distribution and the heat absorption in the target tissue. Since water is a dominant tissue component in both the healthy liver and the malignant tumor the wavelength of the laser is chosen in the NIR area (1,064 nm). This is expected to form an absorption contrast in favor of the tumor leading to high temperature and damage of the tumor cells. The new, fast computational model presented here opens for the possibility of evaluating the outcome of LITT by inspection of temperature elds, and comparing these to measured histological damage due to heating. This combination is promising when evaluating the result of LITT prior to the actual treatment.

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Organisations: Biomedical Engineering, Department of Electrical Engineering, Applied functional analysis, Department of Mathematics, Teraherts Technologies and Biophotonics, Department of Photonics Engineering
Authors: Enevoldsen, M. S. (Intern), Skovgaard, O. (Intern), Andersen, P. E. (Intern)
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Adaptive Receive and Transmit Apodization for Synthetic Aperture Ultrasound Imaging

This paper suggests a framework for utilizing adaptive, data-dependent apodization weights on both the receiving and transmitting aperture for Synthetic Aperture (SA) ultrasound imaging. The suggested approach is based on the Minimum Variance (MV) beamformer and consists of two steps. A set of uniquely designed receive apodization weights are applied to pre-summed element data forming a set of adaptively weighted images; these are in SA literature conventionally referred to as low-resolution images. The adaptive transmit apodization is obtained by applying MV across the full set of single emission images before summation. The method is investigated using simulated SA ultrasound data obtained using Field II. Data of 13 point targets distributed at depths from 40 mm to 70 mm, and a 5.5 MHz, 64-element linear array transducer have been used. The investigation has shown that the introduction of adaptive apodization weights on the transmitting aperture provides a main-lobe reduction (estimated at -30 dB) by a factor of 1.8 compared to the method using adaptive apodization weights on the receiving aperture only.

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Organisations: Center for Fast Ultrasound Imaging, Biomedical Engineering, Department of Electrical Engineering, University of Oslo, Bergen Oilfield Services AS
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Holfort.pdf
Adaptive Spectral Doppler Estimation

In this paper, 2 adaptive spectral estimation techniques are analyzed for spectral Doppler ultrasound. The purpose is to minimize the observation window needed to estimate the spectrogram to provide a better temporal resolution and gain more flexibility when designing the data acquisition sequence. The methods can also provide better quality of the estimated power spectral density (PSD) of the blood signal. Adaptive spectral estimation techniques are known to provide good spectral resolution and contrast even when the observation window is very short. The 2 adaptive techniques are tested and compared with the averaged periodogram (Welch’s method). The blood power spectral capon (BPC) method is based on a standard minimum variance technique adapted to account for both averaging over slow-time and depth. The blood amplitude and phase estimation technique (BAPES) is based on finding a set of matched filters (one for each velocity component of interest) and filtering the blood process over slow-time and averaging over depth to find the PSD. The methods are tested using various experiments and simulations. First, controlled flow-rig experiments with steady laminar flow are carried out. Simulations in Field II for pulsating flow resembling the femoral artery are also analyzed. The simulations are followed by in vivo measurement on the common carotid artery. In all simulations and experiments it was concluded that the adaptive methods display superior performance for short observation windows compared with the averaged periodogram. Computational costs and implementation details are also discussed.

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Measurements on microbubbles clearly indicate a relation between the ambient pressure and the acoustic behavior of the bubble. The purpose of this study was to optimize the sensitivity of ambient pressure measurements, using the subharmonic component, through microbubble response simulations. The behavior of two microbubbles corresponding to two different contrast agents was investigated as a function of driving pulse and ambient overpressure, pov. Simulations of Levovist using a rectangular driving pulse show an almost linear reduction in the subharmonic component as pov is increased. For a 20 cycles driving pulse, a reduction of 4.6 dB is observed when changing pov from 0 to 25 kPa. Increasing the pulse duration makes the reduction even more clear. For a pulse with 64 cycles, the reduction is 9.9 dB. This simulation is in good correspondence with measurement results presented by Shi et al. 1999, who found a linear reduction of 9.6 dB. Further simulations of Levovist show that also the shape and the acoustic pressure of the driving pulse are very important factors. The best pressure sensitivity of Levovist was found to be 0.88 dB/kPa. For Sonazoid, a sensitivity of 1.14 dB/kPa has been found, although the reduction is not completely linear as a function of the ambient pressure.
A new tool fixation for external 3D head tracking using the Polaris Vicra system with the HRRT PET scanner

Objectives: The Polaris Vicra system (Northern Digital Inc.) is used for external 3D head registration with the Siemens HRRT brain PET. Our new tool fixation using a standard bandaid with a velcro-strap implies an improved frame repositioning. Methods: Head movements during serial PET 15O-water studies for up to 75 min (3-8 injections) were registered by the Polaris system in 4 volunteers. The tracking tool was fixed. Scans were divided into subframes based on the registered movements and reconstructed using the 3D-OSEM PSF method. The reconstructed subframes were repositioned to a reference position and pairwise similarity of subframes was evaluated before and after the repositioning. Results: Registered movements during scans were less than 4.3mm with. Images were compared before/after motion correction. Conclusions: Our new velcro band-aid fixation is suitable for clinical use: easy to use, disposable, comfortable, independent of head size and has low cost. It is reliable with only a limited contact area with the movable structures of the head. Registered movements corresponded to those seen on the PET images and correlations between scans were improved after repositioning based on the tracked head position.

Angular Spectrum Simulation of Pulsed Ultrasound Fields

The optimization of non-linear ultrasound imaging should in a first step be based on simulation, as this makes parameter studies considerably easier than making transducer prototypes. Such a simulation program should be capable of simulating non-linear pulsed fields for arbitrary transducer geometries for any kind of focusing and apodization. The Angular Spectrum Approach (ASA) is capable of simulating monochromatic non-linear acoustic wave propagation. However, for ultrasound imaging the time response of each specific point in space is required, and a pulsed ASA simulation with multi temporal frequencies must be performed. Combining it with Field II, the generation of non-linear simulation for any geometry with any excitation array transducer becomes feasible. The purpose of this paper is to make a general pulsed simulation software using the modified ASA. Linear and phased array transducers are used to create the source plane, which is 2 mm from the transducer surface. Field II generates pulses for all the points in the source plane, and the 3D matrix data (1D time, 2D space) are obtained. The pulses in the simulated plane are calculated by the modified ASA, which is the 3D inverse Fourier transform of the values in a series of planes corresponding to each temporal frequency. The values in the planes are the multiplications between the 2D spatial Fourier transform of the pressure in the
source plane and the ASA propagator for every temporal frequency components. The beam focusing is produced by Field II in the source plane. A rectangular plane matched to the shape of the transducer surface is chosen as the source. The plane covering 12.7?156.3 mm2 has 33?407 points with a spatial sampling interval of 1/2 wavelength. A comparison of ASA to Field II at the focal point (0, 0, 64) mm for a 64-element, 2 MHz linear array transducer has been made in the paper, and the root mean square (RMS) error is 2.7%. For further validation, 3 randomly selected points in the simulated plane have RMS errors of 12.5%, 13.3%, 23.4% at the positions (3.9, -1.5, 64), (-1.9, 1.9, 64), (6.2, -4.2, 64) mm. The RMS error of the pulses for all points in the simulated plane is 10.9%. The good agreement between ASA and Field II simulation for the pulsed ultrasound fields obtained in this paper makes it possible to expand Field II to non-linear pulsed fields.

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APES Beamforming Applied to Medical Ultrasound Imaging
Recently, adaptive beamformers have been introduced to medical ultrasound imaging. The primary focus has been on the minimum variance (MV) (or Capon) beamformer. This work investigates an alternative but closely related beamformer, the Amplitude and Phase Estimation (APES) beamformer. APES offers added robustness at the expense of a slightly lower resolution. The purpose of this study was to evaluate the performance of the APES beamformer on medical imaging data, since correct amplitude estimation often is just as important as spatial resolution. In our simulations we have used a 3.5 MHz, 96 element linear transducer array. When imaging two closely spaced point targets, APES displays nearly the same resolution as the MV, and at the same time improved amplitude control. When imaging cysts in speckle, APES offers speckle statistics similar to that of the DAS, without the need for temporal averaging.

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Authors: Blomberg, A. E. A. (Ekstern), Holfort, I. K. (Intern), Austeng, A. (Ekstern), Synnevåg, J. (Ekstern), Holm, S. (Ekstern), Jensen, J. A. (Intern)
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A probabilistic model of RNA conformational space

The increasing importance of non-coding RNA in biology and medicine has led to a growing interest in the problem of RNA 3-D structure prediction. As is the case for proteins, RNA 3-D structure prediction methods require two key ingredients: an accurate energy function and a conformational sampling procedure. Both are only partly solved problems. Here, we focus on the problem of conformational sampling. The current state of the art solution is based on fragment assembly methods, which construct plausible conformations by stringing together short fragments obtained from experimental structures. However, the discrete nature of the fragments necessitates the use of carefully tuned, unphysical energy functions, and their non-probabilistic nature impairs unbiased sampling. We offer a solution to the sampling problem that removes these important limitations: a probabilistic model of RNA structure that allows efficient sampling of RNA conformations in continuous space, and with associated probabilities. We show that the model captures several key features of RNA structure, such as its rotameric nature and the distribution of the helix lengths. Furthermore, the model readily generates native-like 3-D conformations for 9 out of 10 test structures, solely using coarse-grained base-pairing information. In conclusion, the method provides a theoretical and practical solution for a major bottleneck on the way to routine prediction and simulation of RNA structure and dynamics in atomic detail.

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Organisations: Biomedical Engineering, Department of Electrical Engineering, University of Leeds, University of Copenhagen
Authors: Frellsen, J. (Ekstern), Moltke, I. (Ekstern), Thiim, M. (Ekstern), Mardia, K. (Ekstern), Ferkinghoff-Borg, J. (Intern), Hamelryck, T. (Ekstern)
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Broadband Minimum Variance Beamforming for Ultrasound Imaging

A minimum variance (MV) approach for near-field beamforming of broadband data is proposed. The approach is implemented in the frequency domain, and it provides a set of adapted, complex apodization weights for each frequency subband. The performance of the proposed MV beamformer is tested on simulated data obtained using Field II. The method is validated using synthetic aperture data and data obtained from a plane wave emission. Data for 13 point targets and a circular cyst with a radius of 5 mm are simulated. The performance of the MV beamformer is compared with delay-and-sum (DS) using boxcar weights and Harming weights and is quantified by the full width at half maximum (FWHM) and the peak-side-lobe level (PSL). Single emission (DS boxcar, DS Harming, MV) provide a PSL of {-16, -36, -49} dB and a FWHM of {0.79, 1.33, 0.08} mm. Using all 128 emissions, (DS boxcar, DS Harming, MV) provides a PSL of {-32, -49, -65} dB and a FWHM of {0.08, 0.08, 0.08} mm.
dB, and a FWHM of \{0.63, 0.97, 0.08\} mm. The contrast of the beamformed single emission responses of the circular cyst was calculated as \{-18, -37, -40\} dB. The simulations have shown that the frequency subband MV beamformer provides a significant increase in lateral resolution compared with DS, even when using considerably fewer emissions. An increase in resolution is seen when using only one single emission. Furthermore, the effect of steering vector errors is investigated. The steering vector errors are investigated by applying an error of the sound speed estimate to the ultrasound data. As the error increases, it is seen that the MV beamformer is not as robust compared with the DS beamformer with boxcar an Harming weights. Nevertheless, it is noted that the DS does not outperform the MV beamformer. For errors of 2% and 4% of the correct value, the FWHM are \{0.81, 1.25, 0.34\} mm and \{0.89, 1.44, 0.46\} mm, respectively.

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Evaluation Study of Fast Spectral Estimators Using In-vivo Data

Spectrograms in medical ultrasound are usually estimated with Welch's method (WM). To achieve sufficient spectral resolution and contrast, WM uses an observation window (OW) of up to 256 emissions per estimate. Two adaptive filterbank methods have been suggested to reduce the OW: Blood spectral Power Capon (BPC) and the Blood Amplitude and Phase EStimation method (BAPES). Ten volunteers were scanned over the carotid artery. From each dataset, 28 spectrograms were produced by combining four approaches (WM with a Hanning window (W.HAN), WM with a boxcar window (W.BOX), BPC and BAPES) and seven OWs (128, 64, 32, 16, 8, 4, 2). The full-width-at-half-maximum (FWHM) and the ratio between main and side lobe levels were calculated for each spectrogram. Furthermore, all 280 randomized spectrograms were presented to nine radiologists for visual evaluation: useful/not useful. BAPES and BPC compared to WM had better resolution (lower FWHM) for all OW0.05) at OW 128 and 64, while W.BOX scored less (p

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Feasibility of Seizure Prediction from Intracranial EEG Recordings

Purpose: The current project evaluated the feasibility of providing an algorithm that could warn a patient of a forthcoming seizure based on iEEG recordings. Method: The mean phase coherence (MPC) feature (Mormann F et al. Phys Nonlinear Phenom 2000;3-4:358-369.) was implemented and tested in a rigorously, out-of-sample manner. The MPC-feature is based on the synchronization measure, explained through the analytic signal approach where the Hilbert transform is used to find the instantaneous phase of an arbitrary signal. By a relative comparison between two different iEEG channels the phase synchronization was calculated. The feature was employed on the FSPEEG database containing 21 patients with 4.1 seizures in average (Winterhalder M et al. Epilepsy Behav. 2003;4(3):318-325.) to assess its predictive performance. Results: A sensitivity of 55% and a specificity of 62% were obtained after a unified optimization of threshold value and localization of electrodes for all patients. These results are just better than a random predictor. To improve the results the parameters need to be optimized for each patient individually. Before this can be done, a larger database with more seizures recorded per patient is needed. Conclusion: It was shown that it is possible to anticipate an epileptic seizure to some degree. While the obtained results are still far from clinically applicable, they suggest that by optimization of personal parameters, at least some patients will be able to gain advantage of seizure prediction. The field still needs further investigation though.
High Resolution Ultrasound Imaging Using Adaptive Beamforming with Reduced Number of Active Elements

In this paper, the adaptive, minimum variance (MV) beamformer is applied to ultrasound data. Due to near-field properties, the energy of the ultrasound data reduces towards the edges of the transducer. The influence of this near-field effect is demonstrated, and a method to reduce this influence is proposed. By reducing the number of active sensor elements, an increased resolution can be obtained with the MV beamformer. This observation is directly opposite the well-known relation between the spatial extent of the aperture and the achievable resolution. The investigations are based on Field II simulated data using a 128-element transducer with a large spatial extent. The results show that an increased resolution can be obtained, when using only the central part of the transducer compared to using the entire spatial extent. Using the central 32 or 48 elements provides an increased resolution compared to using all 128 elements.
Information theoretical quantification of cooperativity in signalling complexes

Background: Intra-cellular information exchange, propelled by cascades of interacting signalling proteins, is essential for the proper functioning and survival of cells. Now that the interactome of several organisms is being mapped and several structural mechanisms of cooperativity at the molecular level in proteins have been elucidated, the formalization of this fundamental quantity, i.e. information, in these very diverse biological contexts becomes feasible. Results: We show here that Shannon’s mutual information quantifies information in biological system and more specifically the cooperativity inherent to the assembly of macromolecular complexes. We show how protein complexes can be considered as particular instances of noisy communication channels. Further we show, using a portion of the p27 regulatory pathway, how classical equilibrium thermodynamic quantities such as binding affinities and chemical potentials can be used to quantify information exchange but also to determine engineering properties such as channel noise and channel capacity. As such, this information measure identifies and quantifies those protein concentrations that render the biochemical system most effective in switching between the active and inactive state of the intracellular process. Conclusion: The proposed framework provides a new and original approach to analyse the effects of cooperativity in the assembly of macromolecular complexes. It shows the conditions, provided by the protein concentrations, for which a particular system acts most effectively, i.e. exchanges the most information. As such this framework opens the possibility of grasping biological qualities such as system sensitivity, robustness or plasticity directly in terms of their effect on information exchange. Although these parameters might also be derived using classical thermodynamic parameters, a recasting of biological signalling in terms of information exchange offers an alternative framework for visualising network cooperativity that might in some cases be more intuitive.
In vivo comparison of three ultrasound vector velocity techniques to MR phase contrast angiography

The objective of this paper is to validate angle independent vector velocity methods for blood velocity estimation. Conventional Doppler ultrasound (US) only estimates the blood velocity along the US beam direction where the estimate is angle corrected assuming laminar flow parallel to vessel boundaries. This results in incorrect blood velocity estimates, when angle of insonation approaches 90° or when blood flow is non-laminar. Three angle independent vector velocity methods are evaluated in this paper: directional beamforming (DB), synthetic aperture flow imaging (STA) and transverse oscillation (TO). The performances of the three methods were investigated by measuring the stroke volume in the right common carotid artery of 11 healthy volunteers with magnetic resonance phase contrast angiography (MRA) as reference. The correlation with confidence intervals (CI) between the three vector velocity methods and MRA were: DB vs. MRA: R = 0.84 (p <0.01, 95% CI: 0.49–0.96); STA vs. MRA: R = 0.71 (p <0.05, 95% CI: 0.19–0.92) and TO vs. MRA: R = 0.91 (p <0.01, 95% CI: 0.69–0.98). No significant differences were observed for any of the three comparisons (DB vs. MRA: p = 0.65; STA vs. MRA: p = 0.24; TO vs. MRA: p = 0.36). Bland–Altman plots were additionally constructed, and mean differences with limits of agreements (LoA) for the three comparisons were: DB vs. MRA = 0.17 ml (95% CI: −0.61–0.95) with LoA = −2.11–2.44 ml; STA vs. MRA = −0.55 ml (95% CI: −1.54–0.43) with LoA = −3.42–2.32 ml; TO vs. MRA = 0.24 ml (95% CI: −0.32–0.81) with LoA = −1.41–1.90 ml. According to the results, reliable volume flow estimates can be obtained with all three methods. The three US vector velocity techniques can yield quantitative insight into flow dynamics...
and visualize complex flow patterns, which potentially can give the clinician a novel tool for cardiovascular disease assessment.

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Authors: Hansen, K. L. (Intern), Udesen, J. (Intern), Oddershede, N. (Intern), Henze, L. (Ekstern), Thomsen, C. (Ekstern), Jensen, J. A. (Intern), Nielsen, M. B. (Ekstern)
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In-vivo Examples of Flow Patterns With The Fast Vector Velocity Ultrasound Method

Purpose: Conventional ultrasound methods for acquiring color flow images of the blood motion are limited by a relatively low frame rate and are restricted to only giving velocity estimates along the ultrasound beam direction. To circumvent these limitations, the Plane Wave Excitation (PWE) method has been proposed. Material and Methods: The PWE method can estimate the 2D vector velocity of the blood with a high frame rate. Vector velocity estimates are acquired by using the following approach: The ultrasound is not focused during the ultrasound transmission, and a full speckle image of the blood can be acquired for each pulse emission. The pulse is a 13 bit Barker code transmitted simultaneously from each transducer element. The 2D vector velocity of the blood is found using 2D speckle tracking between segments in consecutive speckle images. Implemented on the experimental scanner RASMUS and using a 100 CPU linux cluster for post processing, PWE can achieve a frame of 100 Hz where one vector velocity sequence of approximately 3 sec, takes 10 h to store and 48 h to process. In this paper a case study is presented of in-vivo vector velocity estimates in different complex vessel geometries. Results: The flow patterns of six bifurcations and two veins were investigated. It was shown: 1. that a stable vortex in the carotid bulb was present opposed to other examined bifurcations, 2. that retrograde flow was present in the superficial branch of the femoral artery during diastole, 3. that retrograde flow was present in the subclavian artery and antegrade in the common carotid artery during diastole, 4. that vortices were formed in the sinus pockets behind the venous valves in both antegrade and retrograde flow, and 5. that secondary flow was present in various vessels. Conclusion: Using a fast vector velocity ultrasound method, in-vivo scans have been recorded where complex flow patterns were visualized in greater detail than previously visualized by conventional color flow imaging techniques.
In Vivo Validation of a Blood Vector Velocity Estimator with MR Angiography

Conventional Doppler methods for blood velocity estimation only estimate the velocity component along the ultrasound beam direction. This implies that a Doppler angle under examination close to 90° results in unreliable information about the true blood direction and blood velocity. The novel method transverse oscillation (TO), which combines estimates of the axial and the transverse velocity components in the scan plane, makes it possible to estimate the vector velocity of the blood regardless of the Doppler angle. The present study evaluates the TO method with magnetic resonance phase contrast angiography (MRA) by comparing in vivo measurements of stroke volume. Eleven healthy volunteers were included in this prospective study. From the obtained data sets recorded with the 2 modalities, vector velocity sequences were constructed and stroke volume calculated. Angle of insonation was approximately 90° for TO measurements. The correlation between the stroke volume estimated by TO and MRA was 0.91 (p <0.01) with the equation for the line of regression: MRA = 1.1•TO-0.4. A Bland-Altman plot was additionally constructed where the mean difference was 0.2 ml with limits of agreement at −1.4 ml and 1.9 ml. The results indicate that reliable vector velocity estimates can be obtained in vivo using the presented angle-independent 2-D vector velocity method. The TO method can be a useful alternative to conventional Doppler systems by avoiding the angle artifact, thus giving quantitative velocity information.

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Motion Correction of Single-Voxel Spectroscopy by Independent Component Analysis Applied to Spectra From Nonanesthetized Pediatric Subjects

For single-voxel spectroscopy, the acquisition of the spectrum is typically repeated n times and then combined with a factor in order to improve the signal-to-noise ratio. In practice, the acquisitions are not only affected by random noise but also by physiologic motion and subject movements. Since the influence of physiologic motion such as cardiac and respiratory motion on the data is limited, it can be compensated for without data loss. Individual acquisitions hampered by subject movements, on the other hand, need to be rejected if no correction or compensation is possible. If the individual acquisitions are stored, it is possible to identify and reject the motion-disturbed acquisitions before averaging. Several automatic algorithms were investigated using a dataset of spectra from nonanesthetized infants with a gestational age of 40 weeks. Median filtering removed most subject movement artifacts, but at the cost of increased sensitivity to random noise. Neither independent component analysis nor outlier identification with multiple comparisons has this problem. These two algorithms are novel in this context. The peak height values of the metabolites were increased compared to the mean of all acquisitions for both methods, although primarily for the ICA method. Magn Reson Med, 2009. © 2009 Wiley-Liss, Inc.

General information
State: Published
Organisations: Cognitive Systems, Department of Informatics and Mathematical Modeling, Biomedical Engineering, Department of Electrical Engineering
Authors: de Nijs, R. (Intern), Miranda, M. J. (Ekstern), Hansen, L. K. (Intern), Hanson, L. G. (Intern)
Pages: 1147-1154
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Main Research Area: Technical/natural sciences

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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.77 SJR 1.89 SNIP 1.411
Multi-modal Intelligent Seizure Acquisition (MISA) system - A new approach towards seizure detection based on full body motion measures

Many epilepsy patients cannot call for help during a seizure, because they are unconscious or because of the affection of their motor system or speech function. This can lead to injuries, medical complications and at worst death. An alarm
system setting off at seizure onset could help to avoid hazards. Today no reliable alarm systems are available. A Multi-modal Intelligent Seizure Acquisition (MISA) system based on full body motion data seems as a good approach towards detection of epileptic seizures. The system is the first to provide a full body description for epilepsy applications. Three test subjects were used for this pilot project. Each subject simulated 15 seizures and in addition performed some predefined normal activities, during a 4-hour monitoring with electromyography (EMG), accelerometer, magnetometer and gyroscope (AMG), electrocardiography (ECG), electroencephalography (EEG) and audio and video recording. The results showed that a non-subject specific MISA system developed on data from the modalities: accelerometer (ACM), gyroscope and EMG is able to detect 98% of the simulated seizures and at the same time mistakes only 4 of the normal movements for seizures. If the system is individualized (subject specific) it is able to detect all simulated seizures with a maximum of 1 false positive. Based on the results from the simulated seizures and normal movements the MISA system seems to be a promising approach to seizure detection.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Danish Epilepsy Center
Authors: Conradsen, I. (Intern), Beniczky, S. (Ekstern), Wolf, P. (Ekstern), Terney, D. (Ekstern), Sams, T. (Intern), Sørensen, H. B. D. (Intern)
Pages: 2591-2595
Publication date: 2009

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Publisher: IEEE
Main Research Area: Technical/natural sciences
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Source: orbit
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Publication: Research - peer-review › Article in proceedings – Annual report year: 2009

New Insight into Erythrocyte through In Vivo Surface-Enhanced Raman Spectroscopy
The article presents a noninvasive approach to the study of erythrocyte properties by means of a comparative analysis of signals obtained by surface-enhanced Raman spectroscopy (SERS) and resonance Raman spectroscopy (RS). We report step-by-step the procedure for preparing experimental samples containing erythrocytes in their normal physiological environment in a mixture of colloid solution with silver nanoparticles and the procedure for the optimization of SERS conditions to achieve high signal enhancement without affecting the properties of living erythrocytes. By means of three independent techniques, we demonstrate that under the proposed conditions a colloid solution of silver nanoparticles does not affect the properties of erythrocytes. For the first time to our knowledge, we describe how to use the SERS-RS approach to study two populations of hemoglobin molecules inside an intact living erythrocyte: submembrane and cytosolic hemoglobin (Hb(sm) and Hb(c)). We show that the conformation of Hbsm differs from the conformation of Hbc. This finding has an important application, as the comparative study of Hbsm and Hbc could be successfully used in biomedical research and diagnostic tests.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Moscow Lomonosov State University, University of Copenhagen
Authors: Brazhe, N. A. (Ekstern), Abdali, S. (Intern), Brazhe, A. R. (Ekstern), Luneva, O. G. (Ekstern), Bryzgalova, N. Y. (Ekstern), Parshina, E. Y. (Ekstern), Sosnovtseva, O. V. (Ekstern), Maksimov, G. V. (Ekstern)
Pages: 3206-3214
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Non-invasive estimation of blood pressure using ultrasound contrast agents

Local blood pressure measurements provide important information on the state of health of organs in the body and can be used to diagnose diseases in the heart, lungs, and kidneys. This paper presents an experimental setup for investigating the ambient pressure sensitivity of a contrast agent using diagnostic ultrasound. The setup resembles a realistic clinical setup utilizing a single array transducer for transmit and receive. The ambient pressure sensitivity of SonoVue (Bracco, Milano, Italy) was measured twice using two different acoustic driving pressures, which were selected based on a preliminary experiment. To compensate for variations in bubble response and to make the estimates more robust, the relation between the energy of the subharmonic and the fundamental component was chosen as a measure over the subharmonic peak amplitude. The preliminary study revealed the growth stage of the subharmonic component to occur at acoustic driving pressures between 300 and 500 kPa. Based on this, the pressure sensitivity was investigated using a driving pressure of 485 and 500 kPa. At 485 kPa, a linear pressure sensitivity of 0.42 dB/kPa was found having a linear correlation coefficient of 0.94. The second measurement series at 485 kPa showed a sensitivity of 0.41 dB/kPa with a correlation coefficient of 0.89. Based on the measurements at 500 kPa, this acoustic driving pressure was concluded to be too high causing the bubbles to be destroyed. The pressure sensitivity for these two measurement series were 0.42 and 0.25 dB/kPa with linear correlation coefficients of 0.98 and 0.93, respectively.
Non-linear models in focus localization, seizure detection and prediction

One of the most devastating problems for epilepsy patients is the unpredictable nature of seizures. Not knowing when or where a seizure occurs has severe consequences in social interaction, ability to work, driving a car, go swimming etc. Traditionally the patient and the doctor work together to reduce the amount of seizures, but if only the seizures could be predicted many patients would live a better life even with the same amount of seizures. Most of the research in this area is based on continuous EEG-recordings. Doing the right analysis on the EEG-signal is essential. In the presentation I will introduce different methods developed in collaboration between DTU and Rigshospitalet for seizure prediction and detection. Prediction of seizure onset with nonlinear signal processing has shown promising results in recent years. The goal is to make an attention-device that gives a message when a seizure is approaching. The primary obstacle is the lack of sufficient large databases to make a patient-specific algorithm rather than a “one-size-fits-all” approach. At Rigshospitalet, a research project is carried out that aims at collecting enough data to be able to do this. The next couple of years will probably show whether we should put our hopes up for a seizure prediction algorithm. Seizure detection is a more established field of nonlinear EEG-analysis. Some kinds of epilepsy give none or few clinical symptoms and are thus difficult for the treating physician, relatives, and the patient him- or herself to know when and how often there is seizure activity in the brain. It is therefore interesting to make an objective and automatic detection of the quantity of seizure activity, which is not reliable on competence or fatigue by the epileptologist. With the best algorithm it has been possible to obtain a 100 % detection rate with false alarms amounting to merely 0.02 per hour. While these numbers only apply to seizures of a certain type, a general algorithm has achieved an 83 % detection rate with the same number of false alarms per hour.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Henriksen, J. (Intern)
Publication date: 2009
Event: Paper presented at Danish Epilepsy Society & the Danish Society of Clinical Neurophysiology Annual Meeting, Odense, Denmark,.
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Source: orbit
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On the Nature of the Intrinsic Connectivity of the Cat Motor Cortex: Evidence for a Recurrent Neural Network Topology
Capaday C, Ethier C, Brizzi L, Sik A, van Vreeswijk C, Gingras D. On the nature of the intrinsic connectivity of the cat motor cortex: evidence for a recurrent neural network topology. J Neurophysiol 102: 2131-2141, 2009. First published July 22, 2009; doi: 10.1152/jn.91319.2008. The details and functional significance of the intrinsic horizontal connections between neurons in the motor cortex (Mcx) remain to be clarified. To further elucidate the nature of this intracortical connectivity pattern, experiments were done on the Mcx of three cats. The anterograde tracer biocytin was ejected iontophoretically in layers II, III, and V. Some 30-50 neurons within a radius of similar to 250 µm were thus stained. The functional output of the motor cortical point at which biocytin was injected, and of the surrounding points, was identified by
microstimulation and electromyographic recordings. The axonal arborizations of the stained neurons were traced under camera lucida. The axon collaterals were extensive, reaching distances of

**General information**

State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering
Authors: Capaday, C. (Intern), Ethier, C. (Ekstern), Brizzi, L. (Ekstern), Sik, A. (Ekstern), van Vreeswijk, C. (Ekstern), Gingras, D. (Ekstern)
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.198 SNIP 1.063 CiteScore 2.96
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.383 SNIP 1.159 CiteScore 3.15
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ISI indexed (2013): ISI indexed yes
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Scopus rating (2011): SJR 2.848 SNIP 1.222 CiteScore 3.53
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.788 SNIP 1.143
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 3.217 SNIP 1.235
Web of Science (2009): Indexed yes
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Scopus rating (2008): SJR 3.355 SNIP 1.294
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 3.121 SNIP 1.429
Scopus rating (2006): SJR 2.877 SNIP 1.4
Scopus rating (2005): SJR 3.073 SNIP 1.442
Scopus rating (2004): SJR 2.922 SNIP 1.263
Scopus rating (2003): SJR 3.158 SNIP 1.396
Scopus rating (2002): SJR 2.668 SNIP 1.363
Scopus rating (2001): SJR 2.645 SNIP 1.376
Scopus rating (2000): SJR 2.917 SNIP 1.446
Scopus rating (1999): SJR 2.973 SNIP 1.447
Original language: English
Parameter sensitivity study of a Field II multilayer transducer model on a convex transducer

A multilayer transducer model for predicting a transducer impulse response has in earlier works been developed and combined with the Field II software. This development was tested on current, voltage, and intensity measurements on piezoceramics discs (Bæk et al. IUS 2008) and a convex 128 element ultrasound imaging transducer (Bæk et al. ICU 2009). The model benefits from its 1D simplicity and has shown to give an amplitude error around 1.7-2 dB. However, any prediction of amplitude, phase, and attenuation of pulses relies on the accuracy of manufacturer supplied material characteristics, which may be inaccurate estimates. The previous test cases have assumed the simulation parameters to be exact as received from the manufacturer. In this paper the influence of a deviation in the accuracy of the different parameters is studied by comparing simulation and measurement. The long term objective is a quantitative calibrated model for a complete ultrasound system. This includes a sensitivity study as presented here.

Statement of Contribution/Methods

The study alters 35 different model parameters which describe a 128 element convex transducer from BK Medical Aps. The changes are within ±20 % of the values supplied by the manufacturer, which are considered the zero reference (ZR). Simulations of a system consisting of a transmit unit, a five material layer transducer, and the FIELD II predicted pressure are performed by altering in turn the value of a single parameter in steps of 2 %. The remaining simulation parameters are held fixed at the ZR. The influence of the parameter change is determined by calculating the pressure and the intensity at distance of 112 mm on an element’s center axis and comparing it with hydrophone measurements. These are performed with a water bath hydrophone setup using an Agilent MSO6014A oscilloscope that is set to average consecutive pulses 48 times for noise reduction of the hydrophone output. A commercial transmitter unit is used to drive the transducer with a 10 cycle tone burst at a frequency of 4.0 MHz and a maximum excitation amplitude of 31 volt.

Results

Predictions using the ZR give a pressure pulse error (PPE) and an intensity error (IE) of 32 % and 23 %, respectively, relative to the measured. Altering the piezoelectric permittivity +12 % from ZR decreases the PPE to 30 % and the IE to 2 % relative to the measured. Changing the stiffness constant of the lens -4 % from ZR increases the PPE and the IE with 6 % and 1 %, respectively. Performing the same with the ceramic stiffness the PPE is lowered 1.5 % and the IE is lowered 12 %. Discussion and Conclusions

PPEs are found mainly to be sensitive to lens properties and piezoceramic properties, but minor sensitive to changes in matching layers. IEs are mainly sensitive to the piezoceramic properties. The study shows that minor changes can improve predictions significantly.
Patient-specific Methodologically Rigorous Test of the Mean Phase Coherence for Seizure Prediction

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering
Authors: Duun-Henriksen, J. (Intern), Kjær, T. W. (Ekstern), Madsen, R. E. (Ekstern), Thomsen, C. E. (Intern), Sørensen, H. B. D. (Intern)
Publication date: 2009

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Main Research Area: Technical/natural sciences
Conference: 4th International Workshop on Seizure Prediction, Kansas City, MO, United States, 03/06/2009 - 03/06/2009
Source: orbit
Source-ID: 283725
Publication: Research - peer-review › Article in proceedings – Annual report year: 2009

Purpose: Due to a confined amount of recordings in existing EEG databases, only few papers have described a patient-specific rigorously methodological test of features for seizure prediction. By extraction of intracranial EEG from epilepsy patients with at least 6 seizures, this study has conducted such a test using the mean phase coherence (MPC) feature.

Methods: The MPC was implemented as described by Mormann et al., 2000. It was tested in a generic rigorously methodological way on the FSPEEG database, Winterhalder et al., 2003. 10 patients were used for training of the algorithm’s optimal settings, while the remaining 11 patients were used for testing. With new iEEG extractions from Copenhagen University Hospital, it was possible to obtain training and test sets with adequate amounts of seizures from individual patients. Preictal data from 4 patients was extracted from 11, 7, 7, and 6 seizures respectively together with at least 24 h of interictal data from each individual. With a variant of the leave-one-out training and test method, the optimal amount of training seizures was determined. Results: The generic test on the FSPEEG database resulted in a {sensitivity, false prediction ratio} of {0.55, 0.3/h}. For the 4 new patients the generic results were {0.91, 0.55/h}, {0.85, 0.71/h}, {0.29, 0.49/h}, and {0, 0.36/h} which is comparable to the FSPEEG database. The patient-specific approach yielded {0.81, 0.17/h}, {0.57, 0.13/h}, {0.81, 0.13/h}, and {0.60, 0.50/h} respectively, meaning that the patient-specific approach resulted in a mean improvement of {0.19, 0.30/h}. It was found that 4 seizures were optimal for training. Conclusions: By making the seizure prediction algorithm patient-specific, great improvements were obtained in this preliminary study. 3 out of 4 patients showed clinically applicable results. It is therefore expected that many epilepsy patients can benefit from patient-specific seizure prediction, although there is still room for further improvements.

Performance of the Transverse Oscillation method using beamformed data from a commercial scanner

Blood velocity estimates using conventional color flow imaging (CFI) or Doppler techniques are angle dependent. One of the proposed techniques to overcome this limitation is the Transverse Oscillation (TO) method, which also estimates the lateral velocity components. The performance of this is evaluated on a commercial platform. Beamformed data are acquired using a commercial BK Medical scanner as opposed to the previously reported results obtained with the experimental scanner RASMUS. The implementation is evaluated using an in-house circulating flow rig by calculating the relative mean standard deviation and bias of the velocity components. The relative mean standard deviation decreases as the number of shots per estimate increases and a value of 5% is obtained for 64 shots per estimate. For a center frequency of 5 MHz at 60°, 75°, and 90°, the relative mean bias varies from 21% to 27% and is lowest at a transmit focal depth close to the center of the vessel. The present performance is comparable with the results from the experimental scanner and simulations. It is obtained with only few changes to the conventional CFI setup and further optimization can improve the performance. This illustrates the feasibility of implementing the TO method on a commercial platform for real-time estimation.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging
Authors: Pihl, M. J. (Intern), Nikolov, S. (Ekstern), Haugaard, P. (Ekstern), Hemmsen, M. C. (Intern), Jensen, J. A. (Intern)
Precise Time-of-Flight Calculation For 3-D Synthetic Aperture Focusing

Conventional linear arrays can be used for 3D ultrasound imaging, by moving the array in the elevation direction and stacking the planes in a volume. The point spread function (PSF) is larger in the elevation plane, as the aperture is smaller and has a fixed elevation focus. Resolution improvements in elevation can be achieved by applying synthetic aperture (SA) focusing to the beamformed in-plane RF-data. The proposed method uses a virtual source (VS) placed at the elevation focus for postbeamforming. This has previously been done in two steps, in plane focusing followed by SA post-focusing in elevation, because of a lack of a simple expression for the exact time of flight (ToF). This paper presents a new method for calculating the ToF for a 3D case in a single step using a linear array. This method is more flexible than the previously proposed method and is able to beamform a fewer number of points much more efficiently. The method is evaluated using both simulated data and phantom measurements using the RASMUS experimental scanner. Computational cost for the method is higher than the 2-step method for a full volume beamforming, but allows for a reduction by an order of magnitude if three planes are used for real-time visualization. In addition, the need for a temporary storage of beamformed data is removed.
Seizure detection algorithms based on EMG signals

Background: the currently used non-invasive seizure detection methods are not reliable. Muscle fibers are directly connected to the nerves, whereby electric signals are generated during activity. Therefore, an alarm system on electromyography (EMG) signals is a theoretical possibility. Objective: to show whether medical signal processing of EMG data is feasible for detection of epileptic seizures. Methods: EMG signals during generalised seizures were recorded from 3 patients (with 20 seizures in total). Two possible medical signal processing algorithms were tested. The first algorithm was based on the amplitude of the signal. The other algorithm was based on information of the signal in the frequency domain, and it focused on synchronisation of the electrical activity in a single muscle during the seizure. Results: The amplitude-based algorithm reliably detected seizures in 2 of the patients, while the frequency-based algorithm was efficient for detecting the seizures in the third patient. Conclusion: Our results suggest that EMG signals could be used to develop an automatic seizure detection system. However, different patients might require different types of algorithms/approaches.

Similarity measures for protein ensembles

Analyses of similarities and changes in protein conformation can provide important information regarding protein function and evolution. Many scores, including the commonly used root mean square deviation, have therefore been developed to quantify the similarities of different protein conformations. However, instead of examining individual conformations it is in many cases more relevant to analyse ensembles of conformations that have been obtained either through experiments or from methods such as molecular dynamics simulations. We here present three approaches that can be used to compare conformational ensembles in the same way as the root mean square deviation is used to compare individual pairs of structures. The methods are based on the estimation of the probability distributions underlying the ensembles and subsequent comparison of these distributions. We first validate the methods using a synthetic example from molecular dynamics simulations. We then apply the algorithms to revisit the problem of ensemble averaging during structure determination of proteins, and find that an ensemble refinement method is able to recover the correct distribution of conformations better than standard single-molecule refinement.
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BFI (2012): BFI-level 1
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ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
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BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.705 SNIP 1.178
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.614 SNIP 1.046
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
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Some of the factors influencing the Heel Pad Compressibility Index (HPCI): a literature search

**General information**
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Authors: Matteoli, S. (Intern), Wilhjelm, J. E. (Intern), Torp-Pedersen, S. T. (Ekstern)
Publication date: 2009
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Copenhagen University Hospital
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Spatial resolution of the HRRT PET scanner using 3D-OSEM PSF reconstruction

**General information**
State: Published
Organisations: Image Analysis and Computer Graphics, Department of Informatics and Mathematical Modeling, Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Authors: Olesen, O. V. (Intern), Sibomana, M. (Ekstern), Keller, S. H. (Ekstern), Andersen, F. (Ekstern), Jensen, J. A. (Intern), Holm, S. (Ekstern), Svarer, C. (Ekstern), Højgaard, L. (Ekstern)
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Conference: Conference Record of the IEEE Nuclear Science Symposium and Medical Imaging Conference, 01/01/2009
Spatial resolution, HRRT, Positron emission tomography, PET
DOIs:
Using COMSOL Multiphysics for Biomechanical Analysis of Stent Technology in Cerebral Aneurysms
This work presents new fluid-structure interaction (FSI) models in both 2D and 3D of the effect of using vascular stents as treatment of cerebral berry aneurysms. The stent is positioned inside the cerebral artery covering the neck of the aneurysm. The stent is expected to alter the blood flow into the aneurysm such that the blood coagulates due to low blood velocity, and rupture of the aneurysm is prevented. A 3D FSI model consisting of three domains (blood, arterial, and aneurismal) is used to investigate the effect of the aneurysm on blood flow. Aspects of stent design such as pore size and shape and strut size, shape, and position are modeled in 2D and 3D FSI models. The models show that pore size and strut shape both have significant influence on stent efficiency.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Technical University of Denmark
Authors: Rasmussen, J. (Intern), Thyregod, J. (Ekstern), Enevoldsen, M. S. (Intern), Henneberg, K. (Intern)
Publication date: 2009

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Cerebral aneurysms, vascular stent, fluid-structure interactions, strut setup
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Using High Energy Lasers to Heat and Kill the Cells in an Internal Cancerous Body Tumor

General information
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Organisations: Department of Mathematics, Applied functional analysis, Department of Electrical Engineering, Biomedical Engineering, Technical University of Denmark
Authors: Skovgaard, O. (Intern), Enevoldsen, M. S. (Intern), Delay, L. J. (Ekstern), Hansen, L. B. (Ekstern)
Publication date: 2009

Publication information
Original language: English
Main Research Area: Technical/natural sciences

Synthetic Aperture Sequential Beamforming and other Beamforming Techniques in Ultrasound Imaging
This thesis consists of various subjects and applications within beamforming in general, and subjects within synthetic aperture focusing. An insight into the software architecture and beamformer design principles of a software beamformation toolbox is given. Some of the many considerations in relation to beamformer development and implementation are shared. In the delay-and-sum beamformer the sample index is not necessarily discrete. Some form of interpolation is needed and the influence on image quality has been investigated. The interpolation schemes investigated include linear, polynomial, and up-sampling and FIR filtering. Directional beamforming for angle estimation of the velocity vector has been investigated using simulations and measurements. Using the measurements more than 96% valid estimates were produced for the flow angles $q = \{60\pm, 75\pm, 90\pm\}$ and with a bias below $2\pm$ and a standard deviation below $5\pm$. The two synthetic aperture imaging techniques described in this thesis are both candidates for a realistic implementation in a commercial scanner. In one technique synthetic aperture focusing (SAF) is applied to 2-dimensional imaging with a single rotating mechanically focused concave element. Emission and reception are done while the transducer element continuously rotates and the received RF signals are stored. The geometrical focal point can be considered as a point source emitting a spherical wave in a limited angular region. For each image point in a high resolution image line (HRL) it
must be determined which emissions that have a wave field that encompasses the image point. These emissions contribute to the HRL, and samples from each of them are selected according to the focusing delays, and added together. Due to the rotation, the synthesized aperture only experiences a moderate expansion. This is not sufficient to reduce the extent of the wide point spread function of a single emission. The advantage of SAF is the increase in SNR. For the setup with focal depth at 20 mm the SAF SNR gain is 11 dB. The other synthetic aperture focusing technique is similar but has been revised toward linear array imaging. The technique is realized using two beamformers, and denoted Synthetic Aperture Sequential Beamforming (SASB). The VS is now created from an electronic focused subaperture in the first beamformer. Receive focusing is a simple fixed focusing with receive focal point in the transmit focal point, and the first beamformer could easily be analog and thereby save many ADC’s. The focused RF-lines from the first beamformer are stored and transferred to the 2nd beamformer. Here it is exploited that a single image point is represented in multiple output lines from the first beamformer. There is an substantial improvement in lateral resolution using SASB compared to dynamic receive focusing (DRF). The improvement in FWHM is at least a factor of 2 and the improvement at -40 dB is at least a factor of 3. At depths until 20 mm the FWHM is superior with DRF. With SASB the resolution is almost constant throughout the range. For DRF the FWHM increases almost linearly with range and the resolution at -40 dB is fluctuating with range. SASB has been applied to data acquired with a commercial scanner and a tissue phantom with wire targets. The images confirm the results from the simulations. At the center of the image the resolution of SASB is superior to DRF and is practically range independent. The resolution in the near field is slightly better for DRF. A decrease in performance at the transducer edges occur for both DRF and SASB. They are more profound for SASB and especially at greater depths it is obvious that the lateral resolution is laterally dependent.

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Synthetic Aperture Vector Flow Imaging
Current ultrasonic blood flow velocity measurement systems are subject to a number of limitations, including limited frame rate, aliasing artifacts, and that only the velocity component along the ultrasound beam is estimated. This dissertation aims at solving some of these problems. The main part of the thesis considers a method for estimating the two-dimensional velocity vector within the image plane. This method, called synthetic aperture vector flow imaging, is first shortly reviewed. The main contribution of this work is partly an analysis of the method with respect to focusing effects, motion effects, and clutter rejection, and partly within in-vivo applications of the method, showing examples from various arteries and veins. Furthermore, two additional projects are described and tested. The first is an encoding method for simultaneously acquiring multiple lines for conventional velocity estimation. The method can be used for increasing the frame rate of color flow maps or alternatively for a new imaging modality entitled quadroplex imaging, featuring a color flow map and two independent spectrograms at a high frame rate. The second is an alternative method for ultrasonic vector velocity estimation. Two different velocity estimators were derived for finding both the axial and lateral velocity components through a multi-dimensional spectrum analysis. The work resulted in four journal papers and six conference papers, which are appended to the dissertation.

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Authors: Oddershede, N. (Intern), Jensen, J. A. (Intern)
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Falanga torture involves repetitive blunt trauma to the soles of the feet and typically leaves few detectable changes. Reduced elasticity in the heel pads has been reported as characteristic sequelae and palpatory testing of heel pad elasticity is therefore part of medicolegal assessment of alleged torture victims. The goal was to test the accuracy of two experienced investigators in determining whether a heel pad model was soft, medium or hard. The skin-to-bone distance in the models varied within the human range.
Duplex scanning using sparse data sequences

The velocity distribution in vessels can be displayed using duplex scanning where B-mode acquisitions are interspaced with the velocity data. This gives an image for orientation, but lowers the maximum detectable velocity by a factor of two. Other pulse sequences either omit the B-mode image or leaves gaps in the velocity data, which makes it difficult to output audio data. The near full velocity range can be maintained and B-mode images shown by using a sparse data sequence with velocity and B-mode samples intermixed. The B-mode samples are placed in a (sparse) periodical pattern, which makes reconstruction of the missing samples possible. The periodic pattern has the length \( T = M + A \) samples, where \( M \) are for B-mode and \( A \) for velocity estimation. The missing samples can now be reconstructed using a filter bank. One filter bank reconstructs one missing sample, so the number of filter banks corresponds to \( M \). The number of sub filters in every filter bank is the same as \( A \). Every sub filter contains fractional delay (FD) filter and an interpolation function. Many different sequences can be selected to adapt the B-mode frame rate needed. The drawback of the method is that the maximum velocity detectable is scaled by the factor \( A/T \). The approach has been investigated using in vivo RF data from the Hepatic vein, Carotid artery and Aorta from a 33 year old healthy male. A B-K Medical 3535 ultrasound scanner has been used in Duplex mode with a BK 8556, 3.2 MHz linear array probe. The sampling frequency, the fprf and the resolution are 15 MHz, 3.5 kHz, and 12 bit sample (8 kHz and 16 bit for the Carotid artery). The resulting data contains 8000 RF lines with 128 samples at a depth of 45 mm for the vein and 50 mm for Aorta. Sparse sequences are constructed from the full data sequences to have both a reference sequence and sparse data sequences. After reconstruction the reference and the reconstructed spectrum are almost identical when characterized by the Signal to Noise Ratio (SNR). This is investigated and optimized by altering the number of filter coefficients, the implementation of the fractional delay filter, and the sparse sequence. The Hepatic vein data are processed with 5 filter coefficients, a FD filter implemented with a Knab window and sequence length \( T \) of 10 RF lines. By removing 7 lines the SNR is calculated to be 30 dB. When reconstruction over half the RF lines possible then to two spectograms can be acquired at the same time. The investigation of Aorta shows, that because the spectrum is wider, it puts some restrains on the selection of the sequence. The shortest sequence for getting a good spectrum consists of 7 lines, with one missing line (14.3%, SNR = 31.6 dB). Using sparse sequences both B-mode and velocity data can be acquired with only a modest degradation in maximum velocity. The reconstruction gives errors below the normal noise level in velocity data, and the full audio signal is precisely reconstructed from the data.
Fast Blood Vector Velocity Imaging using ultrasound: In-vivo examples of complex blood flow in the vascular system

Conventional ultrasound methods for acquiring color flow images of the blood motion are restricted by a relatively low frame rate and angle dependent velocity estimates. The Plane Wave Excitation (PWE) method has been proposed to solve these limitations. The frame rate can be increased, and the 2-D vector velocity of the blood motion can be estimated. The transmitted pulse is not focused, and a full speckle image of the blood can be acquired for each emission. A 13 bit Barker code is transmitted simultaneously from each transducer element. The 2-D vector velocity of the blood is found using 2-D speckle tracking between segments in consecutive speckle images. The flow patterns of six bifurcations and two veins were investigated in-vivo. It was shown: 1) that a stable vortex in the carotid bulb was present opposed to other examined bifurcations, 2) that retrograde flow was present in the superficial branch of the femoral artery during diastole, 3) that retrograde flow was present in the subclavian artery and antegrade in the common carotid artery during diastole, 4) that vortices were formed in the buckets behind the venous valves in both antegrade and retrograde flow, and 5) that secondary flow was present in various vessels. The in-vivo results have revealed complex flow patterns not previously visualized with ultrasound imaging and indicate a flow complexity in both simple and complex vessel geometries.

Feasibility of non-linear simulation for Field II using an angular spectrum approach

Simulation of non-linear fields is most often restricted to single element, circularly symmetric sources, which is not used in clinical scanning. To obtain a general and valuable simulation, array transducers of any geometry with any excitation, focusing, and apodization should be modeled. Field II is restricted to simulate these for the linear case and the purpose of this paper is to develop a general frame work for extending it to non-linear simulation. The extension to the non-linear domain is made by using the angular spectrum approach (ASA), where the field is calculated in a plane close to the transducer surface. This calculation is performed using Field II and, thus, includes modeling array transducers of any geometry with any excitation, focusing, and apodization. The propagation in the linear or non-linear medium is then performed using the angular spectrum approach. The first step in deriving this procedure is to find the accuracy of the approach for linear propagation, where the result can be validated using Field II simulations. The ASA calculations are carried out by 3D fast Fourier transform using Matlab, where lambda=2 is chosen as the spatial sampling rate to reduce aliasing errors. Zero-padding is applied to enlarge the source plane to a (4N - 1) times (4N - 1) matrix to overcome artifacts in terms of the circular convolution. The source plane covering an area of 9 times 9 mm2 with N = 61 samples along both side, is 0.05 mm away from a 5 MHz planar piston transducer, which is simulated by Field II. To determine the accuracy, different sampling intervals and zero-paddings are compared and the errors are calculated with Field II as a reference. It can be seen that zero-padding with 4N - 1 and lambda=2 sampling can both reduce the errors from 25.7% to 12.9% for the near-field and from 18.1% to 5.8% for the far-field, and improve the price of an increase in computation time. The angular spectrum approach in combination with Field II opens for- - the possibility of simulating the non-linear acoustic propagation for any kind of array transducers.
Gas enhanced magnetic resonance angiography of the cerebrum using carbon dioxide and oxygen - preliminary results

Purpose/introduction Standard imaging of the cerebral arteries is performed using intravenous contrast in CT angiography and x-ray angiography. Magnetic resonance angiography (MRA) of the cerebral arteries using intravenous contrast media does not perform well. Contrast in the venous bed and the meninges may obscure the signal from the arteries of interest. It is known that oxygen enhances the T1-weighted signal and that carbon dioxide increases the arterial blood flow. This paper presents preliminary results of gas enhanced MRA using combinations of atmospheric air, O2 and CO2. Subjects and Methods Two healthy volunteers were scanned during inhalation of three different gas mixtures: Gas I (air), Gas II (5% CO2, 21% O2, 74% N2), Gas III (5% CO2, 95% O2). For each gas mixture a time of flight (TOF) series on the cerebral arteries was performed. Following each TOF series an ECG-gated phase contrast sequence was performed to calculate volume flow in the common carotid arteries. MRA data was acquired with a 1.5 T Siemens VISION MR-system (SIEMENS Medical Systems, Germany) using a standard circularly polarized head coil. Reconstructed images of TOF series and volume flow measurements were compared. Results The TOF series showed an increase in MRA signal and vessel conspicuousness, when adding CO2 to air (gas I vs. gas II) and an additional increase was seen on MRA when adding O2 to CO2 (gas II vs. gas III). The increase in MRA signal was present on both volunteers. The volume flow increased as a response to the added CO2 (gas II). Free oxygen (gas III) enhanced the MRA blood signal but invoked a slight decrease in the volume flow. Discussion/conclusion Inhaling gas mixture during MRA examination containing CO2 and O2 increased the cerebral MRA signal. These preliminary results indicate that improved MRA of the cerebrum can be gained when inhaling 5% CO2/95% O2 during examination bringing forth an alternative to CT and x-ray cerebral angiography. Furthermore, gas enhanced MRA could be an alternative to contrast enhanced MRA in other regions of interest than cerebrum.
Precision of Needle Tip Localization Using a Receiver in the Needle

Many medical procedures require the detection, tracking and guidance of (biopsy) needles. The detection of the position of the needle can be challenging because of specular reflection which deflects the sound in a direction away from the transducer surface. To visualize the tip of small needles often motion is introduced to the discomfort of the patient. Vilkomerson and co-workers suggested in 1981 the placement of an ultrasound receiver close to the needle tip. The received echoes are detected by add-on hardware. The maximum echo is assumed to originate from a beam directly above the detector, and the time of flight determines the distance to the transducer. The feasibility of the method was demonstrated by the same group in-vivo. The precision of the method has not been previously discussed in literature. This paper introduces two methods for estimation of the position of the needle tip and investigates their precision. The first method uses conventional imaging. Instead of detecting the maximum echo, as previously suggested, the center of mass is found both across beams and along the received signals, thus decreasing the sensitivity to noise. The second method is based synthetic aperture (SA) scanning. The position of the tip is found via triangulation which involves solving a system of linear equations. The robustness to noise is ensured through averaging a number of estimates. The sensor is a ring of piezo-electric film making it possible to receive waves from any direction. The results were obtained using simulations in Field II. The center frequency is 7 MHz. The transducer array is mechanically focused in elevation plane at 25 mm while the height of the elements is 4.5 mm. The transducer pitch is 202 microns. The sensor is a ring with height of 1 mm and 2 mm diameter. Positions were varied from 10 to 120 mm in depth and from 0 to 20 mm in lateral and elevation direction. The mean error of position estimation is for the case of conventional and SA imaging is 0.2 and 0.05 mm, respectively. The precision of two methods to determine the position of the needle tip is investigated. Using spherical transmissions yields higher accuracy. Both methods can be extended to 3D if the transmissions originate from transducer elements that are not placed on a line. Needles equipped with receivers can be used for deploying brachytherapy seeds ensuring high precision of the procedure.

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Authors: Nikolov, S. I. (Ekstern), Jensen, J. A. (Intern)
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Research interface for experimental ultrasound imaging - the CFU grabber project.
Purpose The acquisition of ultrasound images using new calculation methods usually requires days of post processing. An ultrasound scanner with a research interface developed in collaboration between DTU and BK medicals has made it possible to process US images faster than the current research system RASMUS. Furthermore precise scanner settings are stored for inter- and intra-observer studies. The resulting images are used for clinical evaluation. Method and materials The ultrasound scanners research interface is connected to a graphical grabber card in a Windows PC (Grabber PC). The grabber PC acquires pre processed data from the scanner in real time. Further post processing is required to create the final images. In house software (CFU Grabber tool) was developed to review and store the pre processed data. Using MatLab image processing with a new post post processing method the final image can be produced within 20-30 minutes depending on the method while RASMUS uses up to 72 hours for post processing. Results With a post processing time of 30 minutes images using a new method (Synthetic Aperture Sequential Beamforming) and a conventional method (Dynamic Receive Focusing) was performed. The resulting 3 seconds of image sequences (video) will be evaluated by experts within medical ultrasound imaging. Conclusion The setup makes the data acquisition fast and the scanner setting reproducible and the first in-vivo studies using the new research system are on-going.

General information
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Organisations: Biomedical Engineering, Department of Electrical Engineering, Center for Fast Ultrasound Imaging, Copenhagen University Hospital
Rocking convex array used for 3D synthetic aperture focusing

Volumetric imaging can be performed using 1D arrays in combination with mechanical motion. Outside the elevation focus of the array, the resolution and contrast quickly degrade compared to the azimuth plane, because of the fixed transducer focus. The purpose of this paper is to use synthetic aperture focusing (SAF) for enhancing the elevation focusing for a convex rocking array, to obtain a more isotropic point spread function. This paper presents further development of the SAF method, which can be used with curved array combined with a rocking motion. The method uses a virtual source (VS) for defocused multi-element transmit, and another VS in the elevation focus point. This allows a direct time-of-flight (ToF) to be calculated for a given 3D point. The method is evaluated using simulations from Field II and by measurements using the RASMUS experimental scanner with a 4.5 MHz convex array (GE Kretztechnik, Zipf, Austria). The array has an elevation focus at 60 mm of depth, and the angular rocking velocity is up to 140°/s. The scan sequence uses an fprf of 4500 - 7000 Hz allowing up to 15 cm of penetration. The full width at half max (FWHM) and main-lobe to side-lobe ratio (MLSL) is used as quantitative measurements. The elevation FWHM for simulated scatterers placed at depths of 30 to 140 mm of depth were improved by 26.4% on average, and the MLSL ratio was improved by an average of 8.49 dB for the scatterers using 3D SA focusing. The elevation FWHM for a measured wire phantom was improved by 33.8% on average by applying 3D SA focusing. In-Vivo measurements show an improvement in C-scans matching what is found in simulations and wire phantoms. The method has shown the ability to improve the elevation focus and contrast for a convex rocking array. This was shown for simulations and for phantom and In-Vivo measurements using commercially available equipment.

Teaching the physics of medical imaging: an active learning approach involving imaging of biological tissue

Introduction to medical imaging is an experimentally oriented course in the physics of medical imaging, where the students record, process and analyse 3D data of an unknown piece of formalin fixed animal tissue embedded in agar in order to estimate the tissue types present. Planar X-ray, CT, MRI, ultrasound and SPECT/PET images are recorded, showing the tissue in very different ways. In order for the students to estimate the tissue type, they need to study the physical principles of the imaging modalities. The “true” answer is subsequently revealed by slicing the tissue.
Transverse correlation: An efficient transverse flow estimator - initial results

Color flow mapping has become an important clinical tool, for diagnosing a wide range of vascular diseases. Only the velocity component along the ultrasonic beam is estimated, so to find the actual blood velocity, the beam to flow angle has to be known. Because of the unpredictable nature of vascular hemodynamics, the flow angle cannot easily be found as the angle is temporally and spatially variant. Additionally the precision of traditional methods is severely lowered for high flow angles, and they breakdown for a purely transverse flow. To overcome these problems we propose a new method for estimating the transverse velocity component. The method measures the transverse velocity component by estimating the transit time of the blood between two parallel lines beamformed in receive. The method has been investigated using simulations performed with Field II. Using 15 emissions per estimate, a standard deviation of 1.64% and a bias of 1.13% are obtained for a beam to flow angle of 90 degrees. Using the same setup a standard deviation of 2.21% and a bias of 1.07% are obtained for a beam to flow angle of 75 degrees. Using 20 emissions a standard deviation of 3.4% and a bias of 2.06% are obtained at 45 degrees. The method performs stable down to a signal-to-noise ratio of 0 dB, where a standard deviation of 5.5% and a bias of 1.2% is achieved.
Improved Beamforming for Lateral Oscillations in Elastography Using Synthetic Aperture Imaging

In this paper we present a beamforming technique based on synthetic aperture imaging that enables to improve the radio-frequency (RF) ultrasound images with lateral oscillations for lateral displacement estimation. As described in previous work, in order to increase the accuracy of the lateral displacement estimation using images with lateral oscillations, it is necessary to reduce both the wavelength of the lateral oscillations and the width of the point spread function (PSF). This is reached in this work, by doing emit and receive beamforming using synthetic aperture data. We show that the wavelength of the lateral oscillations can be reduced by a factor 2, and the width of the PSF can be reduced by a factor $\sqrt{2}$. We have used the images obtained by this beamforming technique for lateral displacement estimation in the field of elastography. We show that with this new approach it is possible to improve the lateral displacement estimation by nearly 25% by reducing the standard deviation of the error of the lateral estimation.

General information
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Authors: Liebgott, H. (Ekstern), Basarab, A. (Ekstern), Loizeau, D. (Ekstern), Jensen, J. A. (Intern), Delachartre, P. (Ekstern)
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Copyright 2006 IEEE. Personal use of this material is permitted. However, permission to reprint/republish this material for advertising or promotional purposes or for creating new collective works for resale or redistribution to servers or lists, or to
Medical ultrasound imaging

The paper gives an introduction to current medical ultrasound imaging systems. The basics of anatomic and blood flow imaging are described. The properties of medical ultrasound and its focusing are described, and the various methods for two- and three-dimensional imaging of the human anatomy are shown. Both systems using linear and non-linear propagation of ultrasound are described. The blood velocity can also be non-invasively visualized using ultrasound and the basic signal processing for doing this is introduced. Examples for spectral velocity estimation, color flow imaging and the new vector velocity images are presented.

General information

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Spectral velocity estimation using autocorrelation functions for sparse data sets

The distribution of velocities of blood or tissue is displayed using ultrasound scanners by finding the power spectrum of the received signal. This is currently done by making a Fourier transform of the received signal and then showing spectra in an M-mode display. It is desired to show a B-mode image for orientation, and data for this has to acquired interleaved with the flow data. The power spectrum can be calculated from the Fourier transform of the autocorrelation function $R_y(k)$, where its span of lags $k$ is given by the number of emission $N$ in the data segment for velocity estimation. The lag corresponds to the difference in pulse number, so that for lag $k$ data from emission $i$ is correlated with $i + k$. The autocorrelation for lag $k$ can be averaged over $N-k$ pairs of emissions. It is possible to calculate $R_y(k)$ for a sparse set of emissions, as long as all combinations of emissions cover all lags in $R_y(k)$. A sparse set of emissions inter-spaced with B-mode emissions can, therefore, be used for estimating $R_y(k)$. The sequence ‘$v$ B $v$ v B’ gives 2 B-mode emissions (B) for every 3 velocity emissions (v) and is denoted a 3:2 sequence. All combinations on lags are present $k=0123...$, if the sequence is continually repeated. The variance on the estimate of $R_y(k)$ is determined by the number of emission pairs for the value of $k$, and it can be lowered by averaging the RF data over the range gate. Many other sequences can be devised with this property giving 3:3, 3:4, and 5:8 or even random sequences, so that the ratio between B-mode frame rate and spectral precision can be selected.

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Authors: Jensen, J. A. (Intern)
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Frequency division transmission imaging and synthetic aperture reconstruction

In synthetic transmit aperture imaging only a few transducer elements are used in every transmission, which limits the signal-to-noise ratio (SNR). The penetration depth can be increased by using all transmitters in every transmission. In this paper, a method for exciting all transmitters in every transmission and separating them at the receiver is proposed. The coding is done by designing narrow-band linearly frequency modulated signals, which are approximately disjointed in the frequency domain and assigning one waveform to each transmitter. By designing a filterbank consisting of the matched filters corresponding to the excitation waveforms, the different transmitters can be decoded at the receiver. The matched filter of a specific waveform will allow information only from this waveform to pass through, thereby separating it from the other waveforms. This means that all transmitters can be used in every transmission, and the information from the different transmitters can be separated instantaneously. Compared to traditional synthetic transmit aperture (STA) imaging, in which the different transmitters are excited sequentially, more energy is transmitted in every transmission, and a better signal-to-noise-ratio is attained. The method has been tested in simulation, in which the resolution and contrast was compared to a standard synthetic transmit aperture system with a single sinusoid excitation. The resolution and contrast was comparable for the two systems. The method also has been tested using the experimental ultrasound scanner RASMUS. The resolution was evaluated using a string phantom. The method was compared to a conventional STA using both sinusoidal excitation and linear frequency modulated (FM) signals as excitation. The system using the FM signals and the frequency division approach yielded the same performance concerning both axial (of ap 3 lambda) and lateral resolution (of ap 4.5 lambda). A SNR measurement showed an increase in SNR of 6.5 dB compared to the system using the conventional STA method and FM signal excitation.

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Authors: Gran, F. (Intern), Jensen, J. A. (Intern)
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Methods and devices for hyperpolarising and melting NMR samples in a cryostat

The present invention relates to devices and method for melting solid polarised sample while retaining a high level of polarisation. In an embodiment of the present invention a sample is polarised in a sample-retaining cup 9 in a strong magnetic field in a polarising means 3a, 3b, 3c in a cryostat 2 and then melted inside the cryostat 2 by melting means such as a laser 8 connected by an optical fibre 4 to the interior of the cryostat.
Parameter study of 3D synthetic aperture post-beamforming procedure.
A method to increase the image resolution and dynamic range is to use the acquired data from several emissions (lines) and to beamform the collected RF signals treating the focal point in transmit as a virtual source of a spherical wave. The transducer is swept mechanically over the region of interest to scan a full volume. The same beamformation procedure is applied both in the azimuth and the elevation planes. This paper presents a study of the influence of the position of the transmit focus on the image resolution, the signal-to-noise ratio and penetration depth. The investigation is based on simulations and measurements. The system used in this work is a research scanner developed at the department. The transducer is a 7.5 MHz linear array with a pitch of 208 μm and a fixed focus in the elevation direction at 25 mm. The field is simulated for points placed at every 5 mm between 10 and 150 mm depths. 100 different positions of the transmit focus are investigated. For every transmit focus the image is beamformed and evaluated. Finally the gain in signal-to-noise ratio and penetration depth are investigated experimentally for the setup, with which the best resolution is achieved. Simulations indicate that the size of the point spread function at a depth of 60 mm is decreased from 3 mm to 0.66 mm and from 4 mm to 2.5 mm in the azimuth and elevation planes, respectively. The gain in signal-to-noise ratio measured in a tissue mimicking phantom is 10 dB. The penetration depth increases from 70 to 100 mm. The method can be applied in applications, where the image quality is of prime importance, such as in the classification of atherosclerotic lesions in the carotid artery.

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Web of Science (2018): Indexed yes
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Scopus rating (2017): SNIP 1.714 SJR 0.973 CiteScore 2.72
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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.51 SJR 0.834 SNIP 1.728
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Scopus rating (2015): SJR 0.708 SNIP 1.655 CiteScore 2.23
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Scopus rating (2013): SJR 0.67 SNIP 1.727 CiteScore 2.12
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Real-time synthetic aperture imaging: opportunities and challenges

Synthetic aperture (SA) ultrasound imaging has not been introduced in commercial scanners mainly due to the computational cost associated with the hardware implementation of this imaging modality. SA imaging redefines the term beamformed line. Since the acquired information comes from all points in the region of interest it is possible to beamform the signals along a desired path, thus, improving the estimation of blood flow. The transmission of coded excitations makes it possible to achieve higher contrast and larger penetration depth compared to "conventional" scanners. This paper presents the development and implementation of the signal processing stages employed in SA imaging: compression of received data acquired using codes, and beamforming. The goal was to implement the system using commercially available field programmable gate arrays. The compression filter operates on frequency modulated pulses with duration of up to 50 mus sampled at 70 MHz. The beamformer can process data from 256 channels at a pulse repetition frequency of 5000 Hz and produces 192 lines of 1024 complex samples in real time. The lines are described by their origin, direction, length and distance between two samples in 3D. This parametric description makes it possible to quickly change the image geometry during scanning, thus enabling adaptive imaging and precise flow estimation. The paper addresses problems such as large bandwidth and computational load and gives the solutions that have been adopted for the implementation.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Nikolov, S. (Intern), Tomov, B. G. (Intern), Jensen, J. A. (Intern)
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Publication date: 2006
Synthetic Aperture Ultrasound Imaging

The paper describes the use of synthetic aperture (SA) imaging in medical ultrasound. SA imaging is a radical break with today's commercial systems, where the image is acquired sequentially one image line at a time. This puts a strict limit on the frame rate and the possibility of acquiring a sufficient amount of data for high precision flow estimation. These constrictions can be lifted by employing SA imaging. Here data is acquired simultaneously from all directions over a number of emissions, and the full image can be reconstructed from this data. The talk will demonstrate the many benefits of SA imaging. Due to the complete data set, it is possible to have both dynamic transmit and receive focusing to improve contrast and resolution. It is also possible to improve penetration depth by employing codes during ultrasound transmission. Data sets for vector flow imaging can be acquired using short imaging sequences, whereby both the correct velocity magnitude and angle can be estimated. A number of examples of both phantom and in-vivo SA images will be presented measured by the experimental ultrasound scanner RASMUS to demonstrate the many benefits of SA imaging.

General information

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Jensen, J. A. (Intern), Nikolov, S. (Intern), Gammelmark, K. L. (Ekstern), Pedersen, M. H. (Intern)
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Scopus rating (2015): SJR 0.708 SNIP 1.655 CiteScore 2.23
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.848 SNIP 2.156 CiteScore 2.41
Web of Science (2014): Indexed yes
Use of vibrational spectroscopy to study protein and DNA structure, hydration, and binding of biomolecules: A combined theoretical and experimental approach

We report on our work with vibrational absorption, vibrational circular dichroism, Raman scattering, Raman optical activity, and surface-enhanced Raman spectroscopy to study protein and DNA structure, hydration, and the binding of ligands, drugs, pesticides, or herbicides via a combined theoretical and experimental approach. The systems we have studied systematically are the amino acids (L-alanine, L-tryptophan, and L-histidine), peptides (N-acetyl L-alanine N'-methyl amide, N-acetyl L-tryptophan N'-methyl amide, N-acetyl L-histidine N'-methyl amide, L-alanyl L-alanine, tri-L-serine, N-acetyl L-alanine L-pioline L-tyrosine N'-methyl amide, Leu-enkephalin, cyclo-(gly-L-pro), N-acetyl (L-alanine)(n) N'N'-methyl amide), 3-methyl indole, and a variety of small molecules (dichlobenil and 2,6-dochlorobenzamide) of relevance to the protein systems under study. We have used molecular mechanics, the SCC-DFTB, SCCDFTB+disp, RHF, MP2, and DFT methodologies for the modeling studies with the goal of interpreting the experimentally measured vibrational spectra for these molecules to the greatest extent possible and to use this combined approach to understand the structure, function, and electronic properties of these molecules in their various environments. The application of these spectroscopies to biophysical and environmental assays is expanding, and therefore a thorough understanding of the phenomenon from a rigorous theoretical basis is required. In addition, we give some exciting and new preliminary results which allow us to extend our methods to even larger and more complex systems. The work presented here is the current state of the art to this ever and fast changing field of theoretical spectroscopic interpretation and use of VA, VCD, Raman, ROA, EA, and ECD spectroscopies.
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Scopus rating (2016): CiteScore 2.24 SJR 0.959 SNIP 0.902
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.686 SNIP 0.693 CiteScore 1.64
BFI (2014): BFI-level 1
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BFI (2013): BFI-level 1
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BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.603 SNIP 0.709 CiteScore 1.21
ISI indexed (2011): ISI indexed yes
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BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.636 SNIP 0.704
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Scopus rating (2009): SJR 0.717 SNIP 0.771
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Scopus rating (2007): SJR 0.79 SNIP 0.71
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Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.633 SNIP 0.665
Scopus rating (2004): SJR 0.796 SNIP 0.767
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.834 SNIP 0.811
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.866 SNIP 0.799
Scopus rating (2001): SJR 0.914 SNIP 0.691
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.792 SNIP 0.732
Identification of pulse echo impulse responses for multi source transmission

In this paper a method for acquiring data from several simultaneously transmitting elements in synthetic transmit aperture (STA) ultrasound imaging is proposed. Several transmitters are excited simultaneously using pseudo-random sequences. The received signal at a given time point and receiver is a mixture of the information corresponding to several transmitters. There is, thus, no direct way of determining which information corresponds to which transmitter, preventing proper focusing. In this paper we decode the received signal by estimating the pulse echo impulse responses between every transmitter and receiver pair, using a least squares estimator. The decoding is done instantaneously, making information from several transmitters available after only one transmission. This limits the influence of motion artifacts both in the decoding step and when the STA focusing scheme is applied. The method is evaluated using the simulation tool Field II. Three point spread functions are simulated where axial movement of 1 m/s is present. The axial resolution for the moving scatterer is 0.249 mm (-3dB) and 0.291 mm (-6dB), which is compared to a standard STA transmission scheme with sequential excitation of the transmitters using a chirp excitation. The axial resolution was in this case 0.260 mm (-3dB) and 0.611 mm (-6dB). Also a blood vessel is simulated with an angle of 45° to the acoustic axis with a peak flow of 1 m/s. The velocity is estimated with a mean bias of 2.57% and a mean standard deviation of 0.505% relative to the peak velocity of the flow.

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Authors: Gran, F. (Intern), Jensen, J. A. (Intern)
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Apparatus and method for velocity estimation in synthetic aperture imaging

The invention relates to an apparatus for flow estimation using synthetic aperture imaging. The method uses a Synthetic Transmit Aperture, but unlike previous approaches a new frame is created after every pulse emission. In receive mode parallel beam forming is implemented. The beam formed RF data is added to the previously created RF lines obtained by the same transmit sequence. The apparatus comprises a pulser (1) to generate a pulsed voltage signal, that is fed to the emit beam former (2). The emit beam former (2) is connected to the emitting transducer array (3). The ultrasound is reflected by the object (4) and received by the elements of the transducer array (5). All of these signals are then combined in the beam processor (6) to focus all of the beams in the image in both transmit and receive mode and the simultaneously focused signals are used for updating the image in the processor (7). The update signals are used in the velocity estimation processor (8) to correlate the individual measurements to obtain the displacement between high-resolution images and thereby determine the velocity.

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Authors: Jensen, J. A. (Intern)
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Publication: Research › Patent – Annual report year: 2002

Compact beamforming in medical ultrasound scanners

This Ph.D. project was carried out at the Center for Fast Ultrasound Imaging, Technical University of Denmark, under the supervision of Prof. Jørgen Arendt Jensen, Assoc. Prof. Jens Sparse and Prof. Erik Bruun. The goal was to investigate methods for efficient beamforming, which make it possible to fit a large number of channels on a single integrated circuit. The use of oversampled analog-to-digital (A/D) converters with the corresponding beamforming was identified as a particularly promising approach, since it provides both inexpensive and compact A/D conversion and allows for much more compact implementation of the beamformer compared to the case where conventional A/D conversion is used. The compact and economic beamforming is a key aspect in the progress of medical ultrasound imaging. Currently, 64 or 128 channels are widely used in scanners, top-of-the-range scanners have 256 channels, and even more channels are necessary for 3-dimensional (3D) diagnostic imaging. On the other hand, there is a demand for inexpensive portable
devices for use outside hospitals, in field conditions, where power consumption and compactness are important factors. The thesis starts with an introduction into medical ultrasound, its basic principles, system evolution and its place among medical imaging techniques. Then, ultrasound acoustics is introduced, as a necessary base for understanding the concepts of acoustic focusing and beamforming, which follow. The necessary focusing information for high-quality imaging is large, and compressing it leads to better compactness of the beamformers. The existing methods for compressing and recursive generation of focusing data, along with original work in the area, are presented in Chapter 4. The principles and the performance limitations of the oversampled delta-sigma converters are given in Chapter 5, followed by an overview of the present architectures of oversampled beamformers. Then, a new architecture is introduced, which has the potential of achieving the highest image quality that an oversampling beamformer can provide. That architecture has been implemented using VHDL, and estimates for its performance have been obtained. The results indicate that a 32-channel beamformer reaches the target operation frequency of 140 MHz, thereby providing diagnostic image with dynamic range of 60 dB for an excitation central frequency of 3 MHz. That image quality is comparable to that of the very good scanners currently on the market. The performance results have been achieved with the use of a simple oversampled converter of second order. The use of a higher order oversampled converter will allow higher pulse frequency to be used while the high dynamic range in the end image is preserved. The logic resource utilization of a Xilinx FPGA device XCV2000E-7 is less than 45 % when a 32-channel beamformer is implemented. The maximum number of channels that can fit in that FPGA device is 57, due to the fact that too many of the available gates take part in the routing when the channel number is increased.

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Organisations: Biomedical Engineering, Department of Electrical Engineering, Computer Science and Engineering, Department of Informatics and Mathematical Modeling, Electronics, Center for Fast Ultrasound Imaging
Authors: Tomov, B. G. (Intern), Sparsø, J. (Intern), Jensen, J. A. (Intern), Bruun, E. (Intern)
Publication date: Aug 2003

Investigation of the feasability for 3D synthetic aperture imaging
This paper investigates the feasibility of implementing real-time synthetic aperture 3D imaging on the experimental system developed at the Center for Fast Ultrasound Imaging using a 2D transducer array. The target array is a fully populated 32 × 32 3 MHz array with a half wavelength pitch. The elements of the array are grouped in blocks of 16 × 8, which can simultaneously be accessed by the 128 channels of the scanner. Using 8-to-1 high-voltage analog multiplexors, any group of 16 × 8 elements can be accessed. Simulations are done using Field II using parameters from a 32 x 32 elements experimental array made by Vermon with a center frequency of 2.93 MHz, fractional bandwidth of 58 %, and a pitch of 300 µm. The simulations show, that using all of the 128 elements a spherical wave within ±50 degrees sector can be created. The level of the edge waves is reduced by applying apodization with an elliptic footprint. The results of simulations show that the angular resolution at -6dB is 2.7 degrees, and is determined by the distance between the outer-most transmit elements. The peak gratinglobe levels are −23.5, −25, 27.2, −44.5 dB below the main peak for 64, 100, 144, and 169 transmit events, respectively. The number of scanned volumes per second for these cases are 78, 50, 34 and 30, respectively.

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Synthetic aperture tissue and flow ultrasound imaging

This Ph.D. project was carried out at the Center for Fast Ultrasound Imaging, Technical University of Denmark. The goal was to improve existing imaging techniques in order to make them suitable for real-time three-dimensional ultrasound scanning. This dissertation focuses on the synthetic aperture imaging applied to medical ultrasound. It is divided into two major parts: tissue and blood flow imaging. Tissue imaging using synthetic aperture algorithms has been investigated for about two decades, but has not been implemented in medical scanners yet. Among the other reasons, the conventional scanning and beamformation methods are adequate for the imaging modalities in clinical use - the B-mode imaging of tissue structures, and the color mapping of blood flow. The acquisition time, however, is too long, and these methods fail to perform real-time three-dimensional scans. The synthetic transmit aperture, on the other hand, can create a B-mode image with as little as 2 emissions, thus significantly speeding-up the scan procedure. The first part of the dissertation describes the synthetic aperture tissue imaging. It starts with an overview of the efforts previously made by other research groups. A classification of the existing methods is made, and a new imaging technique, the “recursive ultrasound imaging” is suggested. The technique makes it possible to create a new image after every emission. This opens further the possibility for visualizing the blood flow. Various aspects of the scan procedure are considered, among them: the use of sparse one- and two-dimensional arrays; the use of multiple elements in transmit to create virtual sources of ultrasound; the use of virtual sources of ultrasound to improve the resolution of the images in the elevation plane; the use of temporal and spatial encoding to increase the signal to noise ratio. In many of the mentioned areas, the author presents the existing state of the art, and adds his personal contributions. The second part describes blood flow estimation using synthetic aperture techniques. It starts by introducing the velocity estimator based on the time shift measurement of the received signals. This estimator fails to estimate the velocity when applied on the radio frequency signals formed by synthetic aperture techniques. The failure is caused by the motion artifacts, and the second part continues by developing a new model for them. Based on this model a novel motion compensation scheme is presented. The velocity can successfully be estimated from the motion compensated images. The standard deviation and the bias are both within 2 %. The estimation of blood flow using synthetic transmit aperture ultrasound is further extended by developing a scheme of how to modify the existing blood flow estimators. In the new approach images n and n+N, n+1 and n+1+N are cross correlated, where N is the number of emissions for one image. These images experience the same phase distortion due to motion and therefore have a high correlation without motion compensation. The estimate of the cross-correlation i is improved by averaging the estimates obtained from the pairs of frames [n, n+N], [n+1, n+1+N], and so on up to [n+N &n+2N &n100000;1, n+2N &n100000;1]. The advantage of the approach is that a color flow map can be created for all directions in the image simultaneously at every emission, which makes it possible to average over a large number of lines. This makes stationary echo canceling easier and significantly improves the velocity estimates. Only 8 emissions per plane are necessary to create the color flow map. Scanning 12 cm in depth, up to 800 planes can be obtained, making it possible for real-time three-dimensional tissue and blood-flow imaging.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Nikolov, S. (Intern), Jensen, J. A. (Intern)
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Ultrasound imaging using coded signals

Modulated (or coded) excitation signals can potentially improve the quality and increase the frame rate in medical ultrasound scanners. The aim of this dissertation is to investigate systematically the applicability of modulated signals in medical ultrasound imaging and to suggest appropriate methods for coded imaging, with the goal of making better anatomic and flow images and three-dimensional images. On the first stage, it investigates techniques for doing high-resolution coded imaging with improved signal-to-noise ratio compared to conventional imaging. Subsequently it investigates how coded excitation can be used for increasing the frame rate. The work includes both simulated results using Field II, and experimental results based on measurements on phantoms as well as clinical images. Initially a mathematical foundation of signal modulation is given. Pulse compression based on matched filtering is discussed. Correlation and compression properties of coded signals are shown to depend on a single parameter of the coded signals: the time-bandwidth product. It is shown that, due to attenuation in the tissues, the matched filter output is related to the ambiguity function of the excitation signal. Although a gain in signal-to-noise ratio of about 20 dB is theoretically possible for the time-bandwidth product available in ultrasound, it is shown that the effects of transducer weighting and tissue
attenuation reduce the maximum gain at 10 dB for robust compression with low sidelobes. Frequency modulation and phase modulation are considered separately and their resolution, sidelobes, expected signal-to-noise gain and performance in tissue imaging are discussed in detail. A method to achieve low compression sidelobes by reducing the ripples of the amplitude spectrum of the FM signals is described. Application of coded excitation in array imaging is evaluated through simulations in Field II. The low degree of the orthogonality among coded signals for ultrasound systems is first discussed, and the effect of mismatched filtering in the cross-correlation properties of the signals is evaluated. In linear array imaging it is found that the frame rate can be doubled without any degradation in image quality, by using two coded sequences that have a cross-correlation of at least 11 dB. Other coding schemes that can increase the frame rate by nearly 5 times with a small compromise in resolution are discussed. Coded synthetic transmit aperture imaging with only 4 emissions is shown to yield the same signal-to-noise ratio as with conventional phased-array imaging which uses 51 emissions. Further frequency-division coding can make it possible to obtain images with acceptable resolution with only two emissions. Finally, a novel coding technique which uses pulse train excitation is presented.

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A new architecture for a single-chip multi-channel beamformer based on a standard FPGA
A new architecture for a compact medical ultrasound beamformer has been developed. Combination of novel and known principles has been utilized, leading to low processing power requirements and simple analog circuitry. Usage of a field programmable gate array (FPGA) for the digital signal processing provides programming flexibility. First, sparse sample processing is performed by generating the in-phase and quadrature beamformed signals. Hereby only 512 samples are beamformed for each line in an image. That leads to a 15-fold decrease in the number of operations and enables the use of Delta-Sigma (ΔΣ) modulation analog-to-digital converters (ADC). Second, simple second-order ΔΣ modulation ADC with classic topology is used. This allows for simple analog circuitry and a very compact design. Several tens of these together with the corresponding preamplifiers can be fitted together onto a single analog integrated circuit. Third, parameter driven delay generation is used, using 3 input parameters per line per channel for either linear array imaging or phased array imaging. The delays are generated on the fly. The delay generation logic also determines the digital apodization by using 2 additional parameters. The control logic consists of few adders and counters and requires very limited resources. Fourth, the beamformer is fully programmable. Any channel can be set to use an arbitrary delay curve, and any number of these channels can be used together in an extendable modular multi-channel system. A prototype of the digital logic is implemented using a Xilinx Virtex-E series FPGA. A 5 MHz center frequency is used along with an oversampling ratio of 14. The sampling clock frequency used is 140 MHz and the number of channels in a single Xilinx 1 million gate FPGA XC6000E is 32. The beamformer utilizes all of the BlockRAM of the device and 33% of its Core Logic Block (CLB) resources. Both simulation results and processed echo data from a phantom are presented.

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Authors: Tomov, B. G. (Intern), Jensen, J. A. (Intern)
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A new estimator for vector velocity estimation [medical ultrasonics]

A new estimator for determining the two-dimensional velocity vector using a pulsed ultrasound field is derived. The estimator uses a transversely modulated ultrasound field for probing the moving medium under investigation. A modified autocorrelation approach is used in the velocity estimation. The new estimator automatically compensates for the axial velocity when determining the transverse velocity. The estimation is optimized by using a lag different from one in the estimation process, and noise artifacts are reduced by averaging RF samples. Further, compensation for the axial velocity can be introduced, and the velocity estimation is done at a fixed depth in tissue to reduce the influence of a spatial velocity spread. Examples for different velocity vectors and field conditions are shown using both simple and more complex field simulations. A relative accuracy of 10.1% is obtained for the transverse velocity estimates for a parabolic velocity profile for flow transverse to the ultrasound beam and a SNR of 20 dB using 20 pulse-echo lines. The overall bias in the estimates was -4.3%.
A new maximum likelihood blood velocity estimator incorporating spatial and temporal correlation

The blood flow in the human cardiovascular system obeys the laws of fluid mechanics. Investigation of the flow properties reveals that a correlation exists between the velocity in time and space. The possible changes in velocity are limited, since the blood velocity has a continuous profile in time and space. This paper presents a new estimator (STC-MLE), which incorporates the correlation property. It is an expansion of the maximum likelihood estimator (MLE) developed by Ferrara et al. With the MLE a cross-correlation analysis between consecutive RF-lines on complex form is carried out for a range of possible velocities. In the new estimator an additional similarity investigation for each evaluated velocity and the available velocity estimates in a temporal (between frames) and spatial (within frames) neighborhood is performed. An a priori probability density term in the distribution of the observations gives a probability measure of the correlation between the velocities. Both the MLE and the STC-MLE have been evaluated on simulated and in-vivo RF-data obtained from the carotid artery. Using the MLE 4.1% of the estimates deviate significantly from the true velocities, when the performance is
evaluated on the simulated data. These deviating estimates arise, as the search range in the correlation analysis exceeds one wavelength. By performing a similar investigation with the STC-MLE, no highly deviating estimates occur. The allowed search range is therefore larger with the STC-MLE. The performance evaluation on in-vivo data further reveals that the number of highly deviating velocity estimates in the tissue parts of the RF-signals are reduced with the STC-MLE. In general the resulting profiles are continuous and more consistent with the true velocity profile, and the introduction of the correlation property has improved the estimates.

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Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Schlaikjer, M. (Intern), Jensen, J. A. (Intern)
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Source-ID: 60483
Publication: Research - peer-review › Article in proceedings – Annual report year: 2001

**Comparison of PCA and ICA based clutter reduction in GPR systems for anti-personal landmine delaction**
This paper presents statistical signal processing approaches for clutter reduction in stepped-frequency ground penetrating radar (SF-GPR) data. In particular, we suggest clutter/signal separation techniques based on principal and independent component analysis (PCA/ICA). The approaches are successfully evaluated and compared on a real SF-GPR time-series. Field-test data are acquired using a monostatic S-band rectangular waveguide antenna.

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Organisations: Department of Electrical Engineering, Department of Informatics and Mathematical Modeling, Cognitive Systems, Biomedical Engineering, Electromagnetic Systems
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Source: orbit
Experimental investigation of transverse velocity estimation using cross-correlation

A technique for estimating the full flow velocity vector has previously been presented by our group. Unlike conventional estimators, that only detect the axial component of the flow, this new method is capable of estimating the transverse velocity component. The method uses focusing along the flow direction to produce signals that are influenced by the shift of the scatterer's position. The signals are then cross-correlated to find the shift in position and thereby the velocity. The performance of the method is investigated using both a flow phantom and in-vivo measurements.

A flow phantom capable of producing a parabolic flow profile was measured with a B-K Medical 8804 7.5 MHz linear array transducer. A plastic tube with an entrance length of 130 cm and a diameter of 17 mm. was used with an EcoWatt 1 pump generating a volume flow of 93.4 l/h corresponding to a peak velocity in the tube of 0.23 m/s. The volume flow was determined by a Danfoss MAG 1100 flow meter. The velocity profiles were measured for different beam-to-flow angles of 90, 65, and 45 degrees. A Harming apodized beam focused at the vessel was transmitted using 64 elements and the received signals on all elements were sampled at 40 MHz and 12 bits in parallel using our experimental ultrasound scanner. Three hundred and seventy pulse echo measurements were acquired for each angle at a pulse repetition frequency of 5 kHz. The field in a number of points on lines parallel to the flow was calculated by focusing the 64 channels of data. A mean parabolic velocity profile was obtained for purely transverse flow with a mean bias to the true profile of -2.5% relative to the peak velocity and a standard deviation of 13.3% relative to the peak velocity. Twenty pulse-echo lines were used for each estimate and 18 profiles were obtained. For a beam-to-flow angles of 45 and 65 degrees the corresponding numbers were a mean relative bias of less than 4.0% and a relative standard deviation of 3.0% or less, when using 10 pulse-echo lines and 36 profiles. In-vivo measurements have also been performed on the carotid artery on a male volunteer and the flow at an angle of 701 was successfully estimated.

Joint probability discrimination between stationary tissue and blood velocity signals

In CFM-mode the blood velocity estimates are overlaid onto the B-mode image. The velocity estimation gives non-zero velocity estimates in both the surrounding tissue and the vessels. A discrimination algorithm is needed to determine, which estimates represent blood flow and should be displayed. This study presents a new statistical discriminator. Investigation of the RF-signals reveals that features can be derived that distinguish the segments of the signal, which do an do not carry information on the blood flow. In this study 4 features, have been determined: (a) the energy content in the segments before and after echo-canceling, and (b) the amplitude variations between samples in consecutive RF-signals before and after echo-canceling. The statistical discriminator was obtained by computing the probability density functions (PDFs) for each feature through histogram analysis of data. The discrimination is performed by determining the joint probability of the features for the segment under investigation and choosing the segment type that is most likely. The method was tested on
simulated data resembling RF-signals from the carotid artery.

**General information**

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**Mine detection using SF-GPR: A signal processing approach for resolution enhancement and clutter reduction**

Proper clutter reduction is essential for Ground Penetrating Radar data since low signal-to-clutter ratio prevent correct detection of mine objects. A signal processing approach for resolution enhancement and clutter reduction used on Stepped-Frequency Ground Penetrating Radar (SF-GPR) data is presented, and the effects of combining clutter reduction with resolution enhancement are examined using simulated SF-GPR data examples. The resolution enhancement method is based on methods from optical signal processing and is largely carried out in the frequency domain to reduce the computational burden. The clutter reduction method is based on basis function decomposition of the SF-GPR time-series from which the clutter and the signal are separated.

**General information**

**State:** Published  
**Organisations:** Department of Electrical Engineering, Electromagnetic Systems, Biomedical Engineering, Technical University of Denmark  
**Authors:** Karlsen, B. (Intern), Jakobsen, K. B. (Intern), Larsen, J. (Ekstern), Sørensen, H. B. D. (Intern)  
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**DOIs:** 10.1117/12.445535  
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Spatial filters for focusing ultrasound images
Traditionally focusing is done by taking out one sample in the received signal from each transducer element and then sum these signals. This method does not take into account the temporal or spatial spread of the received signal from a point scatterer and does not make an optimal focus of the data. A new method for making spatial matched filter focusing of RF ultrasound data is proposed based on the spatial impulse response description of the imaging. The response from a scatterer at any given point in space relative to the transducer can be calculated, and this gives the spatial matched filter for beamforming the received RF signals from the individual transducer elements. The matched filter is applied on RF signals from individual transducer elements, thus properly taking into account the spatial spread of the received signal. The method can be applied to any transducer and can also be used for synthetic aperture imaging for single element transducers. It is evaluated using the Field II program. Data from a single 3 MHz transducer focused at a distance of 80 mm is processed. Far from the transducer focal region, the processing greatly improves the image resolution: the lateral slice of the autocovariance function of the image shows a -6 dB width reduction by a factor of 3.3 at 20 mm and by a factor of 1.8 at 30 mm. Other simulations use a 64 elements, 3 MHz, linear array. Different receiving conditions are compared and this shows that the effect of the filter is progressively lower, but the approach always yields point spread functions better or equal to a traditional dynamically focused image. Finally, the process was applied to in-vivo clinical images of the liver and right kidney from a 28 years old male. The data was obtained with a single element transducer focused at 100 mm. The improvement in resolution was in this case less evident and further optimization is needed.

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Authors: Jensen, J. A. (Intern), Gori, P. (Ekstern)
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Publication: Research - peer-review › Article in proceedings – Annual report year: 2001

The influence of roughness, angle, range, and transducer type on the echo signal from planar interfaces
The received electrical echo signal from a pulse-echo system insonifying a planar interface was measured for varying degrees of rms roughness [0 to 0.29 mm (0 to 1.7 /spl lambda/)], angles of incidence, /spl theta/, (-7/spl deg/ to 7/spl deg/), and ranges to a planar or focused transducer. The effect of varying a is quantified in terms of the energy of the received signal, E(/spl theta/), and the normalized spectrum of the received signal. E(/spl theta/) is approximately Gaussian when using a planar transducer or a focused transducer with the reflecting interface located at or beyond the focal point. For focused transducers with the interface located closer than the geometrical point of focus, two maxima can sometimes be observed when varying the incident angle. As is generally known, the width of E(spl theta/) is strongly dependent on transducer type, e.g., for a smooth interface, the -3 dB width for a 25.4 mm diameter 5-MHz planar and focused transducer was approximately 0.5/spl deg/ and 4/spl deg/ (at the focal point), respectively. E(0/spl deg/) as a function of surface roughness, R/sub q/, was nearly linear on a decibel scale, with a slope of -109 dB/(R/sub q//spl lambda/) and -61 dB/(Rq//spl lambda/) for planar and focused transducers, respectively. The characteristic nulls present in the normalized spectra of the echo signal at non-normal incidence tend to vanish with increasing R/sub q/ when using planar transducers. For focused transducers, the normalized spectra change from relatively flat to monotonically decreasing as R/sub q/ increases, and they exhibit reduced amplitude with increased incident angle.

General information
Velocity estimation using synthetic aperture imaging [blood flow]

Presented an approach for synthetic aperture blood flow ultrasound imaging. Estimates with a low bias and standard deviation can be obtained with as few as eight emissions. The performance of the new estimator is verified using both simulations and measurements. The results demonstrate that a fully functioning synthetic aperture scanner can be made.

Estimation of blood velocity vectors using ultrasound

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State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, Center for Fast Ultrasound Imaging
Authors: Munk, P. (Ekstern), Jensen, J. A. (Intern)
Number of pages: 206
Publication date: 2000
Estimation of vector velocity

Using a pulsed ultrasound field, the two-dimensional velocity vector can be determined with the invention. The method uses a transversally modulated ultrasound field for probing the moving medium under investigation. A modified autocorrelation approach is used in the velocity estimation. The new estimator automatically compensates for the axial velocity, when determining the transverse velocity by using fourth order moments rather than second order moments. The estimation is optimized by using a lag different from one in the estimation process, and noise artifacts are reduced by using averaging of RF samples. Further, compensation for the axial velocity can be introduced, and the velocity estimation is done at a fixed depth in tissue to reduce spatial velocity dispersion.

Fast simulation of ultrasound images

Realistic B-mode and flow images can be simulated with scattering maps based on optical, CT, or MR images or parametric flow models. The image simulation often includes using 200,000 to 1 million point scatterers. One image line typically takes 1800 seconds to compute on a state-of-the-art PC, and a whole image can take a full day. Simulating 3D images and 3D flow takes even more time. A 3D image of 64 by 64 lines can take 21 days, which is not practical for iterative work. This paper presents a new fast simulation method based on the Field II program. In imaging the same spatial impulse response is calculated for each of the image lines, and making 100 lines, thus, gives 100 calculations of the same impulse response delayed differently for the different lines. Doing the focusing after this point in the simulation can make the calculation faster. This corresponds to full synthetic aperture imaging. The received response from each element is calculated, when emitting with each of the elements in the aperture, and then the responses are subsequently focused. This is the approach taken in this paper using a modified version of the Field II program. A 64 element array, thus, gives 4096 responses. For a 7 MHz 64 element linear array the simulation time for one image line is 471 seconds for 200,000 scatterers on a 800 MHz AMD Athlon PC, corresponding to 17 hours for one image with 128 lines. Using the new
approach, the computation time is 10,963 seconds, and the beamforming time is 9 seconds, which makes the approach
5.5 times faster. For 3D images with 64 by 64 lines, the total conventional simulation time for one volume is 517 hours,
whereas the new approach makes the simulation in 6,810 seconds. The time for beamforming is 288 seconds, and the
new approach is, thus, 262 times faster. The simulation can also be split among a number of PCs for speeding up the
simulation. A full 3D one second volume simulation then takes 7,500 seconds on a 32 CPU 600 MHz Pentium III PC
cluster.

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High-Frequency Dynamic Nuclear Polarization in the Nuclear Rotating Frame
A proton dynamic nuclear polarization (DNP) NMR signal enhancement \( (1) \) close to thermal equilibrium, \( (1) = 0.89 \), has been
obtained at high field \( (B0 = 5 \text{ T}, \nu_{epr} = 139.5 \text{ GHz}) \) using 15 mM trityl radical in a 40:60 water/glycerol frozen solution at 11
K. The electron-nuclear polarization transfer is performed in the nuclear rotating frame with microwave irradiation during a
nuclear spin-lock pulse. The growth of the signal enhancement is governed by the rotating frame nuclear spin–lattice
relaxation time \( (T_1p) \), which is four orders of magnitude shorter than the nuclear spin–lattice relaxation time \( (T_{1n}) \). Due to
the rapid polarization transfer in the nuclear rotating frame the experiment can be recycled at a rate of \( 1/T_1p \) and is not
limited by the much slower lab frame nuclear spin–lattice relaxation rate \( (1/T_{1n}) \). The increased repetition rate allowed in
the nuclear rotating frame provides an effective enhancement per unit time \( 1/2 \) of \( t = 197 \). The nuclear rotating frame-DNP
experiment does not require high microwave power; significant signal enhancements were obtained with a low-power (20
mW) Gunn diode microwave source and no microwave resonant structure. The symmetric trityl radical used as the
polarization source is water-soluble and has a narrow EPR linewidth of 10 G at 139.5 GHz making it an ideal polarization
source for high-field DNP/NMR studies of biological systems.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Farrar, C. T. (Ekstern), Hall, D. A. (Ekstern), Gerfen, G. J. (Ekstern), Rosay, M. (Ekstern), Ardenkjaer-Larsen, J.
H. (Intern), Griffin, R. G. (Ekstern)
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Main Research Area: Technical/natural sciences

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BFI (2018): BFI-level 1
Recursive ultrasound imaging

A method and an apparatus for recursive ultrasound imaging is presented. The method uses a Synthetic Transmit Aperture, but unlike previous approaches a new frame is created at every pulse emission. In receive, parallel beam forming is implemented. The beam formed RF data is added to the previously created RF lines. To keep the level of the signal, the RF data obtained previously, when emitting with the same element is subtracted from the RF lines. Up to 5000 frames/sec can be achieved for a tissue depth of 15 cm with a speed of sound of \( c = 1540 \) m/s. The high frame rate
makes continuous imaging data possible, which can significantly enhance flow imaging. A point spread function $2^\circ$ wide at -6 dB and grating lobes of $\text{amp}(F) -50 \text{ dB}$ is obtained with a 64 elements phased array with a central frequency $f_\text{c} = 3$ MHz using a sparse transmit aperture using only 10 elements ($N_\text{tx} = 10$) during pulse emission. The corresponding images have the quality of a dynamically focused image in transmit and receive. The dynamic focusing gives a small sampling volume and the capability to view small blood vessels and obtain the velocity profiles within the vessels with lower variance than with normal imaging.

### Vector velocity estimation using directional beam forming and cross-correlation

The two-dimensional velocity vector using a pulsed ultrasound field can be determined with the invention. The method uses a focused ultrasound field along the velocity direction for probing the moving medium under investigation. Several pulses are emitted and the focused received fields along the velocity direction are cross-correlated. The time shift between received signals is found from the peak in the cross-correlation function and the velocity is thereby determined.
1H DNP at 1.4 T of Water Doped with a Triarylmethyl-Based Radical

Recently a triarylmethyl-based (TAM) radical has been developed for research in biological and other aqueous systems, and in low magnetic fields, 10 mT or less, large 1H dynamic nuclear polarization (DNP) enhancements have been reported. In this paper the DNP properties of this radical have been investigated in a considerably larger field of 1.4 T, corresponding to proton and electron Larmor frequencies of 60 MHz and 40 GHz, respectively. To avoid excessive microwave heating of the sample, an existing DNP NMR probe was modified with a screening coil, wound around the sample capillary and with its axis perpendicular to the electric component of the microwave field. It was found that with this probe the temperature increase in the sample after 4 s of microwave irradiation with an incident power of 10 W was only 16°C. For the investigations, 10 mM of the TAM radical was dissolved in deionized, but not degassed, water and put into a 1-mm i.d. and 6-mm long capillary tube. At 26°C the following results were obtained: (I) The relaxivity of the radical is 0.07 (mMs)^−1, in accordance with the value extrapolated from low-field results; (II) The leakage factor is 0.63, the saturation factor at maximum power is 0.85, and the coupling factor is −0.0187. It is shown that these results agree very well with an analysis where the electron–dipolar interactions are the dominant DNP mechanism, and where the relaxation transitions resulting from these interactions are governed by translational diffusion of the water molecules. Finally, the possibilities of combining DNP with magnetic resonance microscopy (MRM) are discussed. It is shown that at 26°C the overall DNP-enhanced proton polarization should become maximal in an external field of 0.3 T and become comparable to the thermal equilibrium polarization in a field of 30 T, considerably larger than the largest high-resolution magnet available to date. It is concluded that DNP MRM in this field, which corresponds to a standard microwave frequency of 9 GHz, has the potential to significantly increase the sensitivity in NMR and MRI experiments of small aqueous samples doped with the TAM radical.

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Authors: Wind, R. A. (Ekstern), Ardenkjær-Larsen, J. H. (Intern)
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BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.113 SNIP 1.013 CiteScore 2.26
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.103 SNIP 0.937 CiteScore 2.41
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
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BFI (2011): BFI-level 1
A New Method for Estimation of Velocity Vectors

The paper describes a new method for determining the velocity vector of a remotely sensed object using either sound or electromagnetic radiation. The movement of the object is determined from a field with spatial oscillations in both the axial direction of the transducer and in one or two directions transverse to the axial direction. By using a number of pulse emissions, the inter-pulse movement can be estimated and the velocity found from the estimated movement and the time between pulses. The method is based on the principle of using transverse spatial modulation for making the received signal influenced by transverse motion. Such a transverse modulation can be generated by using apodization on individual transducer array elements together with a special focusing scheme. A method for making such a field is presented along with a suitable two-dimensional velocity estimator. An implementation usable in medical ultrasound is described, and simulated results are presented. Simulation results for a flow of 1 m/s in a tube rotated in the image plane at specific angles (0, 15, 35, 55, 75, and 90 degrees) are made and characterized by the estimated mean value, estimated angle, and the standard deviation in the lateral and longitudinal direction. The average performance of the estimates for all angles is: mean velocity 0.99 m/s, longitudinal S.D. 0.015 m/s, and lateral S.D. 0.196 m/s. For flow parallel to the transducer the results are: mean velocity 0.95 m/s, angle 0.10, longitudinal S.D. 0.020 m/s, and lateral S.D. 0.172 m/s.

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BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.73 SJR 0.986 SNIP 1.402
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.814 SNIP 1.494 CiteScore 2.43
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.088 SNIP 1.627 CiteScore 2.18
Web of Science (2014): Indexed yes
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BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.802 SNIP 1.479 CiteScore 1.87
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**Apparatus and method for determining movements and velocities of moving objects**

With an apparatus according to the invention it is possible to detect an object's velocity transverse to the direction of propagation of an interacting field. Such transverse movement is detected by applying a field that oscillates spatially in the transverse direction. The method used in the apparatus is applicable where wave energy is used to sense or detect an object by its scattering properties when using either sound waves or electro-magnetic waves. The movement can be detected according to the field properties. The field represented by the sampling pulse must feature a spatial oscillation in the directions, where the velocity components are of interest. Such a transversely oscillating field is e.g. generated by using apodization on individual transducer elements and a special focusing scheme. The apparatus uses waves of either sound or electro-magnetic radiation. The temporal characteristics are determined by the setup of the emitter (1). The spatial characteristics are determined by the transmitter array configuration (3) and the receiver array configuration (5) and the respective beam formers (2) and (6a, 6b, 6c). The transmit array consists of $i(N)$ elements and the receive array consists of $i(M)$ elements. The transmit beam former and the receive beam former are configured to obtain the spatially oscillating field. The signal received from the interacting objects (4) is processed by the velocity estimator processor (7) for calculation of the velocity vector components by estimating the shift in position as a function of time and the velocity is derived herefrom.

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DE 69710725  
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US 6148224  
JP 2001503853  
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**Bibliographical note**


**Electron paramagnetic resonance and dynamic nuclear polarization of char suspensions: surface science and oximetry**

Carbon chars have been synthesized in our laboratory from a variety of starting materials, by means of a highly controlled pyrolysis technique. These chars exhibit electron paramagnetic resonance (EPR) line shapes which change with the local oxygen concentration in a reproducible and stable fashion; they can be calibrated and used for oximetry. Biological stability and low toxicity make chars good sensors for in vivo measurements. Scalar and dipolar interactions of water protons at the surfaces of chars may be utilized to produce dynamic nuclear polarization (DNP) of the nuclear spin population in conjunction with electron Zeeman pumping. Low-frequency EPR, DNP and DNP-enhanced MRI all show promise as oximetry methods when used with carbon chars.

**General information**
EPR and DNP Properties of Certain Novel Single Electron Contrast Agents Intended for Oximetric Imaging

Parameters of relevance to oximetry with Overhauser magnetic resonance imaging (OMRI) have been measured for three single electron contrast agents of the triphenylmethyl type. The single electron contrast agents are stable and water soluble. Magnetic resonance properties of the agents have been examined with electron paramagnetic resonance (EPR), nuclear magnetic resonance (NMR), and dynamic nuclear polarization (DNP) at 9.5 mT in water, isotonic saline, plasma, and blood at 23 and 37°C. The relaxivities of the agents are about 0.2–0.4 mM⁻¹s⁻¹ and the DNP enhancements extrapolate close to the dipolar limit. The agents have a single, narrow EPR line, which is analyzed as a Voigt function. The linewidth is measured as a function of the agent concentration and the oxygen concentration. The concentration broadenings are about 1–3 μT/mM and the Lorentzian linewidths at infinite dilution are less than 1 μT in water at room temperature. The longitudinal electron spin relaxation rate is calculated from the DNP enhancement curves. The oxygen broadening in water is about 50 μT/mM O₂ at 37°C. These agents have good properties for oximetry with OMRI.
Overhauser-enhanced MR imaging (OMRI)

Purpose. To evaluate a new single-electron contrast agent for Overhauser-enhanced MR imaging. The contrast agents that are currently available give enhancement factors that are too low to make the technique a valid option for routine clinical use. Material and Methods. MR images were generated directly following the injection of the substance into rats. The MR scanner was operated at a main magnetic field of 0.01 T and equipped with a separate rf-transmitter tuned to the electron paramagnetic resonance frequency of the contrast agent. Results. As expected, the images generated show a high level of enhancement in areas where the contrast agent was present, and a maximum enhancement of 60 times the normal proton signal was obtained in the vascular area. The signal-to-noise ratios in the images were superior to those previously attained. Conclusion: The new contrast agent makes it possible to generate MR images with both morphological and functional information at 0.01 T. The signal-to-noise ratios found in the generated images were of the same order as, or better than, those obtained with the standard clinical routine.

General information
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Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Golman, K. (Ekstern), Leunbach, I. (Ekstern), Ardenkjaer-Larsen, J. (Intern), Ehnholm, G. (Ekstern), Wistrand, L. (Ekstern), Petersson, J. (Intern), Jarvi, A. (Ekstern), Vahasalo, S. (Ekstern)
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A program for the simulation of ultrasound systems is presented. It is based on the Tupholme-Stepanishen method, and is fast because of the use of a far-field approximation. Any kind of transducer geometry and excitation can be simulated, and both pulse-echo and continuous wave fields can be calculated for both transmit and pulse-echo. Dynamic apodization and focusing are handled through time lines, and different focusing schemes can be simulated. The versatility of the program is ensured by interfacing it to Matlab. All routines are called directly from Matlab, and all Matlab features can be used. This makes it possible to simulate all types of ultrasound imaging systems.

**Field:** A Program for Simulating Ultrasound Systems

An ultrasound system simulation program is presented. It is based on the Tupholme-Stepanishen method and is fast due to the use of a far-field approximation. Any transducer geometry and excitation can be simulated, and both pulse-echo and continuous wave fields can be calculated for both transmit and pulse-echo. Dynamic apodization and focusing are handled through time lines, and different focusing schemes can be simulated. The versatility of the program is ensured by interfacing it to Matlab. All routines are called directly from Matlab, and all Matlab features can be used. This makes it possible to simulate all types of ultrasound imaging systems.
In vivo imaging of a stable paramagnetic probe by pulsed-radiofrequency electron paramagnetic resonance spectroscopy

Imaging of free radicals by electron paramagnetic resonance (EPR) spectroscopy using time domain acquisition as in nuclear magnetic resonance (NMR) has not been attempted because of the short spin-spin relaxation times, typically under 1 μs, of most biologically relevant paramagnetic species. Recent advances in radiofrequency (RF) electronics have enabled the generation of pulses of the order of 10-50 ns. Such short pulses provide adequate spectral coverage for EPR studies at 300 MHz resonant frequency. Acquisition of free induction decays (FID) of paramagnetic species possessing inhomogeneously broadened narrow lines after pulsed excitation is feasible with an appropriate digitizer/averager. This report describes the use of time-domain RF EPR spectrometry and imaging for in vivo applications. FID responses were collected from a water-soluble, narrow line width spin probe within phantom samples in solution and also when infused intravenously in an anesthetized mouse. Using static magnetic field gradients and back-projection methods of image reconstruction, two-dimensional images of the spin-probe distribution were obtained in phantom samples as well as in a mouse. The resolution in the images was better than 0.7 mm and devoid of motional artifacts in the in vivo study. Results from this study suggest a potential use for pulsed RF EPR imaging (EPRI) for three-dimensional spatial and spectral-spatial imaging applications. In particular, pulsed EPRI may find use in vivo studies to minimize motional artifacts from cardiac and lung motion that cause significant problems in frequency-domain spectral acquisition, such as in continuous...
wave (cw) EPR techniques

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering, National Cancer Institute
Authors: Murugesan (Ekstern), Cook (Ekstern), Devasahayam (Ekstern), Afeworki (Ekstern), Subramanian (Ekstern), Tschudin (Ekstern), Ardenkjær-Larsen, J. H. (Intern), Mitchell (Ekstern), Russo (Ekstern), Krishna (Ekstern)
Pages: 409-414
Publication date: 1997
Main Research Area: Technical/natural sciences

Publication information
Journal: Magnetic Resonance in Medicine
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Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.77 SJR 1.89 SNIP 1.411
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.52 SJR 1.945 SNIP 1.451
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.329 SNIP 1.481 CiteScore 3.54
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.015 SNIP 1.382 CiteScore 3.32
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.039 SNIP 1.433 CiteScore 3.46
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.158 SNIP 1.553 CiteScore 3.61
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.16 SNIP 1.461 CiteScore 3.45
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.356 SNIP 1.606
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.331 SNIP 1.553
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.468 SNIP 1.5
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 2.397 SNIP 1.536
Scopus rating (2006): SJR 2.319 SNIP 1.756
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 2.298 SNIP 1.833
Web of Science (2005): Indexed yes
Estimation of blood velocities using ultrasound: A Signal Processing Approach

Ultrasound systems are especially useful in estimating blood velocities in the human body because they are noninvasive and can display an estimate in real time. This book offers a comprehensive treatment of this relatively new, important technology. The book begins with an introduction to ultrasound, flow physics, and the circulatory system. Next, the interaction of ultrasound with blood is discussed. The special contribution of the book lies in the remaining chapters, which offer a lucid, thorough description of continuous and pulsed wave systems, the latest systems for doing color flow imaging, and, finally, some of the more recent experimental techniques. The authors shows that the Doppler shift, usually considered the way velocity is detected, actually, plays a minor role in pulsed systems. Rather, it is the shift of position of signals between pulses that is used in velocity estimation.

An Analysis of Pulsed Wave Ultrasound Systems for Blood Velocity Estimation

Pulsed wave ultrasound systems can be used for determining blood's velocity non-invasively in the body. A region of interest is selected, and the received signal is range gated to measure data from the region. One complex sample value is acquired for each pulse emission after complex demodulation of the received signal. The time evolution and distribution of velocity can then be found by using samples from a number of pulse-echo lines. Making a short-time Fourier transform of the data reveals the velocity distribution in the range gate over time. Such systems are called Doppler ultrasound systems implying that they use the classical Doppler effect. The velocity is typically on the order of 0.5 to 1 m/s giving a relative shift of 2 to 4 kHz of the center frequency of the received spectrum for a 3 MHz transducer. Finding such a shift is impossible since the unknown frequency shift from attenuation in tissue can be tens of kilohertz. Some recent reviews and articles state that the Doppler effect is used, and contradictory and wrong results and erroneous system diagrams arise from this assumption. Research done in the last feen years has revealed that it is the movement of the scatterers between pulse emissions, that is used for nding the velocity. This finding gives new insight into the role of the complex demodulation stage, and shows that this can be replaced by a matched Ier and quadrature RF sampling. A derivation of this result is presented in this paper, and it reveals how the bandwidth of the pulse and the number of pulse emissions aect the result. The nal equation for the received signal is quite complicated, and a simplified interpretation is therefore also given. This readily reveals the inuence from transducer bandwidth, attenuation, non-linear eects, classical Doppler eect, and scattering.
Automation of seizure duration estimation during ECT: Use of fractal dimension

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, National Institute of Mental Health and Neuroscience, Indian Institute of Science
Authors: B N, G. (Ekstern), N, J. (Ekstern), Narayana, D. (Ekstern), Puthusserypady, S. (Intern)
Publication date: 1995

Host publication information
Title of host publication: Proceedings of the 14th Annual Conference of BME Society of India: an International Meeting
Main Research Area: Technical/natural sciences
Conference: 14th Annual Conference of the Biomedical Engineering Society of India. An International Meeting, 15/02/1995 - 15/02/1995
Source: orbit
Source-ID: 265969
Publication: Research - peer-review › Article in proceedings – Annual report year: 1995

Comparisons between PW Doppler system and enhanced FM Doppler system
This paper presents a new implementation of an echo-ranging FM Doppler system with improved performance, relative to the FM Doppler system reported previously. The use of long sweeps provides a significant reduction in peak to average power ratio compared to pulsed wave (PW) emission. A PW Doppler system exploits the direct relationship between arrival time of the received signal and range from the transducer. In the FM Doppler systems, a similar relationship exists in the spectral domain of the demodulated received signals, so that range is represented by frequency. Thus, a shift in location of moving scatterers between consecutive emissions corresponds to a frequency shift in the spectral signature. The improvement relative to the earlier version of the FM Doppler system is attained by utilizing cross-correlation of real spectra rather than of magnitude spectra for assessing flow velocity. This approach requires a priori knowledge of the envelope of the received sweep from a point scatterer.

General information
State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering
Authors: Wilhjelm, J. E. (Intern), Pedersen, P. C. (Ekstern)
Pages: 1549-1552
Publication date: 1995

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Publisher: IEEE
ISBN (Print): 07-80-32940-6
Main Research Area: Technical/natural sciences
Electronic versions: Wilhjelm.pdf
DOIs: 10.1109/ULTSYM.1995.495850
Discriminative training of self-structuring hidden control neural models
This paper presents a new training algorithm for self-structuring hidden control neural (SHC) models. The SHC models were trained non-discriminatively for speech recognition applications. Better recognition performance can generally be achieved, if discriminative training is applied instead. Thus we developed a discriminative training algorithm for SHC models, where each SHC model for a specific speech pattern is trained with utterances of the pattern to be recognized and with other utterances. The discriminative training of SHC neural models has been tested on the TIDIGITS database.

Neural network for sonogram gap filling
In duplex imaging both an anatomical B-mode image and a sonogram are acquired, and the time for data acquisition is divided between the two images. This gives problems when rapid B-mode image display is needed, since there is not time for measuring the velocity data. Gaps then appear in the sonogram and in the audio signal, rendering the audio signal useless, thus making diagnosis difficult. The current goal for ultrasound scanners is to maintain a high refresh rate for the B-mode image and at the same time attain a high maximum velocity in the sonogram display. This precludes the intermixing of the B-mode and sonogram pulses, and time must be shared between the two. Gaps will appear frequently in the sonogram since, e.g., half the time is spent on B-mode acquisition. The information in the gaps can be filled from the available information through interpolation. One possibility is to use a neural network for predicting mean frequency of the velocity signal and its variance. The neural network then predicts the evolution of the mean and variance in the gaps, and the sonogram and audio signal are reconstructed from these. The technique is applied on in-vivo data from the carotid artery. The neural network is trained on part of the data and the network is pruned by the optimal brain damage procedure in order to reduce the number of parameters in the network, and thereby reduce the risk of overfitting. The neural predictor is compared to using a linear filter for the mean and variance time series, and is shown to yield better results, i.e., the variances of the predictions are lower. The ability of the neural predictor to reconstruct both the sonogram and the audio signal, when only 50% of the time is used for velocity data acquisition, is demonstrated for the in-vivo data.
Artifacts in blood velocity estimation using ultrasound and cross-correlation

Estimation of blood velocities using ultrasound and time-domain cross-correlation is investigated. The measurement principle is introduced, and the basic properties of the cross-correlation function are discussed. Expressions for the variance of the estimates of the peak location are given, showing the influence of integration time, transducer bandwidth and signal-to-noise ratio. It is also shown that the technique can be implemented using only the sign of the signals. A simple simulation program is used in order to study the exact influence from the different parameters. Using the program, it is shown that any velocity can result from the estimation with a certain probability regardless of the true velocity, when the signal-to-noise ratio is low. This is due to the non-linear estimation technique employed and shows that estimation variance yields little information for this estimator. Graphs are given for the probability of correct estimation, when the different parameters are varied.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Jensen, J. A. (Intern)
Pages: S165-70
Publication date: 1994
Main Research Area: Technical/natural sciences

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Journal: Medical & Biological Engineering & Computing
Volume: 32
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Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.12 SJR 0.661 CiteScore 2.04
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.713 SNIP 1.273 CiteScore 2.05
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.821 SNIP 1.238 CiteScore 2.14
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.64 SNIP 1.324 CiteScore 2.16
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.679 SNIP 1.239 CiteScore 2.19
Estimation of in-vivo pulses in medical ultrasound
An algorithm for the estimation of one-dimensional in-vivo ultrasound pulses is derived. The routine estimates a set of ARMA parameters describing the pulse and uses data from a number of adjacent rf lines. Using multiple lines results in a decrease in variance on the estimated parameters and significantly reduces the risk of terminating the algorithm at a local minimum. Examples from use on synthetic data confirms the reduction in variance and increased chance of successful minimization termination. Simulations are also reported indicating the relation between the one-dimensional pulse and the three-dimensional, attenuated ultrasound field for a concave transducer. Pulses are estimated from in-vivo liver data showing good resemblance to a pulse measured as the response from a planar reflector and then properly attenuated. The main application for the algorithm is to function as a preprocessing stage for deconvolution algorithms using parametric pulses.
Nonparametric estimation of ultrasound pulses

An algorithm for nonparametric estimation of 1D ultrasound pulses in echo sequences from human tissues is derived. The technique is a variation of the homomorphic filtering technique using the real cepstrum, and the underlying basis of the method is explained. The algorithm exploits prior knowledge about the structure of RF line echo data and can employ a number of adjacent RF lines from an image. The prime application of the algorithm is to yield a pulse suitable for deconvolution algorithms. This will enable these algorithms to properly take into account the frequency dependence of the attenuation and its variation within a patient and among patients. It is also possible to use the estimated pulse for attenuation estimation, and the consistency of the assumptions underlying the proposed technique is demonstrated by its ability to recover low variance attenuation estimates in the normal liver from in vivo pulse-echo data. Estimates are given for 8 different patients.
Two-dimensional random arrays for real time volumetric imaging

Two-dimensional arrays are necessary for a variety of ultrasonic imaging techniques, including elevation focusing, 2-D phase aberration correction, and real time volumetric imaging. In order to reduce system cost and complexity, sparse 2-D arrays have been considered with element geometries selected ad hoc, by algorithm, or by random process. Two random sparse array geometries and a sparse array with a Mills cross receive pattern were simulated and compared to a fully sampled aperture with the same overall dimensions. The sparse arrays were designed to the constraints of the Duke University real time volumetric imaging system, which employs a wide transmit beam and receive mode parallel processing to increase image frame rate. Depth-of-field comparisons were made from simulated on-axis and off-axis beamplots at ranges from 30 to 160 mm for both coaxial and offset transmit and receive beams. A random array with Gaussian distribution of transmitters and uniform distribution of receivers was found to have better resolution and depth-of-field than both a Mills cross array and a random array with uniform distribution of both transmit and receive elements. The Gaussian random array was constructed and experimental system response measurements were made at several ranges. Comparisons of B-scan images of a tissue mimicking phantom show improvement in resolution and depth-of-field consistent with simulation results.
Deconvolution of In Vivo Ultrasound B-Mode Images

An algorithm for deconvolution of medical ultrasound images is presented. The procedure involves estimation of the basic one-dimensional ultrasound pulse, determining the ratio of the covariance of the noise to the covariance of the reflection signal, and finally deconvolution of the rf signal from the transducer. Using pulse and covariance estimators makes the approach self-calibrating, as all parameters for the procedure are estimated from the patient under investigation. An example of use on a clinical, in-vivo image is given. A 2 × 2 cm region of the portal vein in a liver is deconvolved. An increase in axial resolution by a factor of 2.4 is obtained. The procedure can also be applied to whole images, when it is ensured that the rf signal is properly measured. A method for doing that is outlined.

General information

State: Published
Organisations: Biomedical Engineering, Department of Electrical Engineering, Section for Vessels, National Institute of Aquatic Resources, Technical University of Denmark
Authors: Jensen, J. A. (Intern), Stage, B. (Intern), Mathorne, J. (Ekstern), Gravesen, T. (Ekstern)
Pages: 122-133
Publication date: 1993
Main Research Area: Technical/natural sciences

Publication information

Journal: Ultrasonic Imaging
Volume: 15
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Ratings:
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.921 SJR 0.692 CiteScore 2.06
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.745 SNIP 0.906 CiteScore 1.75
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.61 SNIP 0.736 CiteScore 1.76
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.915 SNIP 0.996 CiteScore 1.63
Range/velocity limitations for time-domain blood velocity estimation

The traditional range/velocity limitation for blood velocity estimation systems using ultrasound is elucidated. It is stated that the equation is a property of the estimator used, not the actual physical measurement situation, as higher velocities can be estimated by the time domain cross-correlation approach. It is demonstrated that the time domain technique under certain measurement conditions will yield unsatisfactory results, when trying to estimate high velocities. Various methods to avoid these artifacts using temporal and spatial clustering techniques are suggested. The improvement in probability of correct detection is derived, and several examples of simulations are shown.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Jensen, J. A. (Intern)
Pages: 741-749
Publication date: 1993
Main Research Area: Technical/natural sciences

Publication information
Journal: Ultrasound in Medicine & Biology
Volume: 19
Issue number: 9
ISSN (Print): 0301-5629
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
Stationary echo canceling in velocity estimation by time-domain cross-correlation

The application of stationary echo canceling to ultrasonic estimation of blood velocities using time-domain cross-correlation is investigated. Expressions are derived that show the influence from the echo canceler on the signals that enter the cross-correlation estimator. It is demonstrated that the filtration results in a velocity-dependent degradation of the signal-to-noise ratio. An analytic expression is given for the degradation for a realistic pulse. The probability of correct
detection at low signal-to-noise ratios is influenced by signal-to-noise ratio, transducer bandwidth, center frequency, number of samples in the range gate, and number of A-lines employed in the estimation. Quantitative results calculated by a simple simulation program are given for the variation in probability from these parameters. An index reflecting the reliability of the estimate at hand can be calculated from the actual cross-correlation estimate by a simple formula and used in rejecting poor estimates or in displaying the reliability of the velocity estimated.
Calculation of pressure fields from arbitrarily shaped, apodized, and excited ultrasound transducers

A method for simulation of pulsed pressure fields from arbitrarily shaped, apodized and excited ultrasound transducers is suggested. It relies on the Tupholme-Stepanishen method for calculating pulsed pressure fields, and can also handle the continuous wave and pulse-echo case. The field is calculated by dividing the surface into small rectangles and then summing their response. A fast calculation is obtained by using the far-field approximation. Examples of the accuracy of the approach and actual calculation times are given.
Deconvolution of ultrasound images
Based on physical models, it is indicated that the received pressure field in ultrasound B-mode images can be described by a convolution between a tissue reflection signal and the emitted pressure field. This result is used in a description of current image formation and in formulating a new processing scheme. The suggested estimator can take into account the dispersive attenuation, the temporal and spatial variation of the pulse, and the change in reflection strength and signal-to-noise ratio. Details of the algorithm and the estimation of parameters to be used are given. The performance is indicated by two examples. One is for a synthetic signal and the other is for data measured from a tissue mimicking phantom. The
last example shows a finer speckle pattern, giving an increased resolution.
A model for the propagation and scattering of ultrasound in tissue

An inhomogeneous wave equation is derived describing propagation and scattering of ultrasound in an inhomogeneous medium. The scattering term is a function of density and propagation velocity perturbations. The integral solution to the wave equation is combined with a general description of the field from typical transducers used in clinical ultrasound to yield a model for the received pulse-echo pressure field. Analytic expressions are found in the literature for a number of transducers, and any transducer excitation can be incorporated into the model. An example is given for a concave, nonapodized transducer in which the predicted pressure field is compared to a measured field.

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State: Published
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Authors: Jensen, J. A. (Intern)
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Main Research Area: Technical/natural sciences

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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 1.77 SJR 0.695 SNIP 1.224
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.83 SJR 0.819 SNIP 1.271
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.854 SNIP 1.416 CiteScore 1.77
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.887 SNIP 1.402 CiteScore 1.8
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.707 SNIP 1.937 CiteScore 2
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.771 SNIP 1.619 CiteScore 1.75
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.686 SNIP 1.624 CiteScore 1.68
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.734 SNIP 1.511
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 0.778 SNIP 1.692
Estimation of pulses in ultrasound B-scan images

It is shown, based on an expression for the received pressure field in pulsed medical ultrasound systems, that a common one-dimensional pulse can be estimated from individual A-lines. An autoregressive moving average (ARMA) model is suggested for the pulse, and an estimator based on the prediction error method is derived. The estimator is used on a segment of an A-line, assuming that the pulse does not change significantly inside the segment. Several examples of the use of the estimator on synthetic data measured from a tissue phantom and in vitro data measured from a calf's liver are given. They show that a pulse can be estimated even at moderate signal-to-noise ratios.
Phase-processing as a tool for speckle reduction in pulse-echo images

Due to the coherent nature of conventional ultrasound medical imaging systems interference artefacts occur in pulse echo images. These artefacts are generically termed 'speckle'. The phenomenon may severely limit low contrast resolution with clinically relevant information being obscured. Traditional speckle reduction procedures regard speckle correction as a stochastic process and trade image smoothing (resolution loss) for speckle reduction. Recently, a new phase acknowledging technique has been proposed that is unique in its ability to correct for speckle interference with no image resolution tradeoff. The technique is outlined and preliminary in-vivo results are presented.

Sampling system for in vivo ultrasound images

Newly developed algorithms for processing medical ultrasound images use the high frequency sampled transducer signal. This paper describes demands imposed on a sampling system suitable for acquiring such data and gives details about a prototype constructed. It acquires full clinical images at a sampling frequency of 20 MHz with a resolution of 12 bits. The prototype can be used for real time image processing. An example of a clinical in vivo image is shown and various aspects of the data acquisition process are discussed.

On output measurements via radiation pressure

It is shown, by simple physical argument, that measurements of intensity with a radiation pressure balance should not agree with those based on calorimetric techniques. The conclusion is ultimately a consequence of the circumstance that radiation pressure measurements relate to wave momentum, while calorimetric methods relate to wave energy. Measurements with some typical ultrasound fields are performed with a novel type of hydrophone, and these allow an estimate to be made of the magnitude of the discrepancy to be expected between the two types of output measurement in a typical case.
A new principle for a high-efficiency power audio amplifier for use with a digital preamplifier

The use of class-B and class-D amplifiers for converting digital audio signals to analog signals is discussed. It is shown that the class-D amplifier is unsuitable due to distortion. Therefore a new principle involving a switch-mode power supply and a class-B amplifier is suggested. By regulating the supply voltage to the amplifier according to the amplitude of the audio signal, a higher efficiency than can be obtained by the usual principles is achieved. The regulation can be done very efficiently by generating the control signal to the power supply in advance of the audio signal, made possible by a preceding digital signal from the preamplifier. A prototype shows possibilities for further developments.
A new principle for an all-digital preamplifier and equalizer

A new principle for an all-digital preamplifier and equalizer, to be used together with a Compact Disc player, is described. The principle makes it possible to obtain an arbitrary gain transfer function together with a linear phase. The gain can be varied 20 dB from point to point, when specified on a logarithmic frequency axis with 30 divisions from 20 Hz to 20 kHz. The deviation in the passband is a maximum of 0.3 dB. Taking advantage of the digital signal from the preamplifier, a high-efficiency power amplifier can be developed. A prototype of the preamplifier built with commercially obtainable components has shown promising results.
A New Principle for a High Efficiency Power Audio Amplifier for Use with a Digital Preamplifier

The use of class-B and class-D amplifiers for converting digital audio signals to analog signals is discussed. It is shown that the class-D amplifier is unsuitable due to distortion. Therefore, a new principle involving a switch-mode power supply and a class-B amplifier is suggested. By regulating the supply voltage to the amplifier according to the amplitude of the audio signal, a higher efficiency than can be obtained by the current principles is achieved. The regulation can be done very efficiently by generating the control signal to the power supply in advance of the audio signal, made possible by the digital signal from the preamplifier. A prototype shows possibilities for further developments.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Jensen, J. A. (Intern)
Publication date: 1986

Host publication information
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Publisher: Audio Engineering Society
Main Research Area: Technical/natural sciences
Conference: AES Convention , Montreux, Switzerland, 04/03/1986 - 04/03/1986
Amplifiers, Audio frequency, Amplifiers, power type, Electronic circuits, Power supply - applications, Audio equipment, Data conversion, digital to analog, High efficiency power audio amplifier, Digital preamplifier, Control of power supply, Conversion from digital to analog signal;, Switch-mode power supply

Bibliographical note
Paper Number: 2346
Publication: Research - peer-review › Article in proceedings – Annual report year: 1986

A New principle for an all digital preamplifier and equalizer

A new principle for an all digital preamplifier and equalizer, to be used together with a compact disc player, is described. The principle makes it possible to obtain an arbitrary gain transfer function together with a linear phase. The gain can be varied 20 dB from point to point, when specified on a logarithmic frequency axis with 30 divisions from 20 Hz to 20 kHz. The deviation in the passbands is max. 0.2 dB. Taking advantage of the digital signal from the preamplifier, a high-efficiency power amplifier can be developed. A prototype of the preamplifier built with commercially obtainable components has shown promising results.

General information
State: Published
Organisations: Department of Electrical Engineering, Biomedical Engineering
Authors: Jensen, J. A. (Intern)
Publication date: 1986

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Publisher: Audio Engineering Society
Main Research Area: Technical/natural sciences
Conference: AES Convention , Montreux, Switzerland, 04/03/1986 - 04/03/1986
Amplifiers, audio frequency:, Amplifiers, power type, Circuits, power supply - applications, Audio equipment, Data conversion, digital to analog, High efficiency power audio amplifier, Digital preamplifier, Control of power supply, Conversion from digital to analog signal, Switch-mode power supply.

Bibliographical note
Paper no. 2315
Publication: Research - peer-review › Article in proceedings – Annual report year: 1986

Long-Term Cycling of the Magnesium Hydrogen System

Magnesium powder with a grain size of approximately 50μm was hydrogenated for 30 min and dehydrogenated the same time at 390°C, 515 times. A moderate loss in hydrogen storage capacity was observed and was ascribed to a measured decrease in reaction kinetics as the cycle number increased. The time for maximum hydrogen absorption was found to depend significantly on cycle number while the time for maximum desorption was found to be virtually independent of cycle number.

General information
State: Published
Organisations: Risø National Laboratory for Sustainable Energy, Biomedical Engineering, Department of Electrical Engineering
Scopus rating (2001): SJR 0.488 SNIP 1.197
Scopus rating (2000): SJR 0.384 SNIP 0.83
Scopus rating (1999): SJR 0.376 SNIP 0.882
Original language: English

Projects:

**Bindevævs biomekanik og modellering**
Department of Electrical Engineering
Biomedical Engineering
Period: 07/04/2014 → 16/06/2014
Number of participants: 3
Project participant:
- Traberg, Marie Sand (Intern)
- Eriksen, Tine Alkjær (Intern)
- Örn Jensson, Brynjar (Ekstern)

Documents:
- Connective tissue biomechanics and modelling_FinalVersion

Activities:

**Evaluation of respiratory motion correction in PET/CT using a 3D printed phantom**
Period: 22 Oct 2017
Josefine Holm Vilshøll (Speaker)
Hasler S. W. Hasler (Guest lecturer)
L. D. L. Duchstein (Guest lecturer)
Jens E. Wilhjelm (Guest lecturer)
M. N. Lonsdale (Guest lecturer)

Department of Electrical Engineering
Biomedical Engineering
Degree of recognition: International

Related event
**EANM’17: 30th Annual Congress of the European Association of Nuclear Medicine**
21/10/2017 → 25/10/2017
Vienna, Austria
Activity: Talks and presentations

Investigation of echogenic surface enhancements for improved needle visualization in ultrasonography: A PRISMA systematic review
Period: 11 Oct 2017
Caroline Harder Hovgesen (Speaker)
Jens E. Wilhjelm (Guest lecturer)
Peter Vilmann (Guest lecturer)
Evangelos Kalaitzakis (Guest lecturer)
Related event

DMTS Annual meeting
10/10/2017 → 12/10/2017
Vingsted, Denmark
Activity: Talks and presentations › Conference presentations

Studenterinvolvering via ressourcemaessig effektiv peer review i et obligatorisk kursus i fysikken i medicinsk billeddannelse
Period: 30 May 2017
Jens E. Wilhjelm (Speaker)
Sidsel-Marie Winther Prag (Guest lecturer)
Department of Electrical Engineering
Biomedical Engineering
LearningLab DTU

Office for Study Programmes and Student Affairs
Degree of recognition: International
Links:
http://dun-net.dk/aktiviteter/2017/dun-conference-2017/program-sessions/ (Link to program)

Related event

DUN konference 2017
30/05/2017 → 31/05/2017
Vingsted, Denmark
Activity: Talks and presentations › Conference presentations

Danish Cardiovascular Research Academy
Period: 26 May 2016 → 28 May 2016
Jens Christian Brasen (Organizer)
Department of Electrical Engineering
Biomedical Engineering

Description
Organiser of a symposium and chair of the symposium.

Organiser of a symposium and chair of the symposium.

Related event

Danish Cardiovascular Research Academy : 2016 Summer Meeting
26/05/2016 → 28/05/2016
Sønderborg, Denmark
Activity: Attending an event › Participating in or organising a conference

Secretary, ISMRM study group on Detection & Correction of Motion in MRI & MRS (External organisation)
Period: 2015 → 2016
Lars G. Hanson (Participant)
Biomedical Engineering
Department of Electrical Engineering
Copenhagen Center for Health Technology
Description
Research Network of the International Society for Magnetic Resonance in Medicine
Degree of recognition: International

Related external organisation

Secretary, ISMRM study group on Detection &amp; Correction of Motion in MRI &amp; MRS
Activity: Membership › Membership of research networks or expert groups

Endothelial derived hyperpolarization in renal interlobar arteries
Period: 15 Sep 2015
Jens Christian Brasen (Speaker)
Department of Electrical Engineering
Biomedical Engineering

Related event

Meeting on Endothelium-Dependent Hyperpolarizations in Health and Disease
14/09/2015 → 17/09/2015
Nyborg, Denmark
Activity: Talks and presentations › Conference presentations

Meeting on Endothelium-Dependent Hyperpolarizations in Health and Disease
Period: 14 Sep 2015 → 17 Sep 2015
Jens Christian Brasen (Participant)
Department of Electrical Engineering
Biomedical Engineering

Related event

Meeting on Endothelium-Dependent Hyperpolarizations in Health and Disease
14/09/2015 → 17/09/2015
Nyborg, Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

MRI simulation for sequence development, protocol optimisation, and education
Period: 29 Jun 2015 → 1 Jul 2015
Lars G. Hanson (Organizer)
Department of Electrical Engineering
Biomedical Engineering
Copenhagen Center for Health Technology

Description
MRI simulation for sequence development, protocol optimisation, and education
Links:

Related event

MRI simulation for sequence development, protocol optimisation, and education: ESMRMB Lectures on MR
29/06/2015 → 01/07/2015
Kgs. Lyngby, Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

Biosimulation
Period: 1 Jun 2015 → 30 Jun 2015
Visualisation of basic NMR: Quantum and classical aspects
Period: 25 Feb 2015
Lars G. Hanson (Lecturer)
Department of Electrical Engineering
Biomedical Engineering

Description
Invited talk at the MMCE conference, Poland 2015
Documents:
MMCE2015_abstract_LGH
MMCE2015_abstract_LGH.pdf
Links:
http://nmr.cent3.uw.edu.pl/mmce2015/ (Conference homepage)

Related event
Magnetic Moments in Central Europe 2015
25/02/2015 → 01/03/2015
Krynica-Zdrój, Poland
Activity: Talks and presentations › Conference presentations

MR principles, imaging and contrast
Period: 3 Feb 2015
Lars G. Hanson (Lecturer)
Department of Electrical Engineering
Biomedical Engineering

Description
Lecture at PhD course
Documents:
Slides
Links:
http://eprints.drcmr.dk/37/ (Lecture notes)

Related event
Clinical and research applications of diagnostic imaging techniques: MR, PET, SPECT, CT and ultrasound: PhD Course
02/02/2015 → 06/02/2015
Copenhagen, Denmark
Activity: Talks and presentations › Conference presentations

The Scandinavian Physiological Society - The Special Interest Group (SIG) within Vascular Physiology
Period: 28 Jan 2015
Jens Christian Brasen (Participant)
Department of Electrical Engineering
Biomedical Engineering

Related event
The Scandinavian Physiological Society - The Special Interest Group (SIG) within Vascular Physiology
28/01/2015 → …
København, Denmark
Secretary-Elect, ISMRM study group on Detection & Correction of Motion in MRI & MRS (External organisation)
Period: 2014 → 2015
Lars G. Hanson (Secretary)
Department of Electrical Engineering
Biomedical Engineering

Description
Research Network of the International Society for Magnetic Resonance in Medicine
Degree of recognition: International

Related external organisation
Secretary-Elect, ISMRM study group on Detection & Correction of Motion in MRI & MRS

Mathematical Biosciences (Journal)
Period: 23 Oct 2014 → …
Jens Christian Brasen (Reviewer)
Department of Electrical Engineering
Biomedical Engineering

Description
Mathematical Biosciences
Ongoing

Related journal
Mathematical Biosciences
0025-5564
BFI (2018): BFI-level 2, Scopus rating (2017): CiteScore 1.58 SJR 0.663 SNIP 0.954, ISI indexed (2013): ISI indexed yes,
Web of Science (2018): Indexed yes
Central database
Activity: Research › Peer review of manuscripts

Rhythms in complex networks
Period: 1 Sep 2014 → 3 Sep 2014
Jens Christian Brasen ( Participant)
Department of Electrical Engineering
Biomedical Engineering
Links:
http://dsin.ku.dk/calendar/workshop_sep14/Conference_Final.pdf

Related event
Rhythms in complex networks
01/09/2014 → 03/09/2014
Copenhagen, Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

Proceedings of the National Academy of Sciences, Physical Sciences (NASA) (Journal)
Period: 2 Jul 2014 → …
Jens Christian Brasen (Reviewer)
Department of Electrical Engineering
Biomedical Engineering

Related journal

Proceedings of the National Academy of Sciences, Physical Sciences (NASA)
Local database
Activity: Research › Peer review of manuscripts

Mathematical models of (spatial and) temporal dynamics in biological and physiological systems
Period: 22 May 2014
Jens Christian Brasen (Invited speaker)
Department of Electrical Engineering
Biomedical Engineering

Description
Talk at ISOLATE workshop
Links:
http://www.isolate.gu.se/meetings/

Related event

ISOLATE Workshop
15/05/2014 → 23/05/2014
Odense, Denmark
Activity: Talks and presentations › Conference presentations

Kinetik
Period: 18 Feb 2014
Jens Christian Brasen (Guest lecturer)
Department of Electrical Engineering
Biomedical Engineering

Description
På kurset "Modellering af fysiologiske systemer"

Related external organisation

University of Copenhagen
Thorvaldsensvej 40, DK-1871 Frederiksberg C, Copenhagen, Denmark
Activity: Talks and presentations › Guest lectures, external teaching and course activities at other universities

DSMMR Course on MRI Methodology
Period: 20 Jan 2014 → 21 Jan 2014
Lars G. Hanson (Organizer)
Department of Electrical Engineering
Biomedical Engineering

Description
Organizer, DSMMR course on MRI Methodology
Organizer and lecturer

Related event

DSMMR Course on MRI Methodology
20/01/2014 → 21/01/2014
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.
MRI simulation for sequence development, protocol optimisation and education
Period: 2 Dec 2013 → 4 Dec 2013
Lars G. Hanson (Organizer)
Department of Electrical Engineering
Biomedical Engineering

Description
Co-organizer

Co-organizer

Links:

Related event

MRI simulation for sequence development, protocol optimisation and education: ESMRMB Lectures on MR
02/12/2013 → 04/12/2013
Bonn, Germany
Activity: Attending an event › Participating in or organising a conference

BioDynamics 2013
Period: 11 Sep 2013 → 13 Sep 2013
Jens Christian Brasen (Participant)
Department of Electrical Engineering
Biomedical Engineering

Related event

BioDynamics 2013: Where Biology, Medicine & Mathematics meet
11/09/2013 → 13/09/2013
Bristol, United Kingdom
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

14th International Conference on Systems Biology
Period: 30 Aug 2013 → 3 Sep 2013
Jens Christian Brasen (Organizer)
Department of Electrical Engineering
Biomedical Engineering

Description
Organizing Committee

Related event

14th International Conference on Systems Biology
30/08/2013 → 03/09/2013
Copenhagen, Denmark
Activity: Attending an event › Participating in or organising a conference

14th International Conference on Systems Biology
Period: 30 Aug 2013 → 4 Sep 2013
Jens Christian Brasen (Organizer)
Department of Electrical Engineering
Biomedical Engineering

Description
Main Organizer
Related event

14th International Conference on Systems Biology: Workshops
29/08/2013 → 04/09/2013
Kgs. Lyngby, Denmark
Activity: Attending an event › Participating in or organising a conference

4th International Symposium on Dynamic Nuclear Polarization
Lars G. Hanson (Organizer)
Department of Electrical Engineering
Biomedical Engineering

Description
Local co-organizer
Links:
http://www.dnpsymposium.org (Conference homepage)

Related event

4th International Symposium on Dynamic Nuclear Polarization
28/08/2013 → 31/08/2013
Copenhagen, Denmark
Activity: Attending an event › Participating in or organising a conference

Acquisition Strategies for Hyperpolarised Spin Systems
Lars G. Hanson (Organizer)
Department of Electrical Engineering
Biomedical Engineering

Description
Local co-organizer
Links:

Related event

Acquisition Strategies for Hyperpolarised Spin Systems: ESMRMB Lectures on MRI
25/08/2013 → 27/08/2013
Lyngby, Denmark
Activity: Attending an event › Participating in or organising a conference

Basic MRI Physics: A visual introduction for laymen
Lars G. Hanson (Lecturer)
Department of Electrical Engineering
Biomedical Engineering

Description
Invited oral presentation.
Documents:
prod21351622680391.HansonEANM2012.pdf

Related event

25th Annual EANM Congress: European Association of Nuclear Medicine
27/10/2012 → 31/10/2012
Milan, Italy
Activity: Talks and presentations › Conference presentations

**P L o S One (Journal)**
Period: 22 Aug 2011 → …
Jens Christian Brasen (Reviewer)
Department of Electrical Engineering
Biomedical Engineering

**Description**
PLOS One

**Related journal**

**P L o S One**
1932-6203
Indexed in DOAJ
Central database
Activity: Research › Peer review of manuscripts

**Journal of Medical Ultrasonics (External organisation)**
Period: 1 Jan 2010 → …
Jens E. Wilhjelm (Participant)
Department of Electrical Engineering
Biomedical Engineering

**Description**
Editorial board (Overseas)
Degree of recognition: International

**Related external organisation**

**Journal of Medical Ultrasonics**
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

**Ultragarsas (External organisation)**
Period: 1 Jan 2010 → …
Jens E. Wilhjelm (Participant)
Department of Electrical Engineering
Biomedical Engineering

**Description**
Member of editorial board

Body type: Scientific journal
Degree of recognition: International

**Related external organisation**

**Ultragarsas**
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

**International Congress of Ultrasonics (External organisation)**
Period: 1 Jan 2009 → …
Jens E. Wilhjelm (Participant)
Department of Electrical Engineering
Biomedical Engineering

**Description**
Member of the board
Degree of recognition: International

**Related external organisation**
**International Congress of Ultrasonics**
Activity: Membership › Membership of committees, commissions, boards, councils, associations, organisations, or similar

**Prizes:**

**New Investigator Award for Basic Science**
Tommaso di Ianni (Recipient)
Department of Electrical Engineering, Biomedical Engineering

**Description**
American Institute of Ultrasound in Medicine

**Details**
Awarded date: Mar 2017
Prize: Prizes, scholarships, distinctions