Acoustic attenuation imaging of tissue bulk properties with *a priori* information

Fong Ming Hooi, Oliver Kripfgans, and Paul L. Carson^{a)}

Department of Radiology, University of Michigan, Ann Arbor, Michigan 48109-5667, USA

(Received 24 September 2015; revised 24 July 2016; accepted 6 September 2016; published online 29 September 2016)

Attenuation of ultrasound waves traversing a medium is not only a result of absorption and scattering within a given tissue, but also of coherent scattering, including diffraction, refraction, and reflection of the acoustic wave at tissue boundaries. This leads to edge enhancement and other artifacts in most reconstruction algorithms, other than 3D wave migration with currently impractical implementations. The presented approach accounts for energy loss at tissue boundaries by normalizing data based on variable sound speed, and potential density, of the medium using a k-space wave solver. Coupled with *a priori* knowledge of major sound speed distributions, physical attenuation values within broad ranges, and the assumption of homogeneity within segmented regions, an attenuation image representative of region bulk properties is constructed by solving a penalized weighted least squares optimization problem. This is in contradistinction to absorption or to conventional attenuation coefficient based on overall insertion loss with strong dependence on sound speed and impedance mismatches at tissue boundaries. This imaged property will be referred to as the bulk attenuation coefficient. The algorithm is demonstrated on an opposed array setup, with mean-squared-error improvements from 0.6269 to 0.0424 (dB/cm/MHz)² for a cylindrical phantom, and 0.1622 to 0.0256 (dB/cm/MHz)² for a windowed phantom.

© 2016 Acoustical Society of America. [<http://dx.doi.org/10.1121/1.4962983>]

[GH]

Pages: 2113–2122

I. INTRODUCTION

Attenuation imaging quantifies the amplitude reduction of the ultrasound beam as the acoustic wave propagates through the medium.¹ A driving benefit of developing attenuation imaging of the breast is to improve the specificity and sensitivity in detecting and diagnosing breast lesions^{2–10} without cost in data acquisition time. In several studies of ultrasonic transmission tomography of breast cancer, the imaged attenuation coefficient has been a strong contributor, along with speed of sound, for the discrimination of breast cancer from benign lesions.^{6,7} A transmit-receive dataset can be obtained by transmitting with arrays of small elements and recording the radiofrequency (RF) channel data with a receiving array of small elements. Using the same dataset, traditional pulse echo, attenuation, and speed of sound images can be constructed simultaneously for multi-mode screening.^{11–13}

There are varied approaches to ultrasound attenuation tomography of the breast, encompassing different methods of processing attenuation information given the recorded RF signal.^{10,14–16} However, these methods produce attenuation coefficient images that are highly affected by signal losses due to diffraction at boundaries of high sound speed or acoustic impedance change. Like pulse echo imaging, which is highly sensitive to large boundaries, rather than bulk properties of the tissues, the images are highly edge enhanced. Attenuation imaging with arrays of modest total aperture, but phase sensitive elements of several wavelengths in at

least one dimension, are subject to phase cancellation effects and unmeasured signal loss due to scattered waves missing the transducers.

There have been several attempts to address refraction effects, accounting for attenuation due to traversed path-length¹⁵ and using an angular spectrum method¹⁶ that yield some improvements in reconstruction. If one could receive an estimate of all the scattered waves from small inhomogeneities within tissue of interest as well as the scatter from the tissue's boundaries, it would be possible to make an approximate image of the tissue's absorption coefficient. While full-wave inversions do address actual bulk attenuation, and even absorption, instead of simple insertion loss, these algorithms are heavily time and memory consuming,^{17–19} and are performed with the requisite 4π solid angle receiving apertures. Without two-dimensional (2D) arrays and 3D data, these algorithms do not correct for out-of-plane scattering components.

In this paper, we define the attenuation coefficient representative of the bulk properties of identified tissue regions in the breast, i.e., attenuation from local absorption and incoherent scattering of the ultrasonic energy, as the bulk attenuation coefficient μ_B . In Fig. 1(A), μ_B of the blue sphere, representing a region of different tissue properties compared to its background, would include attenuation of detected signals due to absorption of the wave along the red dotted paths as well as the scattering shown as red concentric rings. Waves due to diffraction at the boundary of the sphere, represented by the solid red lines and green concentric circles, often carry a large fraction of the incident energy and are often not detected by the receivers,

^{a)}Electronic mail: pcarson@umich.edu

FIG. 1. (Color online) (A) Waves due to diffraction at tissue boundaries carry a large fraction of incident energy, and are often not detected by receivers. This may affect proper convergence of inversion algorithms. (B) A more severe illustration of scattered energy out of the imaging plane is shown, especially when the imaging plane is not centered on the object.

preventing correct convergence of many inversion algorithms, which usually assume weak interactions. The problem is greatly exacerbated when the imaging plane is not bisecting the sphere, as illustrated in Fig. 1(B), where even more energy is scattered out of the imaging plane, giving less information to aid convergence of the reconstruction toward correct values of attenuation coefficient. With moderately large aperture, 2D arrays rotated fully around the breast and using 3D full-wave inversions,^{18,20,21} much improved sound speed images have been presented for image planes off the center of roughly spherical objects.^{21,22} The attenuation images should also be much improved, but the edges of a cancer or other sound speed objects different from surrounding breast tissues will still have highly enhanced attenuation at the object's boundary. That attenuation will depend on the properties of the surrounding tissue as well as those of the object. One would like an image of attenuation coefficient, μ_B , that is representative of object itself, not of its relative to its surroundings, which, in the breast, are highly variable.

μ_B can be obtained with minimal computation time by properly accounting for the complex wavefronts from the major object boundaries. Constructing a bulk attenuation coefficient map that is representative of the tissue, rather than of the tissue and its contrast with its background, may contribute more diagnostic information. An algorithm for attenuation image reconstruction is proposed where attenuation data are corrected using data from a forward model and a known, potentially 3D, sound speed distribution. Signal loss due to diffraction, coherent scattering and refraction at major tissue borders, without the losses due to bulk attenuation is accounted for in this model in order to compute the losses due to bulk attenuation, μ_B . To construct the attenuation image, a regularized least squares algorithm in weighted space is applied to a misfit function that allows inclusion of

a priori information on major structures in the breast, such as experimental noise and the size, shape, and expected range of attenuation values.

The method is demonstrated on phantoms with objects of cylindrical geometry along an axis normal to the image plane and of low sound speed compared to the background and imaged with a limited transducer aperture as motivated by our Breast Laser and Ultrasound Combined Imaging (BLUCI) system.²³ This system currently acquires B-mode images of the compressed breast in the mammographic geometry with opposed linear arrays. One transducer traverses the top of the compressed breast, while the other traverses the bottom. The algorithm is demonstrated using channel RF data obtained from a pair of commercial linear array transducers mimicking this configuration.

The methods presented here should work well with distinct boundaries in stacks of 2D images acquired with full circular apertures. Such speed of sound images, even from bent ray reconstructions, are often quite good and should work well with the approach proposed here. Speed of sound images with full-wave inversion algorithms should be considerably better, particularly in planes where normal to high contrast speed of sound boundaries are not completely in the image plane. In no case have we seen reconstruction of a bulk attenuation coefficient as defined here.

II. METHODS

The proposed attenuation algorithm depends on the availability of an initial velocity distribution to reconstruct the attenuation profile. This methods section will divide the algorithm into two phases: (1) initial velocity distribution reconstruction and (2) attenuation reconstruction.

While the velocity distribution can be obtained in various ways, this paper will first describe the major elements of a sound speed algorithm²⁴ based on a first-arrival flight-time method adapted from Tarantola,²⁵ since the mechanics of its reconstruction process will be similar to that of the proposed attenuation algorithm. The later section will build upon this first section and describe application to the attenuation algorithm.

A. Initial velocity distribution reconstruction

For sound speed reconstruction, the eikonal equation was chosen as the forward model

$$|\nabla\tau(\vec{x})| = n(\vec{x}), \quad (1)$$

where τ denotes the *eikonal*, n a propagation time-cost, and $\vec{x}$ a point in the propagation domain. In the acoustic context, the time-cost n is the *slowness* (inverse speed) s , and the eikonal is the minimum time required to travel from a source to a given point within the propagation domain.

By minimizing the proposed cost function,

$$2S(\vec{m}) = \|\vec{g}(\vec{m}) - \vec{d}\|_D^2 + \|\vec{m} - \vec{m}_a\|_M^2, \quad (2)$$

where $\vec{g}$ represents the forward operator which, acting on the slowness (inverse velocity) profile, $\vec{m}$, ($\vec{g}(\vec{m})$) yields

predicted flight-time data, $\vec{d}$ represents the measured or simulated flight-time data, and $\vec{m}_a$ is an *a priori* expectation of the profile $\vec{m}$, an estimate of the slowness contrast profile $\vec{m}$ can be obtained.

The cost function is comprised of a weighted data (first term) and model (second term) space, and can be written explicitly as such,

$$2S(\vec{m}) = (\vec{g}(\vec{m}) - \vec{d})^T C_D^{-1} (\vec{g}(\vec{m}) - \vec{d}) + (\vec{m} - \vec{m}_a)^T C_M^{-1} (\vec{m} - \vec{m}_a), \quad (3)$$

where C_D and C_M are the data and profile covariance matrices, respectively. Each covariance matrix allows for inclusion of *a priori* information in the reconstruction. The data covariance matrix (C_D) consists of observed variances of respective flight times (measurement error), while the model covariance matrix (C_M) adjusts for expected sound speed values.

The chosen cost function is predisposed to physically motivated regularization as the covariance matrices can constraint $\vec{m}$ about particular values through appropriate selection of expectation values ($\vec{m}_a$) and variances (diagonal of C_M). $\vec{m}$ can also be correlated with other elements through specification of their covariance (C_M), assigning small correlation coefficients amongst any probable contiguous pixels found from accompanying grayscale B-mode images. B-mode images can be generated using the same dataset for the sound speed reconstructions with a simple delay-and-sum algorithm. Similarly, measurement error can be accounted for in the diagonal of C_D . The construction of a covariance matrix follows the format,

$$C = \begin{pmatrix} \rho_{11}\sigma_1\sigma_1 & \rho_{12}\sigma_1\sigma_2 & \rho_{13}\sigma_1\sigma_3 & \dots \\ \rho_{21}\sigma_2\sigma_1 & \rho_{22}\sigma_2\sigma_2 & \rho_{23}\sigma_2\sigma_3 & \dots \\ \rho_{31}\sigma_3\sigma_1 & \rho_{32}\sigma_3\sigma_2 & \rho_{33}\sigma_3\sigma_3 & \dots \\ \dots & \dots & \dots & \dots \end{pmatrix}, \quad (4)$$

where ρ_{ij} is the correlation coefficient between the i th and j th vector element in $\vec{m}$, and σ_i is the standard deviation set for the i th element. Note that the correlation coefficients on the diagonal will always be equal to 1.

For each iteration, a linearized forward model is used for optimization of the cost function. The eikonal model outputs a time-of-flight map with the given source to receiver locations using the current velocity profile. The path length is then derived by tracing from the receiver in physical space, following the gradient of the flight-time map which provides a direction vector, until it reaches the source. This path length is generated for each transmit-receive pair to construct the path length matrix L , which will be later used in the attenuation reconstruction phase.

The cost function is minimized via nonlinear conjugate gradient updates, whose iterations stop when the problem reaches convergence. The stopping criterion is triggered when the fraction of residual error $|r_n|/|r_0|$ reaches a specified tolerance, where r_n is the residual error, defined as the sum of squared residuals between measured and predicted flight-time data from our forward model for all transmit-receive pairs, at the n th iteration.

For implementation purposes and memory planning, it is important to note that the size of each matrix is dependent on the number of transmitters N_t , receivers N_r , and pixels in the reconstructed image N_i . Measured data, d would correspond to a vector of size $N_t * N_r$, the sound speed profile m would correspond to a vector of size N_i , and the path length matrix L would correspond to be matrix of size $N_t * N_r$ by N_i . Accordingly, the covariance matrices would correspond to a matrix of size N_i by N_i ; however, the memory footprint of this matrix is deceptively large because it is not only sparse and symmetric, but storage of this entire matrix can be avoided in the context of the equation.

The reader is referred to our sound speed paper²⁴ for more specific details in implementation for sound speed images, in particular. Since the proposed attenuation algorithm is based on a similar mechanic, implementation is convenient when coupled with the aforementioned sound speed algorithm. However, it is important to note that the attenuation algorithm is not constrained to only use velocity images produced as such, and can use separately generated velocity distributions as an initial condition as well. If a velocity distribution is readily available, the velocity reconstruction phase can be mostly skipped. The attenuation reconstruction phase delineated in Sec. II B can be implemented independently after an accompanying path length matrix L is computed.

B. Attenuation reconstruction

The cost function for the attenuation algorithm is equivalent to that from the sound speed algorithm found in Eq. (3). For attenuation reconstruction, $\vec{g}$ represents the forward operator which, acting on the attenuation map $\vec{m}$, produces predicted attenuation data $\vec{g}(\vec{m})$, $\vec{d}$ represents the measured attenuation data, and $\vec{m}_a$ represents the *a priori* expectation of the profile $\vec{m}$.

The main differences between implementations for sound speed and attenuation reconstructions are highlighted as such; instead of travel time, which is used for sound speed reconstructions, the input to the algorithm is replaced with attenuation data derived from the raw RF data, in contrast to flight-time. Naturally, the attenuation algorithm also incorporates different physically driven *a priori* information, such as the expected data measurement error, incorporated into C_D , average attenuation, its variance, and probable contiguous locations, as extracted from grayscale B-mode and/or sound speed images, incorporated into C_M .

To derive the proper attenuation input for the algorithm, the complex signal energy ratio is first defined as follows for each recorded RF data line

$$E = \int_{t_1}^{t_2} |I(t)|^2 dt, \quad (5)$$

where t_1 is the first arrival time-of-flight selection, and $t_2 - t_1$ is the time window corresponding to the length of the acoustic pulse. $I(t)$ represents the amplitude envelope of the signal, calculated using the absolute value of the Hilbert transform of the signal.

Attenuation is typically defined as

$$\int_{\text{ray}} a_0 dl = \log_{10} \frac{E_w}{E_o} = C, \quad (6)$$

where W represents water shot data and O represents object shot data. Computing tissue attenuation using a direct ratio of the water shot and the medium shot is insufficient due to the complex beam path of the acoustic wavefront. This direct computation relies on the assumption that the signal is only attenuated by its path through tissue and all remaining energy is collected at the receiver; however, energy is additionally lost to interactions between the acoustic wave front and the medium, including diffraction, refraction, and scattering at major boundaries.

In the presented algorithm, the E_w/E_o term will be normalized by computing lost energy not attributed to energy loss within the bulk tissues of the major structures. Let the corrected energy of the measured object shot $E_o^{m'}$ be defined as

$$E_o^{m'} = AE_o^m, \quad (7)$$

where A is a correction factor that is obtained via the energy ratio found with simulated data,

$$A = \frac{E_w^s}{E_o^s}. \quad (8)$$

The updated numerator in Eq. (6) follows:

$$\log_{10} \frac{E_w^m}{E_o^{m'}} = \log_{10} \frac{E_w^m}{E_o^m} \left(\frac{E_w^s}{E_o^s} \right)^{-1}. \quad (9)$$

If the terms within the log reduce to 1, the attenuation is thereby 0 for that ray as expected. No energy variation between the water shot and the object shot effectively means there is no attenuation. The correction factor will be obtained via a full wave forward model given the sound speed map, which will be described further below.

1. Covariance matrices

The choice of σ_d for C_D , the data covariance matrix, corresponds to the maximum expected error in the data. This error depends on system setup and should be calibrated accordingly. For our experimental setup [Fig. 2(A)], expected noise level is gathered from energy calculations pertaining to water traversing rays, coinciding with edges of each dataset of our phantom setup. σ_d is defined as

$$\sigma_d = |\log_{10}(1 + dE)|, \quad (10)$$

where dE is the max variation found in the energy ratio between simulated and experimental data. For C_M , the model covariance matrix, σ_m is initialized to the maximum expected integrated attenuation in the current reconstruction. Although the reconstructed attenuation values are not strictly Gaussian, as they should never be negative, the algorithm will still converge.²⁶

FIG. 2. (Color online) (A) Transducer locations for simulation and experimental setup. Transmitter and receiver arrays mimic data acquisition of a compressed breast. (B) For experimental data, the speed of sound distribution generated from the same RF dataset used for attenuation imaging is shown for the cylindrical phantom. The map is not a perfect representation of the imaged object, as it shows minimal artifacts in the axial direction due to a limited aperture (vs. complete ring aperture encompassing all viewing angles).

2. Experimental dataset

Attenuation data are acquired experimentally using two linear arrays (L7-4, Philips/ATL, Bothell, WA) mounted opposing each other in a water tank. These arrays are connected to a research ultrasound imaging system (Verasonics, Kirkland, WA) which allows for independent channel and element control for data acquisitions (Fig. 3). The arrays are comprised of 128 elements of 300- μm elements, which at a distance of 5–6 cm allows geometrically for approximately a 30° acceptance angle.

Data are acquired at a center frequency of 3.75 MHz. For each reconstruction, two data acquisitions are obtained: a water shot for system calibration, and an object shot with a phantom made of worm rubber (MF Plastics, Ft. Worth, TX). Each transmitting element is fired once and recorded on all elements of the receiving transducer for a full RF dataset of 128×128 traces. Two different phantom shapes were examined, a 12.5 mm diameter cylindrical phantom to illustrate large refraction artifacts, and a windowed phantom to simulate smaller inclusions (pictured in Fig. 3). The worm rubber

FIG. 3. (Color online) Experimental setup using two linear arrays. The object is placed in between both transducers and the tank is filled with water for data acquisition. This figure shows a close-up picture of the windowed rubber phantom.

phantoms were placed approximately in the center between the two transducers, and had a measured sound speed of 1406 m/s and an attenuation coefficient of 3.2 dB/cm/MHz.

3. Normalizing dataset

To model ultrasound wave propagation and scattering for normalization, the k-wave MATLAB toolbox is used. The algorithm is based on a spectral method which utilizes a perfectly matched layer (PML) as a boundary condition to decrease computation time and storage cost.²⁷

Each transducer element is modeled with an effective element width of 400 μm , slightly larger than the actual width. The source signal is generated empirically using averaged traces recorded from the water shot dataset. The signal is then filtered and smoothed to minimize undesirable transients in the wave computation. The correction factor is computed using the signal computed for each receiver with and without the object in accordance to Eq. (8).

4. Reconstruction method

The traversed ray paths can be obtained by using the eikonal forward model as described in Sec. II A. The derived path length matrix, L , is used to compute $g(\vec{m})$, the forward model of the cost function, approximated as $L\vec{m}$. The cost function in Eq. (2) is minimized similarly to the sound speed reconstructions using nonlinear conjugate gradient updates to obtain an attenuation contrast profile.

Imaging with a limited aperture without spatial regularization results in a large smearing artifact as depicted in our sound speed reconstructions.²⁴ To minimize the effects of limited aperture inversion, local contiguous pixels within the object location are correlated with a coefficient of 0.003 to reduce the smearing artifact, which is specified in C_M , the model covariance matrix. The mean attenuation of each phantom is then calculated over the region of interest (ROI) by averaging a region of 10 by 10 pixels within the center of the phantom. Our reconstruction image was 4.25 cm $\times$ 5.31 cm with square pixels of 75 μm $\times$ 75 μm .

III. RESULTS

A representative image depicting the experimental data and the simulated, normalizing dataset of the cylinder is shown in Fig. 4. RF data recorded when transmitting with the 64th element is shown for both the water and object shots. The experimental and simulated object shots show similar refraction effects, with bands outside the center portion (corresponding to the beam traveling by the edge of the cylinder) depicting large dips in amplitude. There is additional ringing noted in the experimental data, but since the overall energy is small, there is minimal effect when calculating the normalization factor.

The energy ratio profiles for the 64th and 128th transmitting element is shown as well (Fig. 4). The dips in energy in experimental data closely aligns with those from simulation with discrepancies in amplitude. Theoretically, this amplitude discrepancy corresponds to the bulk attenuation of the medium. To quantify this difference, the energy ratios

FIG. 4. (Color online) (A) RF data recorded when transmitting with the 64th element. The experimental and simulated shots show similar refraction effects. (B) The energy ratio is computed for attenuation reconstruction, with the profile for the 64th and 128th transmitting element shown.

are used to compute the correction factor for attenuation in accordance to Eq. (9). Without proper correction, the reconstructed attenuation image would be distorted, especially emphasized while using a limited aperture like that in our BLUCI system.

The matrix of integrated attenuation values for the cylinder are shown in Fig. 5. The x axis corresponds to the receiving element, while the y axis corresponds to the transmitting element. At the index of (64, 64), for example, the plotted data represents the integrated attenuation recorded when transmitting from the 64th element of the transmitter and recording at the 64th element of the receiver.

In the uncorrected dataset, shown in the top row, there are large energy bands recorded corresponding to the edge of the cylinder. These bands are attributed to the impedance

FIG. 5. (Color online) (Top) Uncorrected experimental dataset consisting of an object shot of a cylindrical phantom as described in Sec. II B 2. (Bottom) Corrected dataset result after applying Eq. (8) to the experimental dataset from the top figure.

and speed of sound change at the object's border. Using the energy ratio of simulated data, the attenuation data are corrected to account for this effect, and is shown in the bottom row. The resulting dataset yields a higher attenuation where the beams traverse the center of the cylinder, while largely decreasing the high energy bands that resulted from diffraction at the cylinder's edges.

The resulting attenuation image of the cylinder using a weighted least squares model with *a priori* information is depicted for the uncorrected and corrected dataset in Fig. 6. The cylinder is recovered properly with a corrected dataset at an average of 3.25 dB/cm/MHz; when uncorrected, the resulting image shows attenuation only at the edges of the contrasting cylinder. The mean-squared-error (MSE) for the uncorrected and corrected reconstruction was calculated to

FIG. 6. (Top) Reconstructed attenuation image of the uncorrected dataset for the cylindrical phantom. (Bottom) Reconstructed attenuation image for the corrected dataset. Results are in dB/cm/MHz.

be 0.6269 and 0.0424 (dB/cm/MHz)², respectively. We should note that the effect is drastic and highly emphasized due to the limited aperture setup of our transducers and the size of the phantom in comparison to the aperture.

Similarly, the corrected and uncorrected dataset for the window phantom is depicted in Fig. 7, and the reconstruction in Fig. 8 is shown with an average of 3.02 and 2.96 dB/cm/MHz within the ROI of the windowed phantom, from left to right. The MSE for the uncorrected and corrected reconstruction was calculated to be 0.1622 and 0.0256 (dB/cm/MHz)², respectively. Uncorrected refraction artifacts result in slightly enhanced borders of the phantom and subsequently a lower attenuation value, most notable in the left region of the window with a darker middle region. This effect is less pronounced on the windowed phantom due to the effective

FIG. 7. (Color online) (Top) uncorrected experimental dataset consisting of an object shot of a windowed phantom as described Sec. II B 2. (Bottom) Corrected dataset result after applying Eq. (8) to the experimental dataset from the top figure.

size of the contrast, with refraction effects being milder than that on the cylindrical phantom. The average attenuation using the uncorrected dataset was 0.48 and 0.99 dB/cm/MHz for the left and right regions, respectively.

IV. DISCUSSION

A strong motivation behind the proposed algorithm is to develop a method that can produce reasonable attenuation images with a limited angle dataset as acquired by our BLUCI system, similar to that of limited angle tomography. With limited angle tomography, reflection and refraction phenomena not only present themselves as highly edge enhancing artifacts, but can sometimes result in the wavefront missing the receiving transducers and the object no longer being resolved.

FIG. 8. (Top) Reconstructed attenuation image of the uncorrected dataset for the windowed phantom. (Bottom) Reconstructed attenuation image for the corrected dataset. Results are in dB/cm/MHz.

There are several advantages to imaging the breast in the mammographic geometry. The overall tissue thickness is reduced and thus the imaging depth, compared with that of the uncompressed breast. This enables B-mode imaging with a higher center frequency for increased resolution and soft tissue contrast without excessive signal attenuation. In comparison to a free-floating breast, the reduced thickness and the flattening of some structures decreases the amount of complex acoustic interaction such as refraction and internal reflection.^{28,29} This acquisition mode will also enable co-registration with other modalities including mammography,^{30–34} tomosynthesis,^{35–37} and photoacoustics^{38–40} for improved breast cancer screening.

The proposed algorithm requires an initial assumed velocity distribution. The formation of the attenuation image is reliant on the speed of sound reconstruction for two

reasons: (1) the sound speed reconstruction algorithm provides the path length matrix used in the attenuation inverse problem and most importantly, (2) the sound speed map enables computation of the appropriate normalization accounting for much of the extraneous energy loss. A dataset without bulk attenuation that encompasses complex wave migration due to sound speed is first generated. The simulated dataset containing detected signal attenuation due to only sound speed variations is compared to the recorded experimental dataset, comprised of attenuation due to sound speed variations and medium bulk properties, to obtain a signal energy ratio (Fig. 4). The attenuation inversion is then performed on a normalized dataset using this ratio to generate the bulk attenuation of the medium. Since the reflections at boundaries are actually a function of the acoustic impedances, these calculations could be improved by accounting for the estimated characteristic specific acoustic impedance, $Z_0 = \rho c$. Even in the ray tracing algorithm employed here, the density can be estimated from the speed of sound because the density of breast tissues track linearly with speed of sound.⁴¹

The normalization of attenuation data used energy computations in place of amplitude to decrease the impact of noise and increase robustness of the algorithm. Also, normalizing with a background-object ratio accounts for possible errors that may occur in the forward model that appear in both background and object simulations, including but not limited to receive element sensitivity and numerical artifacts.

The normalized dataset contains some noise, mostly corresponding to edges of the diffracted wavefront (Fig. 5). The algorithm does not aim for a perfect correction since multiple sources of errors may exist; for example, the reconstructed sound speed map may deviate slightly from the true velocity distribution, resulting in an imperfect match with the forward model. Since the modeled wave field is not used directly in the inversion algorithm, but rather as a metric to normalize attenuation data, the field information is sufficiently accurate for our purposes as long as the sound speed reconstruction is successful. Similar to our sound speed reconstructions, the predicted data $\vec{g}(\vec{m})$ and model parameter $\vec{m}$ can be interpreted as jointly Gaussian random variables. The proposed cost function thus allows for some flexibility with both data prediction and measurement via proper specification of the data covariance matrix.

Without proper correction, the resulting attenuation images were highly edge enhanced, especially with the cylinder phantom (Fig. 6). This effect was most pronounced in this experiment because the size and sound speed of the phantom produced a large amount of diffraction and signal loss at large boundaries, in addition to missing viewing angles using a limited aperture. The window phantom exhibited similar characteristics, but was less dramatic due to the size of the strand.

The proposed algorithm is largely based on utilizing known *a priori* information in context of the given cost function. There are several layers of information, with the most crucial being the availability of an accurate sound speed image as it provides the correction factor needed to reduce

edge enhancement of highly attenuative lesions. We are in the early stages of investigating speed of sound imaging with this highly limited angle tomography in order to allow transmission ultrasound imaging in a system that could be combined with digital breast tomosynthesis (DBT). The fidelity of the speed of sound images in complex breasts might be improved by iterative use of segmentation of the reflection and speed of sound images to correct the DBT.³⁷ These DBT images might then be used to correct errors in the speed of sound images because of the approximately linear relationship between density from x rays and speed of sound of breast and other soft tissues.^{41,42} Cross modality segmentation also offers promise.⁴³ As noted, the methods should work well with data from full, circular, cylindrical or spherical apertures. Other *a priori* information include expected values and variances in both the data and model spaces, which are physically motivated and can be extracted from each setup. With the above alone, the discussed algorithm can be applied to general transducer setups with adequate transmitters and receivers.

In regards to the BLUCI setup where data are acquired in a limited aperture setting, the ability to incorporate extra *a priori* information of probable contiguous pixels is necessary in aiding convergence to an accurate value. Garnering detailed *a priori* information from a complex phantom, or actual tissue, will be more challenging. We should note that there is no need to set each pixel to belong to a contiguous region, just that the option is available if a region of pixels is known to be contiguous. For example, pixels attributed to the background regions such as water or gel interfaces would be ideal candidates. Additional investigation will be needed to properly segment the more complex B-mode breast images, and also analyze possible optimal settings when only a few homogenous regions can be identified.

The imaged phantoms were chosen to be relatively simple and symmetric in 3D to demonstrate the working algorithm with reasonable computation times of the normalizing dataset in 2D. To image more complex phantoms and eventually patients, diffraction resulting in energy loss in the elevation dimension need to be considered. The algorithm would follow a similar process as demonstrated in this paper, except with added computation time resulting from modeling a 3D object for normalization. It is important to note that while the overall computational cost of the proposed algorithm is less than a traditional full-wave method, a successful 3D implementation will require the fundamental capability to perform a full-wave 3D simulation. Traditional limitations of 3D modeling include memory constraints of the reconstruction grid, which in turn affect possible frequency choices, and large reduction in computation speed. This modeling will account for energy lost out of the imaging plane, essential for reconstructing accurate attenuation images of objects like those in the human breast that may be subject to significant out-of-plane scattering.

Computation can be made relatively efficient since the problem lends itself to parallelization by dividing the computation tasks based on transmitters. Current rendition of the code is written in MATLAB, and generating the normalizing field on a 4-core 2.93 GHz i7 940 processor took approximately 1.5 min

for each transmit. Sound speed reconstructions were performed on dual 6-core 3.33 GHz Intel Xeon X5680 processors with each iteration taking approximately 3 min. The number of iterations required for convergence depends on the complexity of the imaged object, with the included phantoms taking approximately five iterations. We should note that the reconstruction code is not heavily optimized; for improved speed, the reconstruction code can be ported to more suitable scientific computing languages such as Fortran or C, implemented in a more parallel manner, and also take advantage of recent advancements in graphics processing unit accelerated computing.

Imaging of the compressed breast, versus an uncompressed breast, also decreases the size of the computational domain, easing computation storage and time if one does not take advantage of the ability to increase the ultrasound frequency. Furthermore, the normalizing field, representing the bulk of the computation time, need only be calculated once and does not require iterations. In contrast to full wave inversions, this problem is more tractable and practical as far as computation cost; this method also bypasses the necessity of difficult, full transducer characterization.⁴⁴

V. CONCLUSION

Generating attenuation images indicative of the bulk properties of the medium may be highly beneficial for screening and other medical imaging purposes, decreasing the extent of edge enhanced images to further increase sensitivity and specificity of breast cancer diagnosis. The proposed algorithm suggests improved attenuation reconstructions by focusing on the bulk attenuation coefficient of the medium instead of overall insertion loss, and may alter the interpretation of attenuation images in breast cancer imaging. Future work will include demonstrating the algorithm on more complex phantoms and patients that will require normalization based on 3D models. The extension to 3D should not be too difficult as a 3D stack of 2D speed of sound images is usually acquired in both full and limited angle transmission tomography systems.

ACKNOWLEDGMENTS

This work was supported in part by Grant Nos. NIH BRP 2R01 CA91713, NIH BRP 1R01 CA115267, and NSF CBET 0756338. We wish to thank Mark Haynes and Sacha Verweij for their insight and help in algorithm implementation.

- ¹R. Chivers and C. Hill, "Ultrasonic attenuation in human tissue," *Ultrasound Med. Biol.* **2**, 25–29 (1975).
- ²G. H. Glover, "Computerized time-of-flight ultrasonic tomography for breast examination," *Ultrasound Med. Biol.* **3**, 117–127 (1977).
- ³J. F. Greenleaf, S. A. Johnson, and A. H. Lent, "Measurement of spatial distribution of refractive index in tissues by ultrasonic computer assisted tomography," *Ultrasound Med. Biol.* **3**, 327–339 (1978).
- ⁴J. F. Greenleaf and R. C. Bahn, "Clinical imaging with transmissive ultrasonic computerized tomography," *IEEE Trans. Bio. Med. Eng. BME-28*, 177–185 (1981).
- ⁵A. L. Scherzinger, R. A. Belgam, P. L. Carson, C. R. Meyer, J. V. Sutherland, F. L. Bookstein, and T. M. Silver, "Assessment of ultrasonic computed tomography in symptomatic breast patients by discriminant analysis," *Ultrasound Med. Biol.* **15**, 21–28 (1989).
- ⁶M. P. André, C. H. Barker, N. Sekhon, J. Wiskin, D. Borup, and K. Callahan, "Pre-clinical experience with full-wave inverse-scattering for breast imaging acoustical imaging," in *Acoustical Imaging*, edited by I.

- Akiyama (Springer, Dordrecht, the Netherlands, 2009), Vol. 29, Chap. 10, pp. 73–80.
- ⁷N. Duric, P. Littrup, E. West, B. Ranger, C. Li, and S. Schmidt, "In-vivo imaging of breast cancer with ultrasound tomography: Probing the tumor environment," *Proc. SPIE* **7968**, 796–812 (2011).
- ⁸S. A. Johnson, T. Abbott, R. Bell, M. Berggren, D. Borup, D. Robinson, J. Wiskin, S. Olsen, and B. Hanover, "Non-invasive breast tissue characterization using ultrasound speed and attenuation acoustical imaging," in *Acoustical Imaging*, edited by M. P. André (Springer, Dordrecht, the Netherlands, 2007), Vol. 28, Chap. 17, pp. 147–154.
- ⁹A. C. Kak and K. A. Dines, "Signal processing of broadband pulsed ultrasound: Measurement of attenuation of soft biological tissues," *IEEE Trans. Bio. Med. Eng. BME-25*, 321–344 (1978).
- ¹⁰C. Li, N. Duric, and L. Huang, "Breast imaging using transmission ultrasound: Reconstructing tissue parameters of sound speed and attenuation," in *Proceedings of the 2008 International Conference on BioMedical Engineering and Informatics* (2008), Vol. 2, pp. 708–712.
- ¹¹N. Duric, C. Li, P. Littrup, C. Glide-Hurst, L. Huang, J. Lupinacci, S. Schmidt, O. Rama, L. Bey-Knight, and Y. Xu, "Multi-modal breast imaging with ultrasound tomography," *Proc. SPIE* **6920**, 692000 (2008).
- ¹²J. S. Schreiman, J. J. Gisvold, J. F. Greenleaf, and R. C. Bahn, "Ultrasound transmission computed tomography of the breast," *Radiology* **150**, 523–530 (1984).
- ¹³P. L. Carson, C. R. Meyer, A. L. Scherzinger, and T. V. Oughton, "Breast imaging in coronal planes with simultaneous pulse echo and transmission ultrasound," *Science* **214**, 1141–1143 (1981).
- ¹⁴R. Jirik, R. Stotzka, and T. Takt, "Ultrasonic attenuation tomography based on log-spectrum analysis," *Proc. SPIE* **5750**, 305–314 (2005).
- ¹⁵S. Li, M. Jackowski, D. P. Dione, T. Varslot, L. H. Staib, and K. Mueller, "Refraction corrected transmission ultrasound computed tomography for application in breast imaging," *Med. Phys.* **37**, 2233–2246 (2010).
- ¹⁶S.-W. Huang and P.-C. Li, "Ultrasonic computed tomography reconstruction of the attenuation coefficient using a linear array," *IEEE Trans. Ultrason. Ferr.* **52**, 2011–2022 (2005).
- ¹⁷K. K. Shung, *Ultrasonic Scattering in Biological Tissues* (CRC Press, Boca Raton, FL, 1992), pp. 2–290.
- ¹⁸J. Wiskin, D. T. Borup, q S. A. Johnson, M. Berggren, T. Abbott, and R. Hanover, "Full-wave, non-linear, inverse scattering acoustical imaging," in *Acoustical Imaging*, edited by M. P. André (Springer, Dordrecht, the Netherlands, 2007), Vol. 28, Chap. 20, pp. 183–193.
- ¹⁹R. G. Pratt, L. Huang, N. Duric, and P. Littrup, "Sound-speed and attenuation imaging of breast tissue using waveform tomography of transmission ultrasound data," *Proc. SPIE* **6510**, 65104S (2007).
- ²⁰J. Wiskin, D. Borup, S. Johnson, M. Andre, J. Greenleaf, Y. Parisky, and J. Klock, "Three-dimensional nonlinear inverse scattering: Quantitative transmission algorithms, refraction corrected reflection, scanner design and clinical results," *Proc. Meet. Acoust.* **19**, 075001 (2013).
- ²¹J. Wiskin, "Three-dimensional full-wave nonlinear inverse scattering: Applications to high-resolution breast imaging and quantitative results," in *AIUM Convention* (2016).
- ²²M. Andre, J. Wiskin, D. Borup, S. Johnson, H. Ojeda-Fournier, and L. Olson, "Quantitative volumetric breast imaging with 3D inverse scatter computed tomography," in *2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society* (2012), pp. 1110–1113.
- ²³P. L. Carson, F. Zafar, S. A. Verweij, M. M. Goodsitt, G. L. LeCarpentier, S. Sinha, F. Hooi, M. Roubidoux, and J. B. Fowlkes, "Dual sided automated ultrasound system in the mammographic geometry," in *2011 IEEE International Ultrasonics Symposium* (2011), pp. 2134–2137.
- ²⁴F. Hooi and P. Carson, "First-arrival traveltimes sound speed inversion with a priori information," *Med. Phys.* **41**, 082902 (2014).
- ²⁵A. Tarantola, *Inverse Problem Theory and Methods for Model Parameter Estimation* (Siam, Philadelphia, PA, 2005), pp. 342.
- ²⁶M. Haynes and M. Moghaddam, "large domain, low-contrast acoustic inverse scattering for ultrasound breast imaging," *IEEE Trans. Bio. Med. Eng.* **57**, 2712–2722 (2010).
- ²⁷B. T. Cox, S. Kara, S. R. Arridge, and P. C. Beard, "K-space propagation models for acoustically heterogeneous media: Application to biomedical photoacoustics," *J. Acoust. Soc. Am.* **121**, 3453–3464 (2007).
- ²⁸O. M. Bucci, N. Cardace, L. Crocco, and T. Isernia, "Degree of nonlinearity and a new solution procedure in scalar two-dimensional inverse scattering problems," *J. Opt. Soc. Am. A* **18**, 1832–1843 (2001).
- ²⁹P. L. Carson, B. Wang, G. L. LeCarpentier, M. M. Goodsitt, C. Lashbrook, R. Pinsky, G. Narayanasamy, J. B. Fowlkes, and K. Saitou,

- "Local compression in automated breast ultrasound in the mammographic geometry," in *2010 IEEE International Ultrasonics Symposium* (2010), pp. 1787–1790.
- ³⁰W. A. Berg, J. D. Blume, J. B. Cormack, E. B. Mendelson, D. Lehrer, M. Böhm-Vélez, E. D. Pisano, R. A. Jong, W. P. Evans, M. J. Morton, M. C. Mahoney, L. H. Larsen, R. G. Barr, D. M. Farria, H. S. Marques, and K. Boparai, "Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer," *J. Am. Med. Assoc.* **299**, 2151–2163 (2008).
- ³¹D. Rotten and J. M. Levaillant, "The value of ultrasonic examination to detect and diagnose breast carcinomas. Analysis of the results obtained in 125 tumors using radiographic and ultrasound mammography," *Ultrason. Obst. Gyn.* **2**, 203–214 (1992).
- ³²H. Zhi, B. Ou, B.-M. Luo, X. Feng, Y.-L. Wen, and H.-Y. Yang, "Comparison of ultrasound elastography, mammography, and sonography in the diagnosis of solid breast lesions," *J. Ultrason. Med.* **26**, 807–815 (2007).
- ³³C. K. Kuhl, S. Schradang, C. C. Leutner, N. Morakkabati-Spitz, E. Wardelmann, R. Fimmers, W. Kuhn, and H. H. Schild, "Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer," *J. Clin. Oncol.* **23**, 8469–8476 (2005).
- ³⁴E. Warner, D. B. Plewes, R. S. Shumak, G. C. Catzavelos, L. S. Di Prospero, M. J. Yaffe, V. Goel, E. Ramsay, P. L. Chart, D. E. Cole, G. A. Taylor, M. Cutrara, T. H. Samuels, J. P. Murphy, J. M. Murphy, and S. A. Narod, "Comparison of breast magnetic resonance imaging, mammography, and ultrasound for surveillance of women at high risk for hereditary breast cancer," *J. Clin. Oncol.* **19**, 3524–3531 (2001).
- ³⁵S. P. Poplack, T. D. Tosteson, C. A. Kogel, and H. M. Nagy, "Digital breast tomosynthesis: Initial experience in 98 women with abnormal digital screening mammography," *Am. J. Roentgenol.* **189**, 616–623 (2007).
- ³⁶L. T. Niklason, B. T. Christian, L. E. Niklason, D. B. Kopans, D. E. Castleberry, B. H. Opsahl-Ong, C. E. Landberg, P. J. Slanetz, A. A. Giardino, R. Moore, D. Albagli, M. C. DeJule, P. F. Fitzgerald, D. F. Fobare, B. W. Giambattista, R. F. Kwasnick, J. Liu, S. J. Lubowski, G. E. Possin, J. F. Richotte, C. Y. Wei, and R. F. Wirth, "Digital tomosynthesis in breast imaging," *Radiology* **205**, 399–406 (1997).
- ³⁷S. P. Sinha, M. A. Roubidoux, M. A. Helvie, A. V. Nees, M. M. Goodsitt, G. L. LeCarpentier, J. B. Fowlkes, C. L. Chalek, and P. L. Carson, "Multi-modality 3D breast imaging with x-ray tomosynthesis and automated ultrasound," *Conf. Proc. IEEE Eng. Med. Biol. Soc.* **2007**, 1335–1338 (2007).
- ³⁸Z. Xie, F. Hooi, B. Fowlkes, R. Pinsky, X. Wang, and P. Carson, "Combined photoacoustic and acoustic imaging of human breast specimens in the mammographic geometry," *Ultrasound Med. Biol.* **39**, 2176–2184 (2013).
- ³⁹X. Li, C. Heldermon, L. Yao, L. Xi, and H. Jiang, "High resolution functional photoacoustic tomography of breast cancer," *Med. Phys.* **42**, 5321–5328 (2015).
- ⁴⁰R. Kruger, C. Kuzmiak, R. Lam, D. Reinecke, S. Del Rio, and D. Steed, "Dedicated 3D photoacoustic breast imaging," *Med. Phys.* **40**, 113301 (2013).
- ⁴¹T. D. Mast, "Empirical relationships between acoustic parameters in human soft tissues," *Acoust. Res. Lett. Online* **1**, 37–42 (2000).
- ⁴²D. Fontanarosa, S. Skadi van der Meer, E. Harris, and F. Verhaegen, "A CT based correction method for speed of sound aberration for ultrasound based image guided radiotherapy," *Med. Phys.* **38**, 2665–2673 (2011).
- ⁴³D. Fontanarosa, *Evaluation of Speed of Sound Aberration and Correction for Ultrasound Guided Radiation Therapy, Chap. 7: Automated CT-US Cross-Modality 3D Contouring Algorithm for Prostate* (Datawyse, Universitaire Pers Maastricht, the Netherlands, 2014), 179 pp.
- ⁴⁴M. Haynes, S. Verweij, M. Moghaddam, and P. Carson, "Self-characterization of commercial ultrasound probes in transmission acoustic inverse scattering: Transducer model and volume integral formulation," *IEEE Trans. Ultrason. Ferr.* **61**, 467–480 (2014).