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High Resolution Depth-Resolved Imaging From Multi-Focal Images for Medical Ultrasound

Konstantinos Diamantis, Paul A. Dalgaro, Alan H. Greenaway, Tom Anderson, Jørgen Arendt Jensen and Vassilis Sboros

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

I. INTRODUCTION

In ultrasound, the spatial resolution of current imaging systems is determined by the diffraction limit, depending on the wavelength, the aperture size, and the duration of transmitted pulses [1], [2]. Higher resolution may be achieved with the use of shorter pulses, higher frequencies, or smaller transducer elements, but at the expense of beam penetration depth. High penetration depth, in the order of tens of centimeters, is usually desired to acquire images of most tissue structures. However, if increased resolution could be achieved, there are several cases mainly concerning microvascular diseases [3], where medical ultrasound could provide additional benefits. Nowadays, reaearch towards this direction is often combined with contrast microbubble utilization. With the aid of contrast agents [4] and the a priori knowledge of point source scatter, high resolution images of vascular structure have been obtained [5]–[7]. This was accomplished by applying effective aberration correction methods based on high accuracy position estimation of individual bubbles (2–3 µm diameter).

With those few exceptions, sub-diffraction imaging is still limited in medical ultrasound compared to optical microscopy [8], [9]. Methods like the Single Molecule Localization Microscopy [10] (SMLM) rely on an understanding of optical Point Spread Function (PSF) to achieve down to λ/10 optical resolution. Previous work [11] has used the image sharpness metric to extend SMLM to depth dimension. Image sharpness is a pixel-based measure of image quality, widely used in the past in astronomy for correction of distorted images [12]. This tool has been translated in biological microscopy for the depth estimation of fluorescent particles [13], [14]. The method makes use of multiplane microscopy, for example with a quadratic diffraction grating [15] and a maximum likelihood algorithm. Combined with the sharpness, this approach, provides an average of approximately 14 nm depth resolution when applied to images of unresolved targets that are not background limited (λ=532 nm). In this paper, the technique is introduced in ultrasound imaging and its feasibility is investigated with Field II [16], [17] simulated ultrasound data.

II. METHODS

A. Beamforming

Any commercial transducer can be used for the transmission of ultrasound, which is performed through single plane waves. All the transducer elements are used as both the transmitting and receiving aperture. The unfocused beams offer the advantage of covering the whole image region with only one emission, which allows for high frame rate and multiple acquisitions. After the transmission, the acquired data are stored and receive processing can be utilized to achieve multi-focal images. The transducer element signals can be beamformed offline in multiple ways. The common way to process the received responses is the Delay-And-Sum (DAS) beamformer [18]. The signals are time-delayed, weighted, and summed to form the maximized beamformer output, B(t), that for an array probe with M active elements in receive can be extracted by:

\[ B(t) = \sum_{m=0}^{M-1} w_m(t)x_m(t - \tau_m) = w(t)^H X(t), \]

where \( t \) is the time index, \( w(t) = [w_0(t), w_1(t), ..., w_{M-1}(t)]^H \) is the vector of the apodization weights, \( X(t) = [x_0(t - \tau_0), x_1(t - \tau_1), ..., x_{M-1}(t - \tau_{M-1})]^H \) is the array of the transducer element signals, and \( \tau_m \) is the time delay applied to...
the \( m \)th receiving element, based on its distance from the
focus point. (1) can be implemented separately for any \( \tau_m \),
thus focus in receive. Three different receive foci will result
in three different beamformer outputs that will subsequently
produce different, spatially distinct images of the same
object. A single point scatterer can now move across the
axial direction with a controlled step, and raw scatter data
for each position can be captured. The process is repeated
until the scatterer covers a distance of several millimeters.

**B. Receive Processing Algorithm**

Following similar strategy outlined in [13], for each
position and for each of the three acquired images the
normalized sharpness value is assessed. This metric shows
the degree of aberration on an image or region of an image,
but is dominated by defocus. Its main characteristic is that
it reaches its maximum value at minimum aberration [12].
Image sharpness is usually calculated as the name implies
from images pixel intensities. It is estimated by summing
the squared values of each pixel and is then normalized
by dividing by the squared sum of all pixel intensities.
However, since it is possible to access the data from which
an ultrasound image is formed, the calculation will be made
from the received signals instead. The image intensity is
generally proportional to the square of the signal amplitudes.
Therefore, the sharpness function is redefined by:

\[
S = \sum_{k}^{q} A_k^2 / (\sum_{k}^{q} A_k^2)^2 ,
\]

where \( S \) is the normalized sharpness, \( q \) is the number of raw
samples, and \( A_k \) is the amplitude value of the \( k \)th sample.
All sharpness values plotted together over the point total
displacement will then create three sharpness curves (\( S \)-
curves). One sharpness value from a single \( S \)-curve would
 correspond to two possible \( z \)-positions (Fig. 1). The objective
of the algorithm is to provide a unique estimate of each point
scatterer position. This estimate becomes unambiguous since
each position is characterized by three distinct sharpness
values. The accuracy of the estimation needs to be deter-
mined and extraction of an error is necessary, therefore the
whole procedure is repeated a number of times. Data from
all repetitive simulations are used for the estimation of the
probability density function (PDF), \( P(S_j|z) \), in other words,
the probability that a particular normalized sharpness value,
\( S_j \), will be measured from the raw data of a point source
located at depth \( z \), where \( j \) denotes the focus in receive. Since
the sharpness calculations for each receive focus, do not depend
on each other and with \( z \) being known, the probability
for the set of \( N \) sharpness measurements for all receive foci
when a particle is located at \( z \) can be written as:

\[
L(S_1, S_2, ..., S_N|z) = \prod_{j=1}^{N} P(S_j|z) ,
\]

where \( L \) is the likelihood for the set of sharpness measure-
ments \( S_1, S_2, ..., S_N \) and \( N \) is the number of the different
selected receive foci. The maximum likelihood estimator
(MLE) of the particle depth, \( z \), is the value of \( z \) for which
\( L \) is maximized given an actual dataset \( S_1, S_2, ..., S_N \) and
the calibration PDFs, \( P(S_j|z) \). For the PDF a Gamma distribution
has been selected as it fits best the Lorentzian shape of the \( S \-
curves as depicted in Fig. 1, and the behavior of the variance
on the measured sharpness (Fig. 2), and is given by:

\[
P(S_j|z) = \frac{e^\frac{-S_j}{\bar{S}_j}}{\bar{S}_j^{\alpha} \cdot \beta^{-\alpha} \cdot \Gamma(\alpha)} ,
\]

where \( \alpha = \tilde{S}_j / \sigma_j, \beta = \bar{S}_j / \tilde{S}_j(z), \tilde{S}_j(z) \) represents
the interpolated Lorentzian fit of the mean \( S \)-curve, \( \tilde{S}_j \) the
interpolated Lorentzian fit of the variance, both extracted by
the repetitive simulations, and \( \Gamma(\alpha) \) is the Gamma function.
The estimated depth position is finally compared with the actual
depth that is already known since the movement of the point
is determined by the simulation setup.

**C. Simulation Setup**

A phantom including a single point scatterer at a depth
of 40 mm, is created and used as a target to simulate the
optical particles. The phantom is scanned by single plane
wave emissions, made by a 7 MHz, 192 element, linear array
simulated transducer with \( \lambda \) spacing. The central transducer
element is located above the point target. The speed of sound,
\( c \) is set to 1540 m/s and all the parameters of the scan are
given in Table I. All simulations are carried out with Field
II [16], [17] software and Matlab scripts are utilized for the
data post-processing.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>SIMULATION SETUP PARAMETERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transducer</strong></td>
<td>Linear array</td>
</tr>
<tr>
<td>Transducer type</td>
<td>Linear array</td>
</tr>
<tr>
<td>Transducer element pitch</td>
<td>208 ( \mu )m</td>
</tr>
<tr>
<td>Transducer element kerf</td>
<td>35 ( \mu )m</td>
</tr>
<tr>
<td>Transducer element height</td>
<td>4.5 mm</td>
</tr>
<tr>
<td>Center frequency, ( f_0 )</td>
<td>7 MHz</td>
</tr>
<tr>
<td>Bandwidth</td>
<td>60% fractional</td>
</tr>
<tr>
<td>Speed of sound, ( c )</td>
<td>1540 m/s</td>
</tr>
<tr>
<td>Wavelength, ( \lambda = c/f_0 )</td>
<td>220 ( \mu )m</td>
</tr>
<tr>
<td>Excitation pulse</td>
<td>Two-cycle sinusoid at ( f_0 )</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plane Wave Emission</th>
<th>Hanning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmit apodization</td>
<td>Hanning</td>
</tr>
<tr>
<td>Receive focus depth</td>
<td>39/40/41 mm</td>
</tr>
<tr>
<td>Number of transmitting elements</td>
<td>192</td>
</tr>
<tr>
<td>Number of receiving elements, ( M )</td>
<td>192</td>
</tr>
<tr>
<td>Number of emissions</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Particle Movement</th>
<th>(x, z) = (0, 32.5) mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest point</td>
<td>(x, z) = (0, 47.5) mm</td>
</tr>
<tr>
<td>Lowest point</td>
<td>15 mm (axially only)</td>
</tr>
<tr>
<td>Total distance covered</td>
<td>0.1 mm</td>
</tr>
</tbody>
</table>

Raw data from a single unfocussed emission are acquired
from all 192 channels individually in receive. The data
are stored and then a new phantom is created, with the
point scatterer moved 100 \( \mu \)m with direction away from
the transducers surface until it reaches the depth of 47.5 mm.
The process is followed for the opposite direction as well, until
the point scatterer reaches a depth of 32.5 mm. Therefore, there are 151 acquisitions overall with the point target covering a distance of exactly 15 mm. For each acquisition the data are beamformed with three different foci in receive. The central receive focus has been selected at a depth of 40 mm, that is the target’s initial position and then the two other values are at −1 mm and +1 mm of the starting depth.

III. RESULTS

Using the parameters in Table I a set of three normalized sharpness values is calculated from each of the 151 acquired datasets, leading to the generation of three sharpness curves. The whole simulation is repeated 5 times. Field II would produce identical results from repetitive simulations, and to introduce a level of uncertainty, 10 dB white Gaussian noise has been added to the raw data. This way it is possible to extract the mean \( S \)-curves and their variance that are requisites for the MLE analysis. Mean and variance are shown in Fig. 1 and 2 respectively together with their Lorentzian fits for the case of receive focus at 40 mm. The mean \( S \)-curve presents a correlation coefficient of 0.99 with its Lorentzian fit, preserving the shape of the equivalent optical curves. The same value for the variance curve is significantly lower, at 0.78.

Both in optics and acoustics, sharpness metric changes in a similar manner when a single scatterer moves closer or away from focus. The sharpness variance demonstrates that with the addition of noise, Field II data from successive simulations are similar but not identical. In optics variance is higher around the \( S \)-curve peaks and lower away from them. This characteristic is preserved in ultrasonics as shown in Fig. 2. The Lorentzian fits of all \( S \)-curves and associated variance are then interpolated by a factor of 1000, using a Matlab spline interpolation function and are inserted to the selected PDF model. A set of three sharpness values as measured from one single acquisition are given as inputs to the algorithm, and the output is a prediction of depth position. This is the depth for which, the PDF presents its maximum value. Actual position of point target is known, as it is defined when creating the phantoms. Depth estimations for all 151 datasets, thus particle positions, are extracted and then compared with the ground truth. Since sharpness values are interpolated, the \( z \)-step is modulated accordingly and divided by 1000, taking the value of 0.1 \( \mu m \). The maximum of the PDF will correspond to a depth position of the updated depth vector using the new \( z \)-step. As a result, the error of the estimated depth will be assessed with a tenth of a micron accuracy.

In Fig. 3 the three mean \( S \)-curves are plotted over axial distance and the absolute difference can also be found between estimated and real point position, which shows the accuracy of the proposed method. There is a central region of approximately 4 mm (from 38 mm to 42 mm) where the localization error is on average, 28.6 \( \mu m \) (see arrowed region in Fig. 3b), which almost corresponds to a value one order of magnitude lower than the used wavelength. The average accuracy for the total distance of 15 mm should not be considered, as the algorithm does not provide accurate estimates around both ends of the target’s displacement.
Fig. 3 and particularly the uncertainty bar presents good resemblance with the optics analogue that appears in [13]. In the optics case, the average achieved accuracy also becomes higher around the crossover points of the S-curves. However, it reaches a value almost 40 times lower than the used wavelength, indicating a further improvement compared to the ultrasonics equivalent.

IV. DISCUSSION

A technique for improving the axial resolution of detection of point scatter using an ultrasound imaging method that is similar to those used clinically is suggested. Although, this is subject to further optimization, a localization error of an order of magnitude better than the wavelength was achieved, which is beyond the diffraction limit. The technique can be utilized directly with raw ultrasound data, and appears to be particularly suitable to the detection of single contrast microbubbles [5]–[7], which is a growing field of investigation.

In this example, the sharpness method performs best for a 4 mm region around the peak of the S-curves. This region is equal to 4 times the distance between two successive receive foci. At other parts of the S-curves there is no high difference between two neighbouring sharpness values, that is substantial for the method’s high performance. Further research is needed to determine the optimal parameters, such as focal depths and sampling, that will help optimize the localization error, which appears further improved in the optics analogue. To increase the high-resolution range and possibly at the same time, reduce the uncertainty of the estimates it may be necessary to increase the number of overlapping S-curves to cover axially a whole image. A single image, or signals dataset will then be characterized by a set of several sharpness values. This is straightforward in ultrasound imaging as the receive data can be beamformed accordingly. Therefore the number of S-curves that can be formed is practically unlimited. Importantly, in multipane microscopy this is more difficult to implement as light intensity per image plane drops. This fact is a significant advantage in the acoustics case, especially since the method is intended for real imaging.

On the other hand the Lorentzian fit may not be the optimal choice and the main source of error for the ultrasonics case. Unlike biological microscopy where the sharpness variance is calculated based on optical theory [13], the variance extracted from ultrasound data is only based on the addition of noise to the raw signals. The selection of the most appropriate fit needs to be reconsidered. All the above indicate that a calibration method needs to be generated in order to address the particle location. The validity of the technique needs to be evaluated with an experimental setup that matches the simulation in the first place, and next in real tissue environment where strong aberrations provide a variable and unpredictable point spread function.

V. CONCLUSION

Three or more simultaneous sharpness values can be extracted for each depth position of a moving target. Those values plotted together, form the sharpness curves from which a high accuracy estimate of all those positions can be extracted. This is the basis for the particle tracking technique in biological microscopy and analogous process can be reproduced for Field II simulated ultrasound data. The depth resolution achieved reaches 28.6 µm (0.13λ) for a 4 mm range of the total point displacement. The proposed method, translated from optics, presents encouraging results, but requires further investigation and experimental validation before being suitable for real-time applications.

REFERENCES