A modality-adaptive method for segmenting brain tumors and organs-at-risk in radiation therapy planning

In this paper we present a method for simultaneously segmenting brain tumors and an extensive set of organs-at-risk for radiation therapy planning of glioblastomas. The method combines a contrast-adaptive generative model for whole-brain segmentation with a new spatial regularization model of tumor shape using convolutional restricted Boltzmann machines. We demonstrate experimentally that the method is able to adapt to image acquisitions that differ substantially from any available training data, ensuring its applicability across treatment sites; that its tumor segmentation accuracy is comparable to that of the current state of the art; and that it captures most organs-at-risk sufficiently well for radiation therapy planning purposes. The proposed method may be a valuable step towards automating the delineation of brain tumors and organs-at-risk in glioblastoma patients undergoing radiation therapy.

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An Automatically Generated Texture-based Atlas of the Lungs

Many pulmonary diseases can be characterized by visual abnormalities on lung CT scans. Some diseases manifest similar defects but require completely different treatments, as is the case for Pulmonary Hypertension (PH) and Pulmonary Embolism (PE): both present hypo- and hyper-perfused regions but with different distribution across the lung and require different treatment protocols. Finding these distributions by visual inspection is not trivial even for trained radiologists who currently use invasive catheterism to diagnose PH. A Computer-Aided Diagnosis (CAD) tool that could facilitate the non-invasive diagnosis of these diseases can benefit both the radiologists and the patients. Most of the visual differences in the parenchyma can be characterized using texture descriptors. Current CAD systems often use texture information but the texture is either computed in a patch-based fashion, or based on an anatomical division of the lung. The difficulty of precisely finding these divisions in abnormal lungs calls for new tools for obtaining new meaningful divisions of the lungs. In this paper we present a method for unsupervised segmentation of lung CT scans into subregions that are similar in terms of texture and spatial proximity. To this extent, we combine a previously validated Riesz-wavelet texture descriptor with a well-known superpixel segmentation approach to create a 3D texture-based atlas that we extend to 3D. We demonstrate the feasibility and accuracy of our approach on a simulated texture dataset, and show preliminary results for CT scans of the lung comparing subjects suffering either from PH or PE. The resulting texture-based atlas of individual lungs can potentially help physicians in diagnosis or be used for studying common texture distributions related to other diseases.

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Organisations: Department of Applied Mathematics and Computer Science, Department of Electrical Engineering, Center for Magnetic Resonance, Image Analysis & Computer Graphics, University of Applied Sciences Western Switzerland, University Hospital of Geneva
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A probabilistic atlas of the human thalamic nuclei combining ex vivo MRI and histology
The human thalamus is a brain structure that comprises numerous, highly specific nuclei. Since these nuclei are known to have different functions and to be connected to different areas of the cerebral cortex, it is of great interest for the neuroimaging community to study their volume, shape and connectivity in vivo with MRI. In this study, we present a probabilistic atlas of the thalamic nuclei built using ex vivo brain MRI scans and histological data, as well as the application of the atlas to in vivo MRI segmentation. The atlas was built using manual delineation of 26 thalamic nuclei on the serial histology of 12 whole thalami from six autopsy samples, combined with manual segmentations of the whole thalamus and surrounding structures (caudate, putamen, hippocampus, etc.) made on in vivo brain MR data from 39 subjects. The 3D structure of the histological data and corresponding manual segmentations was recovered using the ex vivo MRI as reference frame, and stacks of blockface photographs
acquired during the sectioning as intermediate target. The atlas, which was encoded as an adaptive tetrahedral mesh, shows a good agreement with previous histological studies of the thalamus in terms of volumes of representative nuclei. When applied to segmentation of in vivo scans using Bayesian inference, the atlas shows excellent test-retest reliability, robustness to changes in input MRI contrast, and ability to detect differential thalamic effects in subjects with Alzheimer's disease. The probabilistic atlas and companion segmentation tool are publicly available as part of the neuroimaging package FreeSurfer.

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**Characterization of highly multiplexed monolithic PET / gamma camera detector modules: Paper**
PET detectors use signal multiplexing to reduce the total number of electronics channels needed to cover a given area. Using measured thin-beam calibration data, we tested a principal component based multiplexing scheme for scintillation detectors. The highly-multiplexed detector signal is no longer amenable to standard calibration methodologies. In this study we report results of a prototype multiplexing circuit, and present a new method for calibrating the detector module with multiplexed data. A 50 × 50 × 10 mm3 LYSO scintillation crystal was affixed to a position-sensitive photomultiplier tube with 6 × 8 position-outputs and one channel that is the sum of the other 64. The 65-channel signal was multiplexed in a resistive circuit, with 65:5 or 65:7 multiplexing. A 0.9 mm beam of 511 keV photons was scanned across the face of the crystal in a 1.52 mm grid pattern in order to characterize the detector response. New methods are developed to reject scattered events and perform depthestimation to characterize the detector response of the calibration data. Photon interaction position estimation of the testing data was performed using a Gaussian Maximum Likelihood estimator and the resolution and scatter-rejection capabilities of the detector were analyzed. We found that using a 7-channel multiplexing scheme (65.7 compression ratio) with 1.67 mm depth bins had the best performance with a beam-contour of 1.2 mm FWHM (from the 0.9 mm beam) near the center of the crystal and 1.9 mm FWHM near the edge of the crystal. The positioned events followed the expected BeerLambert depth distribution. The proposed calibration and positioning method exhibited a scattered photon rejection rate that was a 55% improvement over the summed signal energy-windowing method.

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CT metal artifact reduction using MR image patches

Metal implants give rise to metal artifacts in computed tomography (CT) images, which may lead to diagnostic errors and erroneous CT number estimates when the CT is used for radiation therapy planning. Methods for reducing metal artifacts by exploiting the anatomical information provided by coregistered magnetic resonance (MR) images are of great potential value, but remain technically challenging due to the poor contrast between bone and air on the MR image. In this paper, we present a novel MR-based algorithm for automatic CT metal artifact reduction (MAR), referred to as kerMAR. It combines kernel regression on known CT value/MR patch pairs in the uncorrupted patient volume with a forward model of the artifact corrupted values to estimate CT replacement values. In contrast to pseudo-CT generation that builds on multi-patient modelling, the algorithm requires no MR intensity normalisation or atlas registration. Image results for 7 head-and-neck radiation therapy patients with T1-weighted images acquired in the same fixation as the RT planning CT suggest a potential for more complete MAR close to the metal implants than the oMAR algorithm (Philips) used clinically. Our results further show improved performance in air and bone regions as compared to other MR-based MAR algorithms. In addition, we experimented with using kerMAR to define a prior for iterative reconstruction with the maximum likelihood transmission reconstruction algorithm, however with no apparent improvements.

Impact on proton range estimates using a novel mr-based artifact reduction algorithm

Purpose. Metal implants lead to streak and cupping artifacts in computed tomography (CT) images, causing erroneous CT number estimates for radiation therapy (RT) planning. We recently introduced kerMAR, a novel Magnetic Resonance (MR)-based CT metal artifact reduction algorithm that combines kernel regression on uncorrupted CT value/MR patch pairs with a forward model of the CT metal artifacts. Here, we compare the impact of kerMAR and the clinical oMAR algorithm (Philips) on the proton range in calculated spot scanning (SS) dose plans for proton RT. Methods. We acquired T1w MR and CT image sets of a veal shank phantom with and without metal markers inserted, and applied kerMAR and oMAR to the former. We then created SS plans in Eclipse v. 13.7 (Varian) delivering 150 MeV protons in a 0.55 cm single spot that passed 1) near a metal marker at shallow depth and 2) near two different markers located at shallow (near bone) and deep depths, respectively. Similar images were acquired for 4 head-and-neck (HN) RT patients with dental implants, and plans using the same phantom beam, angled through the artifact corrupted oral cavity, were devised, leading to a configuration most resembling phantom beam 2. We finally recalculated the dose plans for the same beamline settings and monitor units on all CT sets, and compared the proton ranges defined as the depth with 80% of the maximum dose. Results. For
the phantom plans, the following range deviations relative to the metal-free reference plan (uncorrected CT, oMAR, kerMAR) were observed: Plan 1: (0.6, 0.6, 0.6)%; plan 2: (4, 1.8, 2.1)%. The patient plans showed the following deviations from the uncorrected CT plan: kerMAR: (10, 8, 7, 11)%; oMAR: (3, 0.1, 10, 0.2)%. Conclusions. Proton range calculations on a phantom showed similar improvements compared to the uncorrupted reference with kerMAR and oMAR. Similar calculations on HN patients, however, displayed systematic proton range increases when applying kerMAR as compared to oMAR.

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Skull segmentation from MR scans using a higher-order shape model based on convolutional restricted Boltzmann machines
Transcranial brain stimulation (TBS) techniques such as transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS) and others have seen a strong increase as tools in therapy and research within the last 20 years. In order to precisely target the stimulation, it is important to accurately model the individual head anatomy of a subject. Of particular importance is accurate reconstruction of the skull, as it has the strongest impact on the current pathways due to its low conductivity. Thus providing automated tools, which can reliably reconstruct the anatomy of the human head from magnetic resonance (MR) scans would be highly valuable for the application of transcranial stimulation methods. These head models can also be used to inform source localization methods such as EEG and MEG. Automated segmentation of the skull from MR images is, however, challenging as the skull emits very little signal in MR. In order to avoid topological defects, such as holes in the segmentations, a strong model of the skull shape is needed. In this paper we propose a new shape model for skull segmentation based on the so-called convolutional restricted Boltzmann machines (cRBMs). Compared to traditionally used lower-order shape models, such as pair-wise Markov random fields (MRFs), the cRBMs model local shapes in larger spatial neighborhoods while still allowing for efficient inference. We compare the skull segmentation accuracy of our approach to two previously published methods and show significant improvement.

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Organisations: Department of Electrical Engineering, Center for Magnetic Resonance, Department of Applied Mathematics and Computer Science, Image Analysis & Computer Graphics, Cognitive Systems, Hvidovre Hospital
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Systematic comparison of different techniques to measure hippocampal subfield volumes in ADNI2

Objective: Subfield-specific measurements provide superior information in the early stages of neurodegenerative diseases compared to global hippocampal measurements. The overall goal was to systematically compare the performance of five representative manual and automated T1 and T2 based subfield labeling techniques in a sub-set of the ADNI2 population.

Methods: The high resolution T2 weighted hippocampal images (T2-HighRes) and the corresponding T1 images from 106 ADNI2 subjects (41 controls, 57 MCI, 8 AD) were processed as follows. A. T1-based: 1. Freesurfer + Large-Diffeomorphic-Metric-Mapping in combination with shape analysis. 2. FreeSurfer 5.1 subfields using in-vivo atlas. B. T2-HighRes: 1. Model-based subfield segmentation using ex-vivo atlas (FreeSurfer 6.0). 2. T2-based automated multi-atlas segmentation combined with similarity-weighted voting (ASHS). 3. Manual subfield parcellation. Multiple regression analyses were used to calculate effect sizes (ES) for group, amyloid positivity in controls, and associations with cognitive/memory performance for each approach. Results: Subfield volumetry was better than whole hippocampal volumetry for the detection of the mild atrophy differences between controls and MCI (ES: 0.27 vs 0.11). T2-HighRes approaches outperformed T1 approaches for the detection of early stage atrophy (ES: 0.27 vs 0.10), amyloid positivity (ES: 0.11 vs 0.04), and cognitive associations (ES: 0.22 vs 0.19). Conclusions: T2-HighRes subfield approaches outperformed whole hippocampus and T1 subfield approaches. None of the different T2-HighRes methods tested had a clear advantage over the other methods. Each has strengths and weaknesses that need to be taken into account when deciding which one to use to get the best results from subfield volumetry.
analysis of the reconstructed PET images revealed quantification errors (aRC) of 13.2% ± 22.1% for the IPAC with respect to CT-corrected images. The Dixon-based method performed substantially worse, with a mean aRC of 23.1% ± 38.4%.

Conclusion: We have presented a non-TOF emission-based approach for estimating the attenuation map in the presence of metallic implants, to be used for whole-body attenuation correction in integrated PET/MR scanners. The Graphics Processing Unit implementation of the algorithm will be included in the open-source reconstruction toolbox Occiput.io.

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A machine learning method for fast and accurate characterization of depth-of-interaction gamma cameras: Paper
Measuring the depth-of-interaction (DOI) of gamma photons enables increasing the resolution of emission imaging systems. Several design variants of DOI-sensitive detectors have been recently introduced to improve the performance of scanners for positron emission tomography (PET). However, the accurate characterization of the response of DOI detectors, necessary to accurately measure the DOI, remains an unsolved problem. Numerical simulations are, at the state of the art, imprecise, while measuring directly the characteristics of DOI detectors experimentally is hindered by the impossibility to impose the depth-of-interaction in an experimental set-up. In this article we introduce a machine learning approach for extracting accurate forward models of gamma imaging devices from simple pencil-beam measurements, using a nonlinear dimensionality reduction technique in combination with a finite mixture model. The method is purely data-driven, not requiring simulations, and is applicable to a wide range of detector types. The proposed method was evaluated both in a simulation study and with data acquired using a monolithic gamma camera designed for PET (the cMiCE detector), demonstrating the accurate recovery of the DOI characteristics. The combination of the proposed calibration technique with maximum-a posteriori estimation of the coordinates of interaction provided a depth resolution of approximate to 1.14 mm for the simulated PET detector and approximate to 1.74 mm for the cMiCE detector. The software and experimental data are made available at http://occiput.mgh.harvard.edu/depthembedding/.

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High-resolution magnetic resonance imaging reveals nuclei of the human amygdala: manual segmentation to automatic atlas

The amygdala is composed of multiple nuclei with unique functions and connections in the limbic system and to the rest of the brain. However, standard in vivo neuroimaging tools to automatically delineate the amygdala into its multiple nuclei are still rare. By scanning postmortem specimens at high resolution (100-150µm) at 7T field strength (n = 10), we were able to visualize and label nine amygdala nuclei (anterior amygdaloid, cortico-amygdaloid transition area; basal, lateral, accessory basal, central, cortical medial, paralaminar nuclei). We created an atlas from these labels using a recently developed atlas building algorithm based on Bayesian inference. This atlas, which will be released as part of FreeSurfer, can be used to automatically segment nine amygdala nuclei from a standard resolution structural MR image. We applied this atlas to two publicly available datasets (ADNI and ABIDE) with standard resolution T1 data, used individual volumetric data of the amygdala nuclei as the measure and found that our atlas i) discriminates between Alzheimer’s disease participants and age-matched control participants with 84% accuracy (AUC=0.915), and ii) discriminates between individuals with autism and age-, sex- and IQ-matched neurotypically developed control participants with 59.5% accuracy (AUC=0.59). For both datasets, the new ex vivo atlas significantly outperformed (all p <.05) estimations of the whole amygdala derived from the segmentation in FreeSurfer 5.1 (ADNI: 75%, ABIDE: 54% accuracy), as well as classification based on whole amygdala volume (using the sum of all amygdala nuclei volumes; ADNI: 81%, ABIDE: 55% accuracy). This new atlas and the segmentation tools that utilize it will provide neuroimaging researchers with the ability to explore the function and connectivity of the human amygdala nuclei with unprecedented detail in healthy adults as well as those with neurodevelopmental and neurodegenerative disorders.
A generative model for segmentation of tumor and organs-at-risk for radiation therapy planning of glioblastoma patients
We present a fully automated generative method for simultaneous brain tumor and organs-at-risk segmentation in multi-modal magnetic resonance images. The method combines an existing whole-brain segmentation technique with a spatial tumor prior, which uses convolutional restricted Boltzmann machines to model tumor shape. The method is not tuned to any specific imaging protocol and can simultaneously segment the gross tumor volume, peritumoral edema and healthy tissue structures relevant for radiotherapy planning. We validate the method on a manually delineated clinical data set of glioblastoma patients by comparing segmentations of gross tumor volume, brainstem and hippocampus. The preliminary results demonstrate the feasibility of the method.

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A Generative Probabilistic Model and Discriminative Extensions for Brain Lesion Segmentation - With Application to Tumor and Stroke
We introduce a generative probabilistic model for segmentation of brain lesions in multi-dimensional images that generalizes the EM segmenter, a common approach for modelling brain images using Gaussian mixtures and a probabilistic tissue atlas that employs expectation-maximization (EM), to estimate the label map for a new image. Our model augments the probabilistic atlas of the healthy tissues with a latent atlas of the lesion. We derive an estimation algorithm with closed-form EM update equations. The method extracts a latent atlas prior distribution and the lesion posterior distributions jointly from the image data. It delineates lesion areas individually in each channel, allowing for differences in lesion appearance across modalities, an important feature of many brain tumor imaging sequences. We also propose discriminative model extensions to map the output of the generative model to arbitrary labels with semantic and biological meaning, such as "tumor core" or "fluid-filled structure", but without a one-to-one correspondence to the hypo- or hyper-intense lesion areas identified by the generative model. We test the approach in two image sets: the publicly available BRATS set of glioma patient scans, and multimodal brain images of patients with acute and subacute ischemic stroke. We find the generative model that has been designed for tumor lesions to generalize well to stroke images, and the extended discriminative-discriminative model to be one of the top ranking methods in the BRATS evaluation.

General information
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A patch-based pseudo-CT approach for MRI-only radiotherapy in the pelvis

In radiotherapy based only on magnetic resonance imaging (MRI), knowledge about tissue electron densities must be derived from the MRI. This can be achieved by converting the MRI scan to the so-called pseudo-computed tomography (pCT). An obstacle is that the voxel intensities in conventional MRI scans are not uniquely related to electron density. The authors previously demonstrated that a patch-based method could produce accurate pCTs of the brain using conventional T_1-weighted MRI scans. The method was driven mainly by local patch similarities and relied on simple affine registrations between an atlas database of the co-registered MRI/CT scan pairs and the MRI scan to be converted. In this study, the authors investigate the applicability of the patch-based approach in the pelvis. This region is challenging for a method based on local similarities due to the greater inter-patient variation. The authors benchmark the method against a baseline pCT strategy where all voxels inside the body contour are assigned a water-equivalent bulk density. Furthermore, the authors implement a parallelized approximate patch search strategy to speed up the pCT generation time to a more clinically relevant level. The data consisted of CT and T_1-weighted MRI scans of 10 prostate patients. pCTs were generated using an approximate patch search algorithm in a leave-one-out fashion and compared with the CT using frequently described metrics such as the voxel-wise mean absolute error (MAE_vox) and the deviation in water-equivalent path lengths. Furthermore, the dosimetric accuracy was tested for a volumetric modulated arc therapy plan using dose–volume histogram (DVH) point deviations and γ-index analysis. The patch-based approach had an average MAE_vox of 54 HU; median deviations of less than 0.4% in relevant DVH points and a γ-index pass rate of 0.97 using a 1%/1 mm criterion. The patch-based approach showed a significantly better performance than the baseline water pCT in almost all metrics. The approximate patch search strategy was 70x faster than a brute-force search, with an average prediction time of 20.8 min. The authors showed that a patch-based method based on affine registrations and T_1-weighted MRI could generate accurate pCTs of the pelvis. The main source of differences between pCT and CT was positional changes of air pockets and body outline.
Bayesian longitudinal segmentation of hippocampal substructures in brain MRI using subject-specific atlases

The hippocampal formation is a complex, heterogeneous structure that consists of a number of distinct, interacting subregions. Atrophy of these subregions is implied in a variety of neurodegenerative diseases, most prominently in Alzheimer's disease (AD). Thanks to the increasing resolution of MR images and computational atlases, automatic segmentation of hippocampal subregions is becoming feasible in MRI scans. Here we introduce a generative model for dedicated longitudinal segmentation that relies on subject-specific atlases. The segmentations of the scans at the different time points are jointly computed using Bayesian inference. All time points are treated the same to avoid processing bias. We evaluate this approach using over 4700 scans from two publicly available datasets (ADNI and MIRIAD). In test-retest reliability experiments, the proposed method yielded significantly lower volume differences and significantly higher Dice overlap than the cross-sectional approach for nearly every subregion (average across subregions: 4.5% vs. 6.5%, Dice overlap: 81.8% vs. 75.4%). The longitudinal algorithm also demonstrated increased sensitivity to group differences: in MIRIAD (69 subjects: 46 with AD and 23 controls), it found differences in atrophy rates between AD and controls that the cross sectional method could not detect in a number of subregions: right parasubiculum, left and right presubiculum, right subiculum, left dentate gyrus, left CA4, left HATA and right tail. In ADNI (836 subjects: 369 with AD, 215 with early cognitive impairment — eMCI — and 252 controls), all methods found significant differences between AD and controls, but the proposed longitudinal algorithm detected differences between controls and eMCI and differences between eMCI and AD that the cross sectional method could not find: left presubiculum, right subiculum, left and right parasubiculum, left and right HATA. Moreover, many of the differences that the cross-sectional method already found were detected with higher significance. The presented algorithm will be made available as part of the open-source neuroimaging package FreeSurfer.
Brain Tumor Segmentation Using a Generative Model with an RBM Prior on Tumor Shape

In this paper, we present a fully automated generative method for brain tumor segmentation in multi-modal magnetic resonance images. The method is based on the type of generative model often used for segmenting healthy brain tissues, where tissues are modeled by Gaussian mixture models combined with a spatial atlas-based tissue prior. We extend this basic model with a tumor prior, which uses convolutional restricted Boltzmann machines (cRBMs) to model the shape of both tumor core and complete tumor, which includes edema and core. The cRBMs are trained on expert segmentations of training images, without the use of the intensity information in the training images. Experiments on public benchmark data of patients suffering from low- and high-grade gliomas show that the method performs well compared to current state-of-the-art methods, while not being tied to any specific imaging protocol.

Computed tomography synthesis from magnetic resonance images in the pelvis using multiple random forests and auto-context features

In radiotherapy treatment planning that is only based on magnetic resonance imaging (MRI), the electron density information usually obtained from computed tomography (CT) must be derived from the MRI by synthesizing a so-called pseudo CT (pCT). This is a non-trivial task since MRI intensities are neither uniquely nor quantitatively related to electron density. Typical approaches involve either a classification or regression model requiring specialized MRI sequences to solve intensity ambiguities, or an atlas-based model necessitating multiple registrations between atlases and subject scans. In this work, we explore a machine learning approach for creating a pCT of the pelvic region from conventional MRI sequences without using atlases. We use a random forest provided with information about local texture, edges and spatial features derived from the MRI. This helps to solve intensity ambiguities. Furthermore, we use the concept of auto-context by sequentially training a number of classification forests to create and improve context features, which are finally used to train a regression forest for pCT prediction. We evaluate the pCT quality in terms of the voxel-wise error and the radiologic accuracy as measured by water-equivalent path lengths. We compare the performance of our method against two baseline pCT strategies, which either set all MRI voxels in the subject equal to the CT value of water, or in addition transfer the bone volume from the real CT. We show an improved performance compared to both baseline pCTs suggesting that our method may be useful for MRI-only radiotherapy.
Fast and Sequence-Adaptive Whole-Brain Segmentation Using Parametric Bayesian Modeling

Quantitative analysis of magnetic resonance imaging (MRI) scans of the brain requires accurate automated segmentation of anatomical structures. A desirable feature for such segmentation methods is to be robust against changes in acquisition platform and imaging protocol. In this paper we validate the performance of a segmentation algorithm designed to meet these requirements, building upon generative parametric models previously used in tissue classification. The method is tested on four different datasets acquired with different scanners, field strengths and pulse sequences, demonstrating comparable accuracy to state-of-the-art methods on T1-weighted scans while being one to two orders of magnitude faster. The proposed algorithm is also shown to be robust against small training datasets, and readily handles images with different MRI contrast as well as multi-contrast data.

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Regional Hippocampal Atrophy and Higher Levels of Plasma Amyloid-Beta Are Associated With Subjective Memory Complaints in Nondemented Elderly Subjects

Background: Evidence suggests a link between the presence of subjective memory complaints (SMC) and lower volume of the hippocampus, one of the first regions to show neuropathological lesions in Alzheimer's disease. However, it remains unknown whether this pattern of hippocampal atrophy is regionally specific and whether SMC are also paralleled by changes in peripheral levels of amyloid-beta (Aβ).

Methods: The volume of hippocampal subregions and plasma Aβ levels were cross-sectionally compared between elderly individuals with (SMC+; N = 47) and without SMC (SMC−; N = 48). Significant volume differences in hippocampal subregions were further correlated with plasma Aβ levels and with objective memory performance.
Results: Individuals with SMC exhibited significantly higher Aβ1-42 concentrations and lower volumes of CA1, CA4, dentate gyrus, and molecular layer compared with SMC(-) participants. Regression analyses further showed significant associations between lower volume of the dentate gyrus and both poorer memory performance and higher plasma Aβ1-42 levels in SMC(+) participants.

Conclusions: The presence of SMC, lower volumes of specific hippocampal regions, and higher plasma Aβ1-42 levels could be conditions associated with aging vulnerability. If such associations are confirmed in longitudinal studies, the combination may be markers recommending clinical follow-up in nondemented older adults.

Simultaneous Whole-Brain Segmentation and White Matter Lesion Detection Using Contrast-Adaptive Probabilistic Models

In this paper we propose a new generative model for simultaneous brain parcellation and white matter lesion segmentation from multi-contrast magnetic resonance images. The method combines an existing whole-brain segmentation technique with a novel spatial lesion model based on a convolutional restricted Boltzmann machine. Unlike current state-of-the-art lesion detection techniques based on discriminative modeling, the proposed method is not tuned to one specific scanner or imaging protocol, and simultaneously segments dozens of neuroanatomical structures. Experiments on a public benchmark dataset in multiple sclerosis indicate that the method’s lesion segmentation accuracy compares well to that of the current state-of-the-art in the field, while additionally providing robust whole-brain segmentations.
4-D PET-MR with Volumetric Navigators and Compressed Sensing

Hybrid PET-MR scanners acquire multi-modal signals simultaneously, eliminating the requirement of software alignment between the MR and PET imaging data. However, the acquisition of high-resolution MR and PET images requires long scanning times, therefore movement of the subject during the acquisition deteriorates both the PET and the MR images. In this work we have developed an approach for tightly integrated PET-MR imaging, making use of volumetric MR navigators to inform, in real-time, both the MR acquisition and the PET reconstruction. The integrated imaging procedure that we describe exploits the simultaneity of MR and PET in hybrid PET-MR systems, producing inherently-aligned motion-free MR and PET images. We describe the system setup, the algorithm for motion-corrected reconstruction, an adaptive sinogram binning algorithm and software design decisions aimed at integrating tightly the MR and PET subsystems. Application of the integrated motion-corrected acquisition procedure to a phantom study and to a volunteer subject demonstrates the validity of the approach for a variety of motion patterns.

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A computational atlas of the hippocampal formation using ex vivo, ultra-high resolution MRI: Application to adaptive segmentation of in vivo MRI.

Automated analysis of MRI data of the subregions of the hippocampus requires computational atlases built at a higher resolution than those that are typically used in current neuroimaging studies. Here we describe the construction of a statistical atlas of the hippocampal formation at the subregion level using ultra-high resolution, ex vivo MRI. Fifteen autopsy samples were scanned at 0.13 mm isotropic resolution (on average) using customized hardware. The images were manually segmented into 13 different hippocampal substructures using a protocol specifically designed for this study; precise delineations were made possible by the extraordinary resolution of the scans. In addition to the subregions, manual annotations for neighboring structures (e.g., amygdala, cortex) were obtained from a separate dataset of in vivo, T1-weighted MRI scans of the whole brain (1 mm resolution). The manual labels from the in vivo and ex vivo data were combined into a single computational atlas of the hippocampal formation with a novel atlas building algorithm based on Bayesian inference. The resulting atlas can be used to automatically segment the hippocampal subregions in structural MRI images, using an algorithm that can analyze multimodal data and adapt to variations in MRI contrast due to differences in acquisition hardware or pulse sequences. The applicability of the atlas, which we are releasing as part of FreeSurfer (version 6.0), is demonstrated with experiments on three different publicly available datasets with different types of MRI contrast. The results show that the atlas and companion segmentation method: 1) can segment T1 and T2 images, as well as their combination, 2) replicate findings on mild cognitive impairment based on high-resolution T2 data, and 3) can discriminate between Alzheimer's disease subjects and elderly controls with 88% accuracy in standard resolution (1 mm) T1 data, significantly outperforming the atlas in FreeSurfer version 5.3 (86% accuracy) and classification based on whole hippocampal volume (82% accuracy).
An algorithm for optimal fusion of atlases with different labeling protocols

In this paper we present a novel label fusion algorithm suited for scenarios in which different manual delineation protocols with potentially disparate structures have been used to annotate the training scans (hereafter referred to as "atlases"). Such scenarios arise when atlases have missing structures, when they have been labeled with different levels of detail, or when they have been taken from different heterogeneous databases. The proposed algorithm can be used to automatically label a novel scan with any of the protocols from the training data. Further, it enables us to generate new labels that are not present in any delineation protocol by defining intersections on the underlying labels. We first use probabilistic models of label fusion to generalize three popular label fusion techniques to the multi-protocol setting: majority voting, semi-locally weighted voting and STAPLE. Then, we identify some shortcomings of the generalized methods, namely the inability to produce meaningful posterior probabilities for the different labels (majority voting, semi-locally weighted voting) and to exploit the similarities between the atlases (all three methods). Finally, we propose a novel generative label fusion model that can overcome these drawbacks. We use the proposed method to combine four brain MRI datasets labeled with different protocols (with a total of 102 unique labeled structures) to produce segmentations of 148 brain regions. Using cross-validation, we show that the proposed algorithm outperforms the generalizations of majority voting, semi-locally weighted voting and STAPLE (mean Dice score 83%, vs. 77%, 80% and 79%, respectively). We also evaluated the proposed algorithm in an aging study, successfully reproducing some well-known results in cortical and subcortical structures. (C) 2014 The Authors. Published by Elsevier Inc.
Bayesian segmentation of brainstem structures in MRI

In this paper we present a method to segment four brainstem structures (midbrain, pons, medulla oblongata and superior cerebellar peduncle) from 3D brain MRI scans. The segmentation method relies on a probabilistic atlas of the brainstem and its neighboring brain structures. To build the atlas, we combined a dataset of 39 scans with already existing manual delineations of the whole brainstem and a dataset of 10 scans in which the brainstem structures were manually labeled with a protocol that was specifically designed for this study. The resulting atlas can be used in a Bayesian framework to segment the brainstem structures in novel scans. Thanks to the generative nature of the scheme, the segmentation method is robust to changes in MRI contrast or acquisition hardware. Using cross validation, we show that the algorithm can segment the structures in previously unseen T1 and FLAIR scans with great accuracy (mean error under 1mm) and robustness (no failures in 383 scans including 168 AD cases). We also indirectly evaluate the algorithm with an experiment in which we study the atrophy of the brainstem in aging. The results show that, when used simultaneously, the volumes of the midbrain, pons and medulla are significantly more predictive of age than the volume of the entire brainstem, estimated as their sum. The results also demonstrate that the method can detect atrophy patterns in the brainstem structures that have been previously described in the literature. Finally, we demonstrate that the proposed algorithm is able to detect differential effects of AD on the brainstem structures. The method will be implemented as part of the popular neuroimaging package FreeSurfer.
Cone beam computed tomography guided treatment delivery and planning verification for magnetic resonance imaging only radiotherapy of the brain

Background. Radiotherapy based on MRI only (MRI-only RT) shows a promising potential for the brain. Much research focuses on creating a pseudo computed tomography (pCT) from MRI for treatment planning while little attention is often paid to the treatment delivery. Here, we investigate if cone beam CT (CBCT) can be used for MRI-only image-guided radiotherapy (IGRT) and for verifying the correctness of the corresponding pCT.

Material and methods. Six patients receiving palliative cranial RT were included in the study. Each patient had three-dimensional (3D) T1W MRI, a CBCT and a CT for reference. Further, a pCT was generated using a patch-based approach. MRI, pCT and CT were placed in the same frame of reference, matched to CBCT and the differences noted. Paired pCT-CT and pCT-CBCT data were created in bins of 10 HU and the absolute difference calculated. The data were converted to relative electron densities (RED) using the CT or a CBCT calibration curve. The latter was either based on a CBCT phantom (phan) or a paired CT-CBCT population (pop) of the five other patients.

Results. Non-significant (NS) differences in the pooled CT-CBCT, MRI-CBCT and pCT-CBCT transformations were noted. The largest deviations from the CT-CBCT reference were <1 mm and 1°. The average median absolute error (MeAE) in HU was 184 ± 34 and 299 ± 34 on average for pCT-CT and pCT-CBCT, respectively, and was significantly different (p <0.01) in each patient. The average MeAE in RED was 0.108 ± 0.025, 0.104 ± 0.011 and 0.099 ± 0.017 for pCT-CT, pCT-CBCT phan (p <0.01 on 2 patients) and pCT-CBCT pop (NS), respectively.

Conclusions. CBCT can be used for patient setup with either MRI or pCT as reference. The correctness of pCT can be verified from CBCT using a population-based calibration curve in the treatment geometry.

Patch-based generation of a pseudo CT from conventional MRI sequences for MRI-only radiotherapy of the brain

Purpose: In radiotherapy (RT) based on magnetic resonance imaging (MRI) as the only modality, the information on electron density must be derived from the MRI scan by creating a so-called pseudo computed tomography (pCT). This is a nontrivial task, since the voxel-intensities in an MRI scan are not uniquely related to electron density. To solve the task, voxel-based or atlas-based models have typically been used. The voxel-based models require a specialized dual ultrashort echo time MRI sequence for bone visualization and the atlas-based models require deformable registrations of conventional MRI scans. In this study, we investigate the potential of a patch-based method for creating a pCT based on conventional T1-weighted MRI scans without using deformable registrations. We compare this method against two state-of-the-art methods within the voxel-based and atlas-based categories.

Methods: The data consisted of CT and MRI scans of five cranial RT patients. To compare the performance of the different methods, a nested cross validation was done to find optimal model parameters for all the methods. Voxel-wise and geometric evaluations of the pCTs were done. Furthermore, a radiologic evaluation based on water equivalent path
lengths was carried out, comparing the upper hemisphere of the head in the pCT and the real CT. Finally, the dosimetric accuracy was tested and compared for a photon treatment plan.

Results: The pCTs produced with the patch-based method had the best voxel-wise, geometric, and radiologic agreement with the real CT, closely followed by the atlas-based method. In terms of the dosimetric accuracy, the patch-based method had average deviations of less than 0.5% in measures related to target coverage.

Conclusions: We showed that a patch-based method could generate an accurate pCT based on conventional T1-weighted MRI sequences and without deformable registrations. In our evaluations, the method performed better than existing voxel-based and atlas-based methods and showed a promising potential for RT of the brain based only on MRI.


Objective: An increasing number of human in vivo magnetic resonance imaging (MRI) studies have focused on examining the structure and function of the subfields of the hippocampal formation (the dentate gyrus, CA fields 1 – 3, and the subiculum) and subregions of the parahippocampal gyrus (entorhinal, perirhinal, and parahippocampal cortices). The ability to interpret the results of such studies and to relate them to each other would be improved if a common standard existed for labeling hippocampal subfields and parahippocampal subregions. Currently, research groups label different subsets of structures and use different rules, landmarks, and cues to define their anatomical extents. This paper characterizes, both qualitatively and quantitatively, the variability in the existing manual segmentation protocols for labeling hippocampal and parahippocampal substructures in MRI, with the goal of guiding subsequent work on developing a harmonized substructure segmentation protocol. Method: MRI scans of a single healthy adult human subject were acquired both at 3 T and 7 T. Representatives from 21 research groups applied their respective manual segmentation protocols to the MRI modalities of their choice. The resulting set of 21 segmentations was analyzed in a common anatomical space to quantify similarity and identify areas of agreement. Results: The differences between the 21 protocols include the region within which segmentation is performed, the set of anatomical labels used, and the extents of specific anatomical labels. The greatest overall disagreement among the protocols is at the CA1/subiculum boundary, and disagreement across all structures is greatest in the anterior portion of the hippocampal formation relative to the body and tail. Conclusions: The combined examination of the 21 protocols in the same dataset suggests possible strategies towards developing a harmonized subfield segmentation protocol and facilitates comparison between published studies.
The Multimodal Brain Tumor Image Segmentation Benchmark (BRATS)

In this paper we report the set-up and results of the Multimodal Brain Tumor Image Segmentation Benchmark (BRATS) organized in conjunction with the MICCAI 2012 and 2013 conferences. Twenty state-of-the-art tumor segmentation algorithms were applied to a set of 65 multi-contrast MR scans of low- and high-grade glioma patients – manually annotated by up to four raters – and to 65 comparable scans generated using tumor image simulation software. Quantitative evaluations revealed considerable disagreement between the human raters in segmenting various tumor sub-regions (Dice scores in the range 74-85%), illustrating the difficulty of this task. We found that different algorithms worked best for different sub-regions (reaching performance comparable to human inter-rater variability), but that no single algorithm ranked in the top for all subregions simultaneously. Fusing several good algorithms using a hierarchical majority vote yielded segmentations that consistently ranked above all individual algorithms, indicating remaining opportunities for further methodological improvements. The BRATS image data and manual annotations continue to be publicly available through an online evaluation system as an ongoing benchmarking resource.

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Tissue Classification
Computational methods for automatically segmenting magnetic resonance images of the brain have seen tremendous advances in recent years. So-called tissue classification techniques, aimed at extracting the three main brain tissue classes (white matter, gray matter, and cerebrospinal fluid), are now well established. In their simplest form, these methods classify voxels independently based on their intensity alone, although much more sophisticated models are typically used in practice.

This article aims to give an overview of often-used computational techniques for brain tissue classification. Although other methods exist, we concentrate on Bayesian modeling approaches, in which generative image models are constructed and subsequently ‘inverted’ to obtain automated segmentations. This general framework encompasses a large number of segmentation methods, including those implemented in widely used software packages such as SPM, FSL, and FreeSurfer.

A Cautionary Analysis of STAPLE Using Direct Inference of Segmentation Truth
In this paper we analyze the properties of the well-known segmentation fusion algorithm STAPLE, using a novel inference technique that analytically marginalizes out all model parameters. We demonstrate both theoretically and empirically that when the number of raters is large, or when consensus regions are included in the model, STAPLE devolves into thresholding the average of the input segmentations. We further show that when the number of raters is small, the STAPLE result may not be the optimal segmentation truth estimate, and its model parameter estimates might not reflect the individual raters’ actual segmentation performance. Our experiments indicate that these intrinsic weaknesses are frequently exacerbated by the presence of undesirable global optima and convergence issues. Together these results cast doubt on the soundness and usefulness of typical STAPLE outcomes.
An Inference Language for Imaging

We introduce iLang, a language and software framework for probabilistic inference. The iLang framework enables the definition of directed and undirected probabilistic graphical models and the automated synthesis of high performance inference algorithms for imaging applications. The iLang framework is composed of a set of language primitives and of an inference engine based on a message-passing system that integrates cutting-edge computational tools, including proximal algorithms and high performance Hamiltonian Markov Chain Monte Carlo techniques. A set of domain-specific highly optimized GPU-accelerated primitives specializes iLang to the spatial data-structures that arise in imaging applications. We illustrate the framework through a challenging application: spatio-temporal tomographic reconstruction with compressive sensing.

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A voxel-based investigation for MRI-only radiotherapy of the brain using ultra short echo times

Radiotherapy (RT) based on magnetic resonance imaging (MRI) as the only modality, so-called MRI-only RT, would remove the systematic registration error between MR and computed tomography (CT), and provide co-registered MRI for assessment of treatment response and adaptive RT. Electron densities, however, need to be assigned to the MRI images for dose calculation and patient setup based on digitally reconstructed radiographs (DRRs). Here, we investigate the geometric and dosimetric performance for a number of popular voxel-based methods to generate a so-called pseudo CT (pCT).

Five patients receiving cranial irradiation, each containing a co-registered MRI and CT scan, were included. An ultra short echo time MRI sequence for bone visualization was used. Six methods were investigated for three popular types of voxel-based approaches; (1) threshold-based segmentation, (2) Bayesian segmentation and (3) statistical regression. Each approach contained two methods. Approach 1 used bulk density assignment of MRI voxels into air, soft tissue and bone based on logical masks and the transverse relaxation time T2 of the bone. Approach 2 used similar bulk density assignments with Bayesian statistics including or excluding additional spatial information. Approach 3 used a statistical regression correlating MRI voxels with their corresponding CT voxels. A similar photon and proton treatment plan was generated for a target positioned between the nasal cavity and the brainstem for all patients. The CT agreement with the pCT of each method was quantified and compared with the other methods geometrically and dosimetrically using both a number of reported metrics and introducing some novel metrics.

The best geometrical agreement with CT was obtained with the statistical regression methods which performed significantly better than the threshold and Bayesian segmentation methods (excluding spatial information). All methods agreed significantly better with CT than a reference water MRI comparison. The mean dosimetric deviation for photons and protons compared to the CT was about 2% and highest in the gradient dose region of the brainstem. Both the threshold based method and the statistical regression methods showed the highest dosimetric agreement.

Generation of pCTs using statistical regression seems to be the most promising candidate for MRI-only RT of the brain.
Further, the total amount of different tissues needs to be taken into account for dosimetric considerations regardless of their correct geometrical position.

**Improved resolution and reliability in dynamic PET using Bayesian regularization of MRTM2**

This paper presents a mathematical model that regularizes dynamic PET data by using a Bayesian framework. We base the model on the well known two-parameter multilinear reference tissue method MRTM2 and regularize on the assumption that spatially close regions have similar parameters. The developed model is compared to the conventional approach of improving the low signal-to-noise ratio of PET data, i.e., spatial filtering of each time frame independently by a Gaussian kernel. We show that the model handles high levels of noise better than the conventional approach, while at the same time retaining a higher resolution. In addition, it results in a higher reliability between scans on individual subject data, measured by intraclass correlation for absolute agreement.

**N3 Bias Field Correction Explained as a Bayesian Modeling Method**

Although N3 is perhaps the most widely used method for MRI bias field correction, its underlying mechanism is in fact not well understood. Specifically, the method relies on a relatively heuristic recipe of alternating iterative steps that does not optimize any particular objective function. In this paper we explain the successful bias field correction properties of N3 by showing that it implicitly uses the same generative models and computational strategies as expectation maximization (EM).
based bias field correction methods. We demonstrate experimentally that purely EM-based methods are capable of producing bias field correction results comparable to those of N3 in less computation time.

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**An Improved Optimization Method for the Relevance Voxel Machine**
In this paper, we will re-visit the Relevance Voxel Machine (RVoxM), a recently developed sparse Bayesian framework used for predicting biological markers, e.g., presence of disease, from high-dimensional image data, e.g., brain MRI volumes. The proposed improvement, called IRVoxM, mitigates the shortcomings of the greedy optimization scheme of the original RVoxM algorithm by exploiting the form of the marginal likelihood function. In addition, it allows voxels to be added and deleted from the model during the optimization. In our experiments we show that IRVoxM outperforms RVoxM on synthetic data, achieving a better training cost and test root mean square error while yielding sparser models. We further evaluated IRVoxM's performance on real brain MRI scans from the OASIS data set, and observed the same behavior - IRVoxM retains good prediction performance while yielding much sparser models than RVoxM.

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**A Probabilistic, Non-parametric Framework for Inter-modality Label Fusion**
Multi-atlas techniques are commonplace in medical image segmentation due to their high performance and ease of implementation. Locally weighting the contributions from the different atlases in the label fusion process can improve the quality of the segmentation. However, how to define these weights in a principled way in inter-modality scenarios remains an open problem. Here we propose a label fusion scheme that does not require voxel intensity consistency between the atlases and the target image to segment. The method is based on a generative model of image data in which each intensity in the atlases has an associated conditional distribution of corresponding intensities in the target. The segmentation is computed using variational expectation maximization (VEM) in a Bayesian framework. The method was evaluated with a dataset of eight proton density weighted brain MRI scans with nine labeled structures of interest. The results show that the algorithm outperforms majority voting and a recently published inter-modality label fusion algorithm.
A unified framework for cross-modality multi-atlas segmentation of brain MRI

Multi-atlas label fusion is a powerful image segmentation strategy that is becoming increasingly popular in medical imaging. A standard label fusion algorithm relies on independently computed pairwise registrations between individual atlases and the (target) image to be segmented. These registrations are then used to propagate the atlas labels to the target space and fuse them into a single final segmentation. Such label fusion schemes commonly rely on the similarity between intensity values of the atlases and target scan, which is often problematic in medical imaging - in particular, when the atlases and target images are obtained via different sensor types or imaging protocols. In this paper, we present a generative probabilistic model that yields an algorithm for solving the atlas-to-target registrations and label fusion steps simultaneously. The proposed model does not directly rely on the similarity of image intensities. Instead, it exploits the consistency of voxel intensities within the target scan to drive the registration and label fusion, hence the atlases and target image can be of different modalities. Furthermore, the framework models the joint warp of all the atlases, introducing interdependence between the registrations. We use variational expectation maximization and the Demons registration framework in order to efficiently identify the most probable segmentation and registrations. We use two sets of experiments to illustrate the approach, where proton density (PD) MRI atlases are used to segment T1-weighted brain scans and vice versa. Our results clearly demonstrate the accuracy gain due to exploiting within-target intensity consistency and integrating registration into label fusion.
Fast, Sequence Adaptive Parcellation of Brain MR Using Parametric Models

In this paper we propose a method for whole brain parcellation using the type of generative parametric models typically used in tissue classification. Compared to the non-parametric, multi-atlas segmentation techniques that have become popular in recent years, our method obtains state-of-the-art segmentation performance in both cortical and subcortical structures, while retaining all the benefits of generative parametric models, including high computational speed, automatic adaptiveness to changes in image contrast when different scanner platforms and pulse sequences are used, and the ability to handle multi-contrast (vector-valued intensities) MR data. We have validated our method by comparing its segmentations to manual delineations both within and across scanner platforms and pulse sequences, and show preliminary results on multi-contrast test-retest scans, demonstrating the feasibility of the approach.

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Improved inference in Bayesian segmentation using Monte Carlo sampling: Application to hippocampal subfield volumetry

Many segmentation algorithms in medical image analysis use Bayesian modeling to augment local image appearance with prior anatomical knowledge. Such methods often contain a large number of free parameters that are first estimated and then kept fixed during the actual segmentation process. However, a faithful Bayesian analysis would marginalize over such parameters, accounting for their uncertainty by considering all possible values they may take. Here we propose to incorporate this uncertainty into Bayesian segmentation methods in order to improve the inference process. In particular, we approximate the required marginalization over model parameters using computationally efficient Markov chain Monte Carlo techniques. We illustrate the proposed approach using a recently developed Bayesian method for the segmentation of hippocampal subfields in brain MRI scans, showing a significant improvement in an Alzheimer’s disease classification task. As an additional benefit, the technique also allows one to compute informative "error bars" on the volume estimates of individual structures.

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Is Synthesizing MRI Contrast Useful for Inter-modality Analysis?

Availability of multi-modal magnetic resonance imaging (MRI) databases opens up the opportunity to synthesize different MRI contrasts without actually acquiring the images. In theory such synthetic images have the potential to reduce the amount of acquisitions to perform certain analyses. However, to what extent they can substitute real acquisitions in the respective analyses is an open question. In this study, we used a synthesis method based on patch matching to test whether synthetic images can be useful in segmentation and inter-modality cross-subject registration of brain MRI. Thirty-nine T1 scans with 36 manually labeled structures of interest were used in the registration and segmentation of eight proton density (PD) scans, for which ground truth T1 data were also available. The results show that synthesized T1 contrast can considerably enhance the quality of non-linear registration compared with using the original PD data, and it is only marginally worse than using the original T1 scans. In segmentation, the relative improvement with respect to using the PD is smaller, but still statistically significant.

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On Feature Relevance in Image-Based Prediction Models: An Empirical Study

Determining disease-related variations of the anatomy and function is an important step in better understanding diseases and developing early diagnostic systems. In particular, image-based multivariate prediction models and the "relevant features" they produce are attracting attention from the community. In this article, we present an empirical study on the relevant features produced by two recently developed discriminative learning algorithms: neighborhood approximation forests (NAF) and the relevance voxel machine (RVoxM). Specifically, we examine whether the sets of features these methods produce are exhaustive; that is whether the features that are not marked as relevant carry disease-related information. We perform experiments on three different problems: image-based regression on a synthetic dataset for which the set of relevant features is known, regression of subject age as well as binary classification of Alzheimer’s Disease (AD) from brain Magnetic Resonance Imaging (MRI) data. Our experiments demonstrate that aging-related and AD-related variations are widespread and the initial sets of relevant features discovered by the methods are not exhaustive. Our findings show that by knocking-out features and re-training models, a much larger set of disease-related features can be identified.
Predicting the location of human perirhinal cortex, Brodmann's area 35, from MRI

The perirhinal cortex (Brodmann's area 35) is a multimodal area that is important for normal memory function. Specifically, perirhinal cortex is involved in the detection of novel objects and manifests neurofibrillary tangles in Alzheimer's disease very early in disease progression. We scanned ex vivo brain hemispheres at standard resolution (1mm×1mm×1mm) to construct pial/white matter surfaces in FreeSurfer and scanned again at high resolution (120μm×120μm×120μm) to determine cortical architectural boundaries. After labeling perirhinal area 35 in the high resolution images, we mapped the high resolution labels to the surface models to localize area 35 in fourteen cases. We validated the area boundaries determined using histological Nissl staining. To test the accuracy of the probabilistic mapping, we measured the Hausdorff distance between the predicted and true labels and found that the median Hausdorff distance was 4.0mm for the left hemispheres (n=7) and 3.2mm for the right hemispheres (n=7) across subjects. To show the utility of perirhinal localization, we mapped our labels to a subset of the Alzheimer's Disease Neuroimaging Initiative dataset and found decreased cortical thickness measures in mild cognitive impairment and Alzheimer's disease compared to controls in the predicted perirhinal area 35. Our ex vivo probabilistic mapping of the perirhinal cortex provides histologically validated, automated and accurate labeling of architectonic regions in the medial temporal lobe, and facilitates the analysis of atrophic changes in a large dataset for earlier detection and diagnosis.
The Improved Relevance Voxel Machine

The concept of sparse Bayesian learning has received much attention in the machine learning literature as a means of achieving parsimonious representations of features used in regression and classification. It is an important family of algorithms for sparse signal recovery and compressed sensing and enables basis selection from overcomplete dictionaries.

One of the trailblazers of Bayesian learning is MacKay who already worked on the topic in his PhD thesis in 1992 [1]. Later on Tipping and Bishop developed the concept of sparse Bayesian learning [2, 3] and Tipping published the Relevance Vector Machine (RVM) [4] in 2001. While the concept of RVM was intriguing, problems with the approach were the run time which is approximately cubic in the number of basis functions as well as the greedy optimization. Hence, different approaches to overcome these shortcomings were developed, e.g. [5] or [6] as well as Tipping himself in [7] (FastRVM).

Recently, Sabuncu and Van Leemput [8, 9] extended the relevance vector machine by incorporating an additional spatial regularization term in the Gaussian prior on the regression weights or classification features (RVoxM). RVoxM encourages spatial clustering of the relevance voxels and computes predictions as linear combinations of their content. While the model of RVoxM produced nice results on age regression data [8, 9], the algorithm used a simple fixed point optimization scheme, which is not guaranteed to decrease the cost function at every step and is computationally expensive. In addition, RVoxM prunes voxels from the regression model by applying an artificial numerical threshold to the weight hyperparameters and hence has a free parameter that influences model sparsity. Finally, RVoxM can only remove voxels from the model, but not reintroduce them later on. Hence in its current form it is reminiscent of a greedy forward feature selection algorithm.

In this report, we aim to solve the problems of the original RVoxM algorithm in the spirit of [7] (FastRVM). We call the new algorithm Improved Relevance Voxel Machine (IRVoxM). Our contributions are an improvement of the greedy optimization algorithm employed in RVoxM by exploiting the form of the marginal likelihood function and deriving an analytic expression for the optimal hyperparameter of each voxel, given the current hyperparameter of all other voxels. This enables us to maximize the marginal likelihood function in a principled and efficient manner. As a result IRVoxM optimizes the objective function better during training and the resulting models predict better on unseen cases. Finally, IRVoxM enables us to flexibly add and/or remove voxels during the optimization procedure.

A generative model for multi-atlas segmentation across modalities

Current label fusion methods enhance multi-atlas segmentation by locally weighting the contribution of the atlases according to their similarity to the target volume after registration. However, these methods cannot handle voxel intensity inconsistencies between the atlases and the target image, which limits their application across modalities or even across MRI datasets due to differences in image contrast. Here we present a generative model for multi-atlas image segmentation, which does not rely on the intensity of the training images. Instead, we exploit the consistency of voxel intensities within regions in the target volume and their relation to the propagated labels. This is formulated in a probabilistic framework, where the most likely segmentation is obtained with variational expectation maximization (EM). The approach is demonstrated in an experiment where $T_1$-weighted MRI atlases are used to segment proton-density (PD) weighted brain MRI scans, a scenario in which traditional weighting schemes cannot be used. Our method significantly improves the results provided by majority voting and STAPLE.
A generative model for probabilistic label fusion of multimodal data

The maturity of registration methods, in combination with the increasing processing power of computers, has made multi-atlas segmentation methods practical. The problem of merging the deformed label maps from the atlases is known as label fusion. Even though label fusion has been well studied for intramodality scenarios, it remains relatively unexplored when the nature of the target data is multimodal or when its modality is different from that of the atlases. In this paper, we review the literature on label fusion methods and also present an extension of our previously published algorithm to the general case in which the target data are multimodal. The method is based on a generative model that exploits the consistency of voxel intensities within the target scan based on the current estimate of the segmentation. Using brain MRI scans acquired with a multiecho FLASH sequence, we compare the method with majority voting, statistical-atlas-based segmentation, the popular package FreeSurfer and an adaptive local multi-atlas segmentation method. The results show that our approach produces highly accurate segmentations (Dice 86.3% across 22 brain structures of interest), outperforming the competing methods.

Differential correlation of amyloid binding with hippocampal subfield volume loss in cognitively normal participants

Background

Pathological examination has suggested early involvement of CA1 and CA2 in hippocampal cell loss and manual tracing in amnestic MCI has found volume loss at the CA1-CA2 boundary. With the recent development and validation of hippocampus subfield segmentation it is now possible to reliably analyze changes across populations and correlations with other biomarkers. Increased cortical amyloid binding is among the earliest changes in preclinical AD, preceding overall hippocampal atrophy. In this investigation we sought to determine whether hippocampal CA1 and CA2 subfield volume loss correlated with mean amyloid cortical binding potential (MCPB).

Methods

Cognitively normal participants (n = 46; 34 females (74%) were assessed with the clinical dementia rating (CDR) scale = 0 at the Washington University ADRC. Mean and (SD) for age and education were 63.8 (7.6) and 16.1 (2.6) respectively. MRI was performed on a 3T Siemens Trio system with 12-channel head coil; voxel size = 1x1x1 mm obtained sagitally;
Hippocampal subfield segmentation used Freesurfer pipeline (Martinos Center http://surfer.nmr.mgh.harvard.edu/) yielding 7 segments for both left and right hippocampus: CA1, CA2-3, CA4-DG, subiculum, presubiculum, fimbria and hippocampal fissure. Amyloid-β PET imaging was conducted following ≈ 12 mCi of [11C] PIB and 60 min dynamic PET scan in 3D mode (septa retracted). Mean cortical binding potential (MCBP) was determined as previously described.

Results
Pearson correlation revealed the following correlations and trends between MCBP (for amyloid) and hippocampal subvolumes: left CA2-3 r = -0.29 (P = 0.05); right CA2-3 r = -0.25 (P = 0.09); left CA1 r = -0.20 (P = 0.18); right CA1 r = -0.27 (P = 0.07). No other regional volumes were correlated with MCBP.

Conclusions
In this young healthy cognitively normal population there were trends towards the same pattern seen recently in an amnestic MCI population, with significantly smaller subfield volumes in CA 2-3 and subiculum compared with controls. In our study group only 8/46 participants had elevated MCBP (> 0.18 BP). We will extend our sample to a larger and older population, which can be expected to have higher numbers of participants with elevated amyloid.
The Relevance Voxel Machine (RVoxM): A Self-Tuning Bayesian Model for Informative Image-Based Prediction

This paper presents the relevance voxel machine (RVoxM), a dedicated Bayesian model for making predictions based on medical imaging data. In contrast to the generic machine learning algorithms that have often been used for this purpose, the method is designed to utilize a small number of spatially clustered sets of voxels that are particularly suited for clinical interpretation. RVoxM automatically tunes all its free parameters during the training phase, and offers the additional advantage of producing probabilistic prediction outcomes. We demonstrate RVoxM as a regression model by predicting age from volumetric gray matter segmentations, and as a classification model by distinguishing patients with Alzheimer's disease from healthy controls using surface-based cortical thickness data. Our results indicate that RVoxM yields biologically meaningful models, while providing state-of-the-art predictive accuracy.

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Organisations: Department of Informatics and Mathematical Modeling, Image Analysis and Computer Graphics, Massachusetts General Hospital
Contributors: Sabuncu, M. R., Van Leemput, K.
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A Generative Approach for Image-Based Modeling of Tumor Growth

Extensive imaging is routinely used in brain tumor patients to monitor the state of the disease and to evaluate therapeutic options. A large number of multi-modal and multi-temporal image volumes is acquired in standard clinical cases, requiring new approaches for comprehensive integration of information from different image sources and different time points. In this work we propose a joint generative model of tumor growth and of image observation that naturally handles multimodal and longitudinal data. We use the model for analyzing imaging data in patients with glioma. The tumor growth model is based on a reaction-diffusion framework. Model personalization relies only on a forward model for the growth process and on image likelihood. We take advantage of an adaptive sparse grid approximation for efficient inference via Markov Chain Monte Carlo sampling. The approach can be used for integrating information from different multi-modal imaging protocols and can easily be adapted to other tumor growth models.

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Organisations: Massachusetts Institute of Technology, University of Helsinki, Microsoft Research Cambridge, University Hospital Heidelberg, INRIA Sophia Antipolis
Mild Cognitive Impairment: Differential Atrophy in the Hippocampal Subfields

BACKGROUND AND PURPOSE: Hippocampus volumetry is a useful surrogate marker for the diagnosis of Alzheimer disease, but it seems insufficiently sensitive for the aMCI stage. We postulated that some hippocampus subfields are specifically atrophic in aMCI and that measuring hippocampus subfield volumes will improve sensitivity of MR imaging to detect aMCI. MATERIALS AND METHODS: We evaluated episodic memory and hippocampus subfield volume in 15 patients with aMCI and 15 matched controls. After segmentation of the whole hippocampus from clinical MR imaging, we applied a new computational method allowing fully automated segmentation of the hippocampus subfields. This method used a Bayesian modeling approach to infer segmentations from the imaging data. RESULTS: In comparison with controls, subiculum and CA2–3 were significantly atrophic in patients with aMCI, whereas total hippocampus volume and other subfields were not. Total hippocampus volume in controls was age-related, whereas episodic memory was the main explanatory variable for both the total hippocampus volume and the subfields that were atrophic in patients with aMCI. Segmenting subfields increases sensitivity to diagnose aMCI from 40% to 73%. CONCLUSIONS: Measuring CA2–3 and subiculum volumes allows a better detection of aMCI.
from structural brain MRI indicate that RVoxM yields biologically meaningful models that provide excellent predictive accuracy.

A generative model for brain tumor segmentation in multi-modal images
We introduce a generative probabilistic model for segmentation of tumors in multi-dimensional images. The model allows for different tumor boundaries in each channel, reflecting difference in tumor appearance across modalities. We augment a probabilistic atlas of healthy tissue priors with a latent atlas of the lesion and derive the estimation algorithm to extract tumor boundaries and the latent atlas from the image data. We present experiments on 25 glioma patient data sets, demonstrating significant improvement over the traditional multivariate tumor segmentation. © 2010 Springer-Verlag.

Association of intramyocellular, intraperitoneal and liver fat with glucose tolerance in severely obese adolescents
Objective
Impaired glucose tolerance (IGT) is common among obese adolescents. The aim of the present study was to investigate the association between glucose tolerance and intramyocellular, intra-abdominal and liver fat in adolescents presenting with early-onset severe obesity.

Design and methods
We studied 21 adolescents (mean age 13.5 years, range 11.5–15.9 years) referred to secondary care due to severe obesity (relative weight for height >+60% or body mass index >98th percentile for age and sex, before the age of 10 years) and their eight non-obese siblings (mean age 14.4 years, range 11.8–16.7 years). All subjects underwent oral glucose tolerance tests, followed by magnetic resonance spectroscopy (MRS) to measure the intramyocellular fat content in mainly oxidative soleus and mainly glycolytic tibialis anterior muscles. MRS was also used to measure liver fat. Abdominal fat (subcutaneous, intraperitoneal and retroperitoneal) was measured using MR imaging.

Results
Compared with their non-obese siblings, the obese adolescents had increased fat deposition in all anatomic locations studied. Eight obese adolescents had IGT, and they also had increased intramyocellular fat in the soleus (P=0.03) and increased intraperitoneal fat (P=0.04) compared with obese subjects with normal glucose tolerance (NGT). In contrast, no significant difference was seen between obese adolescents with NGT and IGT in liver fat (P=0.9) or intramyocellular fat in the tibialis anterior (P=0.13). In logistic regression analysis, increased soleus intramyocellular fat and intraperitoneal fat were significant predictors of IGT.

Conclusions
IGT in obese adolescents is associated with increased intramyocellular and intraperitoneal fat rather than liver fat.

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Cerebral measurements and their correlation with the onset age and the duration of opioid abuse
The total volume (GM + WM + CSF) of the cerebrum was significantly smaller in patients than in controls (Mann-Whitney U-test, p = 0.026) as well as the absolute volumes of GM and WM (p = 0.014 and p = 0.007, respectively). There was no significant difference in GM and WM volumes normalized with total cerebral volume. In contrast, the absolute volume of CSF did not significantly differ between the groups, but the relative volume of CSF was significantly higher in opioid dependents (p = 0.029). SFR and bifrontal ratio were larger in opioid dependents than in controls (p = 0.005 and p = 0.013). The SFR correlated negatively (p = 0.017, r = -0.569) and the area of vermis cerebelli correlated positively (p = 0.043, r = 0.496) with the onset age of opioid abuse. The length of opioid abuse and the area of vermis cerebellum had a negative correlation (p = 0.038, r = -0.523) even though the areas of cerebellar vermis did not significantly differ between opioid dependents and controls. The authors speculate that the onset of substance abuse in adolescence or early adulthood may have in part disturbed the late brain maturation process, as in normal development, the dorsolateral frontal cortex and superior parts of the temporal lobes are the last to maturate. Also, the cerebellar vermis may be affected by early onset substance abuse. It is possible that the brain is more vulnerable to substance abuse at a young age than later in life.

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Organisations: Helsinki University Central Hospital
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Segmentation of image ensembles via latent atlases

Spatial priors, such as probabilistic atlases, play an important role in MRI segmentation. However, the availability of comprehensive, reliable and suitable manual segmentations for atlas construction is limited. We therefore propose a method for joint segmentation of corresponding regions of interest in a collection of aligned images that does not require labeled training data. Instead, a latent atlas, initialized by at most a single manual segmentation, is inferred from the evolving segmentations of the ensemble. The algorithm is based on probabilistic principles but is solved using partial differential equations (PDEs) and energy minimization criteria. We evaluate the method on two datasets, segmenting subcortical and cortical structures in a multi-subject study and extracting brain tumors in a single-subject multi-modal longitudinal experiment. We compare the segmentation results to manual segmentations, when those exist, and to the results of a state-of-the-art atlas-based segmentation method. The quality of the results supports the latent atlas as a promising alternative when existing atlases are not compatible with the images to be segmented.

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Organisations: Massachusetts Institute of Technology
Contributors: Riklin-Raviv, T., Van Leemput, K., Menze, B. H., Wells, W. M. I., Golland, P.
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Asymmetric image-template registration

A natural requirement in pairwise image registration is that the resulting deformation is independent of the order of the images. This constraint is typically achieved via a symmetric cost function and has been shown to reduce the effects of local optima. Consequently, symmetric registration has been successfully applied to pairwise image registration as well as the spatial alignment of individual images with a template. However, recent work has shown that the relationship between an image and a template is fundamentally asymmetric. In this paper, we develop a method that reconciles the practical advantages of symmetric registration with the asymmetric nature of image-template registration by adding a simple correction factor to the symmetric cost function. We instantiate our model within a log-domain diffeomorphic registration
framework. Our experiments show exploiting the asymmetry in image-template registration improves alignment in the image coordinates. © 2009 Springer-Verlag.

Automated segmentation of hippocampal subfields from ultra-high resolution in vivo MRI
Recent developments in MRI data acquisition technology are starting to yield images that show anatomical features of the hippocampal formation at an unprecedented level of detail, providing the basis for hippocampal subfield measurement. However, a fundamental bottleneck in MRI studies of the hippocampus at the subfield level is that they currently depend on manual segmentation, a laborious process that severely limits the amount of data that can be analyzed. In this article, we present a computational method for segmenting the hippocampal subfields in ultra-high resolution MRI data in a fully automated fashion. Using Bayesian inference, we use a statistical model of image formation around the hippocampal area to obtain automated segmentations. We validate the proposed technique by comparing its segmentations to corresponding manual delineations in ultra-high resolution MRI scans of 10 individuals, and show that automated volume measurements of the larger subfields correlate well with manual volume estimates. Unlike manual segmentations, our automated technique is fully reproducible, and fast enough to enable routine analysis of the hippocampal subfields in large imaging studies. © 2009 Wiley-Liss, Inc.
Encoding Probabilistic Brain Atlases Using Bayesian Inference

This paper addresses the problem of creating probabilistic brain atlases from manually labeled training data. Probabilistic atlases are typically constructed by counting the relative frequency of occurrence of labels in corresponding locations across the training images. However, such an "averaging" approach generalizes poorly to unseen cases when the number of training images is limited, and provides no principled way of aligning the training datasets using deformable registration. In this paper, we generalize the generative image model implicitly underlying standard "averaging" atlases, using mesh-based representations endowed with an explicit deformation model. Bayesian inference is used to infer the optimal model parameters from the training data, leading to a simultaneous group-wise registration and atlas estimation scheme that encompasses standard averaging as a special case. We also use Bayesian inference to compare alternative atlas models in light of the training data, and show how this leads to a data compression problem that is intuitive to interpret and computationally feasible. Using this technique, we automatically determine the optimal amount of spatial blurring, the best deformation field flexibility, and the most compact mesh representation. We demonstrate, using 2-D training datasets, that the resulting models are better at capturing the structure in the training data than conventional probabilistic atlases. We also present experiments of the proposed atlas construction technique in 3-D, and show the resulting atlases' potential in fully-automated, pulse sequence-adaptive segmentation of 36 neuroanatomical structures in brain MRI scans.

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Joint segmentation of image ensembles via latent atlases
Spatial priors, such as probabilistic atlases, play an important role in MRI segmentation. However, the availability of comprehensive, reliable and suitable manual segmentations for atlas construction is limited. We therefore propose a joint segmentation of corresponding, aligned structures in the entire population that does not require a probability atlas. Instead, a latent atlas, initialized by a single manual segmentation, is inferred from the evolving segmentations of the ensemble. The proposed method is based on probabilistic principles but is solved using partial differential equations (PDEs) and energy minimization criteria. We evaluate the method by segmenting 50 brain MR volumes. Segmentation accuracy for cortical and subcortical structures approaches the quality of state-of-the-art atlas-based segmentation results, suggesting that the latent atlas method is a reasonable alternative when existing atlases are not compatible with the data to be processed. © 2009 Springer-Verlag.

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Contributors: Riklin Raviv, T., Van Leemput, K., Wells III, W. M., Golland, P.
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Nonparametric mixture models for supervised image parcellation

We present a nonparametric, probabilistic mixture model for the supervised parcellation of images. The proposed model yields segmentation algorithms conceptually similar to the recently developed label fusion methods, which register a new image with each training image separately. Segmentation is achieved via the fusion of transferred manual labels. We show that in our framework various settings of a model parameter yield algorithms that use image intensity information differently in determining the weight of a training subject during fusion. One particular setting computes a single, global weight per training subject, whereas another setting uses locally varying weights when fusing the training data. The proposed nonparametric parcellation approach capitalizes on recently developed fast and robust pairwise image alignment tools. The use of multiple registrations allows the algorithm to be robust to occasional registration failures. We report experiments on 39 volumetric brain MRI scans with expert manual labels for the white matter, cerebral cortex, ventricles and subcortical structures. The results demonstrate that the proposed nonparametric segmentation framework yields significantly better segmentation than state-of-the-art algorithms.

Predicting the location of entorhinal cortex from MRI

Entorhinal cortex (EC) is a medial temporal lobe area critical to memory formation and spatial navigation that is among the earliest parts of the brain affected by Alzheimer's disease (AD). Accurate localization of EC would thus greatly facilitate early detection and diagnosis of AD. In this study, we used ultra-high resolution ex vivo MRI to directly visualize the architectonic features that define EC rostrocaudally and mediolaterally, then applied surface-based registration techniques to quantify the variability of EC with respect to cortical geometry, and made predictions of its location on in vivo scans. The results indicate that EC can be localized quite accurately based on cortical folding patterns, within 3 mm in vivo, a significant step forward in our ability to detect the earliest effects of AD when clinical intervention is most likely to be effective.
Subjects With Intellectual Disability and Familial Need for Full-Time Special Education Show Regional Brain Alterations: A Voxel-Based Morphometry Study

Subjects attending full-time special education (SE) often have multifactorial background for their cognitive impairment, and brain MRI may show nonspecific changes. As voxel-based morphometry reveals regional volume differences, we applied this method to 119 subjects with cognitive impairments and familial need for full-time SE—graded into three levels from specific disorders of cognitive processes (level 1) to intellectual disability (IQ <70; level 3)—and to 43 age-matched controls attending mainstream education (level 0). Subjects in SE groups had smaller global brain white matter (WM), cerebrospinal fluid, and total brain volume than controls. Compared with controls, subjects with intellectual disabilities in SE level 3 showed greater regional gray matter volumes bilaterally in the ventral and dorsal anterior cingulate cortex and smaller regional gray matter volumes in the left thalamus and cerebellar hemisphere. Further, they had greater WM volume in the left frontoparietal region and smaller WM volumes in the posterior limbs of the internal capsules. Subjects in SE level 1 and 2 groups showed the same tendency, but the results were nonsignificant. In conclusion, compared with controls, subjects with intellectual disabilities showed in voxel-based morphometry analysis several regional brain alterations.
Supervised nonparametric image parcellation

Segmentation of medical images is commonly formulated as a supervised learning problem, where manually labeled training data are summarized using a parametric atlas. Summarizing the data alleviates the computational burden at the expense of possibly losing valuable information on inter-subject variability. This paper presents a novel framework for Supervised Nonparametric Image Parcellation (SNIP). SNIP models the intensity and label images as samples of a joint distribution estimated from the training data in a non-parametric fashion. By capitalizing on recently developed fast and robust pairwise image alignment tools, SNIP employs the entire training data to segment a new image via Expectation Maximization. The use of multiple registrations increases robustness to occasional registration failures. We report experiments on 39 volumetric brain MRI scans with manual labels for the white matter, cortex and subcortical structures. SNIP yields better segmentation than state-of-the-art algorithms in multiple regions of interest. © 2009 Springer-Verlag.

JNCL patients show marked brain volume alterations on longitudinal MRI in adolescence

Juvenile neuronal ceroid lipofuscinosis (JNCL, CLN3) is an inherited lysosomal disease. We used longitudinal MRI, for the first time, to evaluate the rate of brain volume alterations in JNCL. Six patients (mean ages of 12.4 years and 17.3 years) and 12 healthy controls were studied twice with 1.5 T MRI. White matter (WM), gray matter (GM) and CSF volumes were measured from the sets of T1-weighted 3-dimensional MR images using a fully automated image-processing procedure. The brain volume alterations were calculated as percentage change per year. The GM and whole brain volumes decreased and the CSF volume increased significantly more in the patients than in controls (p-values for the null hypothesis of equal means were 0.001, 0.004, and 0.005, respectively). We found no difference in the WM volume change between the populations. In patients, the GM volume decreased 2.4 % (SD 0.5 %, p = 0.0001 for the null hypothesis of zero mean change between observations), the whole brain volume decreased 1.1 % (SD 0.5 %, p = 0.003), and the CSF volume increased 2.7 % (SD 1.8 %, p = 0.01) per year. In normal controls, only the mean white matter volume was significantly altered (0.8 % increase, SD 0.7 %, and p = 0.001). We demonstrated by longitudinal MRI that the annual rate of the gray matter loss in adolescent JNCL patients is as high as 2.4 %.
Model-based segmentation of hippocampal subfields in ultra-high resolution in vivo MRI

Recent developments in MR data acquisition technology are starting to yield images that show anatomical features of the hippocampal formation at an unprecedented level of detail, providing the basis for hippocampal subfield measurement. Because of the role of the hippocampus in human memory and its implication in a variety of disorders and conditions, the ability to reliably and efficiently quantify its subfields through in vivo neuroimaging is of great interest to both basic neuroscience and clinical research. In this paper, we propose a fully-automated method for segmenting the hippocampal subfields in ultra-high resolution MRI data. Using a Bayesian approach, we build a computational model of how images around the hippocampal area are generated, and use this model to obtain automated segmentations. We validate the proposed technique by comparing our segmentation results with corresponding manual delineations in ultra-high resolution MRI scans of five individuals. © 2008 Springer-Verlag Berlin Heidelberg.

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Projects:

Prediction of tumor grade and tumor recurrence from multimodal imaging data
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Law, I., Supervisor
Van Leemput, K., Main Supervisor
01/10/2018 → 30/09/2021
Project: PhD

Computational Imaging Biomarkers of Multiple Sclerosis
Cerni, S., PhD Student, Department of Applied Mathematics and Computer Science
Van Leemput, K., Main Supervisor, Department of Applied Mathematics and Computer Science
Ribbens, A., Supervisor
Siebner, H. R., Supervisor
Marie Curie (EU-stipendium)
01/04/2018 → 31/03/2021
Award relations: Computational Imaging Biomarkers of Multiple Sclerosis
Project: PhD
New Multi-Modal Registration Methods: Application in Fetal Image Reconstruction
Engberg, A. M. E., PhD Student, Department of Mathematics
Van Leemput, K., Main Supervisor, Department of Applied Mathematics and Computer Science
Cuadra, M. B., Supervisor
Thiran, J., Supervisor
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01/11/2016 → 31/10/2019
Award relations: New Multi-Modal Registration Methods: Application in Fetal Image Reconstruction
Project: PhD

CT metal artifact reduction using MRI for radiotherapy
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Van Leemput, K., Main Supervisor, Department of Applied Mathematics and Computer Science
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Samfinansieret - Andet
01/02/2016 → 31/01/2019
Award relations: CT metal artifact reduction using MRI for radiotherapy
Project: PhD

Segmentation and Reconstruction of Multi-Phase Structures using the Derformable Simplicial Complex Method
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Bærentzen, J. A., Main Supervisor
Dahl, V. A., Supervisor
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01/11/2014 → 15/08/2018
Award relations: Segmentation and Reconstruction of Multi-Phase Structures using the Derformable Simplicial Complex Method
Project: PhD

Computational modeling of MR/PET in brain tumor patients for optimized radiation therapy planning
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Eksternt finansieret virksomhed
01/11/2013 → 14/06/2017
Award relations: Computational modeling of MR/PET in brain tumor patients for optimized radiation therapy planning
Project: PhD

Advanced Methods for Biological Shape Analysis
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01/07/2006 → 25/11/2009
Award relations: Advanced Methods for Biological Shape Analysis
Project: PhD
Computing pseudo-CT from MR: Towards MR-only based radiation therapy
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01/08/2013 → 12/12/2016
Award relations: Computing pseudo-CT from MR: Towards MR-only based radiation therapy
Project: PhD

A Neuroimaging study: Consequences of physical exercise on regional brain structure and connectivity in AD
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Award relations: A Neuroimaging study: Consequences of physical exercise on regional brain structure and connectivity in AD
Project: PhD

Computational Analysis of Brain Images: Towards a Useful Tool in Clinical Practice
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01/11/2012 → 24/02/2016
Award relations: Computational Analysis of Brain Images: Towards a Useful Tool in Clinical Practice
Project: PhD

Automated Image-Based Procedures for Radio-Therapy Treatment Evaluation and Daily Dose Re-Planning
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01/01/2010 → 22/11/2013
Award relations: Automated Image-Based Procedures for Radio-Therapy Treatment Evaluation and Daily Dose Re-Planning
Project: PhD