Magnetoacoustic tomography with magnetic induction for high-resolution bioimpedance imaging through vector source reconstruction under the static field of MRI magnet

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(Received 27 September 2013; revised 20 December 2013; accepted for publication 8 January 2014; published 27 January 2014)

Purpose: Magnetoacoustic tomography with magnetic induction (MAT-MI) is an imaging modality to reconstruct the electrical conductivity of biological tissue based on the acoustic measurements of Lorentz force induced tissue vibration. This study presents the feasibility of the authors' new MAT-MI system and vector source imaging algorithm to perform a complete reconstruction of the conductivity distribution of real biological tissues with ultrasound spatial resolution.

Methods: In the present study, using ultrasound beamformation, imaging point spread functions are designed to reconstruct the induced vector source in the object which is used to estimate the object conductivity distribution. Both numerical studies and phantom experiments are performed to demonstrate the merits of the proposed method. Also, through the numerical simulations, the full width half maximum of the imaging point spread function is calculated to estimate of the spatial resolution. The tissue phantom experiments are performed with a MAT-MI imaging system in the static field of a 9.4 T magnetic resonance imaging magnet.

Results: The image reconstruction through vector beamformation in the numerical and experimental studies gives a reliable estimate of the conductivity distribution in the object with a ~ 1.5 mm spatial resolution corresponding to the imaging system frequency of 500 kHz ultrasound. In addition, the experiment results suggest that MAT-MI under high static magnetic field environment is able to reconstruct images of tissue-mimicking gel phantoms and real tissue samples with reliable conductivity contrast.

Conclusions: The results demonstrate that MAT-MI is able to image the electrical conductivity properties of biological tissues with better than 2 mm spatial resolution at 500 kHz, and the imaging with MAT-MI under a high static magnetic field environment is able to provide improved imaging contrast for biological tissue conductivity reconstruction. © 2014 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4862836>]

Key words: magnetoacoustic tomography with magnetic induction (MAT-MI), electrical impedance, vector acoustic tomography, image reconstruction

1. INTRODUCTION

The reconstruction of tissue electrical conductivity distribution has been widely researched as an indicator of underlying physiological and pathological conditions in the tissue. For example, malignant breast cancer tissue exhibits higher electrical conductivity than the normal surrounding tissues,^{1,2} in addition clinical data from 24 740 cases suggest that five-year breast cancer survival rate can reach 96.2% if the tumor is diagnosed when the size is less than 5 mm.³ For these reasons, the development of high spatial resolution imaging techniques for the early detection of small-size tumors is desired. Also, detailed information about tissue electrical properties plays an important role in electromagnetic source imaging⁴ and specific absorption rate (SAR) estimation such as in high field magnetic resonance imaging (MRI).^{5,6} Therefore, several techniques for noninvasive bioimpedance reconstruction have been studied.

Electric impedance tomography (EIT) (Refs. 7–9) is one of the earliest developed techniques for bioimpedance imaging. In EIT, surface electrodes are used to measure voltages induced by different surface injected currents, and the impedance is estimated from the measured voltages. EIT is a low cost, safe, and real time imaging system; however the ill-posed nature of the inverse problem leads to low spatial resolution in the reconstruction. To achieve better spatial resolution and accuracy than EIT, magnetic resonance electrical impedance tomography (MREIT) (Ref. 10) was developed by combining EIT and magnetic resonance current density imaging (MRCDI).¹¹ In MREIT, the magnetic field induced by the injected currents from surface electrodes is measured using a MRI scanner. High spatial resolution conductivity images were obtained in both *in vitro* and *in vivo* experiments.¹⁰ However, MREIT is currently limited by its requirement for high level current injection to obtain an acceptable signal-to-noise (SNR) level. In addition, surface electrodes are used to

inject currents, leading to the “shielding effect” caused by insulating or low conductive regions in the object, such as fat tissue.¹² This problem of the “shielding effect” is avoided in magnetic induction tomography (MIT) (Ref. 13) which uses an oscillating magnetic field to induce currents in a conductive object and measure the secondary magnetic field using small coils placed around the surface. However, the spatial resolution of the MIT technique is still quite limited. Besides these electromagnetic imaging methods, hybrid methods, such as magnetoacoustic tomography (MAT) (Refs. 14 and 15) and Hall effect imaging (HEI) (Ref. 16) were developed for non-invasive impedance imaging with high spatial resolution by combining electromagnetic fields and acoustic fields. In these methods, the electromagnetic and acoustic fields are coupled through Lorentz force to reconstruct the conductivity distribution in the object. These imaging methods also use surface electrodes for current injection or voltage measurements which leads to shielding effects. Magnetoacoustic tomography with magnetic induction (MAT-MI) (Refs. 17–34) is a recently introduced approach to image electrical impedance distribution with high spatial resolution. In MAT-MI, magnetic fields are used to induce currents in the conductive object, and hence the method does not suffer from shielding effects. Ultrasound is generated in the object to be imaged by placing it in a dynamic and static magnetic field. The dynamic field induces eddy currents in the object, and the static field leads to generation of acoustic vibrations from Lorentz force on the induced currents. The acoustic vibrations are at the same frequency as the dynamic magnetic field, which is chosen to match the ultrasound frequency range. This allows us to reconstruct the acoustic source distribution in the object by using possible ultrasound imaging approaches.^{18,36} The conductivity distribution of the object can then be reconstructed from the obtained acoustic source map.^{18,25,30} In previously used MAT-MI image reconstruction methods, the scalar pressure source induced by the Lorentz force is first estimated. A practical ultrasound system uses a bandwidth-limited ultrasound probe for acoustic measurements. As a result only the strong scalar pressure signals from the conductivity boundaries can be reconstructed.^{25,27} Nevertheless, the induced vector current source, unlike the scalar pressure source, is uniformly present throughout the object, and thus can be reliably estimated under limited bandwidth conditions. The estimated current source can then be used to give a complete reconstruction of conductivity distribution in the object.³⁰ A vector beamformer algorithm consisting of weighting and summing of the received signal with appropriate time delays is used to obtain the MAT-MI current source. This is then used to estimate the object conductivity under piecewise homogeneous assumption.

In this paper, we present our work on MAT-MI based conductivity reconstruction in objects with imaging resolution under 2 mm corresponding to 500 kHz center frequency of the ultrasound scanning setup. We use numerical simulations to determine the point spread function (PSF) of the imaging system and measure the full width half maximum (FWHM) of the PSF, which is an estimation of the resolution in the image reconstruction. In MAT-MI imaging, conductivity dis-

tribution of objects over the size of the FWHM of the system is reconstructed faithfully. The previously reported MAT-MI experimental system can only acquire very small amplitude of MAT-MI ultrasound signals, as real biological tissues are poor conductors of electricity which limits the eddy current generation when a safe pulsed magnetic stimulation is applied. Consequently, the imaging quality is degraded by the weak MAT-MI signals. In this study, we obtained increased MAT-MI tissue signals by using a high magnetic field from a MRI scanner for human study. The testing results demonstrated that our imaging system and reconstruction algorithm have the capability of providing MAT-MI high-resolution bioimpedance images.

2. METHODS

2.A. Forward problem description

In MAT-MI, a pulsed magnetic field $\mathbf{B}_1(\mathbf{r}, t)$ is applied to the object space Ω which leads to an induced electrical field $\mathbf{E}(\mathbf{r}, t)$ in the space. If the object is conductive with an isotropic conductivity distribution $\sigma(\mathbf{r})$, the induced electric field gives rise to currents in the object, with current density distribution $\mathbf{J}(\mathbf{r}, t)$ given by $\mathbf{J}(\mathbf{r}, t) = \sigma(\mathbf{r})\mathbf{E}(\mathbf{r}, t)$. The magnetic pulse used in MAT-MI is generated by using approximately microsecond long currents through coils, which lead to MHz magnetic fields resulting in negligible propagation time of the field through the object. This allows the magnetic induction problem in MAT-MI to be considered quasistatic. The skin depth of the corresponding MHz field in general biological tissue is at the level of meters, much larger than the characteristic dimension of the object; so the magnetic diffusion can be ignored.³⁵ This allows the applied magnetic field to be uniquely determined by the coil setup around the object and the separation of the spatial and temporal functions in the electromagnetic field analysis of MAT-MI as in $\mathbf{B}_1(\mathbf{r}, t) = \mathbf{B}_1(\mathbf{r})f(t)$, $\mathbf{E}(\mathbf{r}, t) = \mathbf{E}(\mathbf{r})f'(t)$, where the prime indicates first derivative. In addition to this the microsecond long magnetic stimulation also leads to the displacement currents being much weaker than the ohmic current due to the fact that $\sigma \gg \omega\epsilon$ in biological tissue is in the 1 MHz range,¹⁸ where ω is the angular frequency of the stimulating field and ϵ is the permittivity of the object. For a known conductivity distribution σ the magnetic induction problem can be solved, in order to obtain current density distribution $\mathbf{J}(\mathbf{r}, t)$, using the finite element method (FEM) simulations.³⁵ When a static magnetic field $\mathbf{B}_0(\mathbf{r})$ is applied to the object space, it interacts with the induced currents and leads to Lorentz force based vibrations in the objects. The Lorentz force is determined as $\mathbf{F}(\mathbf{r}, t) = \mathbf{J}(\mathbf{r}, t) \times \mathbf{B}_0(\mathbf{r})$, giving rise to propagating acoustic waves in the medium. The resultant acoustic pressure waves, for which the divergence of the Lorentz force acts as the source, given by $As(\mathbf{r}, t) = \nabla \cdot \mathbf{F}(\mathbf{r}, t)$, is governed by the following wave equation:

$$\nabla^2 p - \frac{1}{c_s^2} \frac{\partial^2 p}{\partial t^2} = As(\mathbf{r}, t), \quad (1)$$

where p is the pressure and c_s is the acoustic speed in the medium. The induced eddy current $\mathbf{J}$ is a smooth function that vanishes outside the object space with its first derivative, so it can be decomposed into a rotational part $\mathbf{J}_c$ and an irrotational part $\nabla\theta$.³⁰ The current $\mathbf{J}$ can be written as

$$\mathbf{J} = \mathbf{J}_c + \nabla\theta. \quad (2)$$

Suppose the static magnetic field $\mathbf{B}_0(\mathbf{r})$ applied to the object space can be assumed to be approximately a constant vector, then $\nabla \times \mathbf{B}_0 \approx 0$. The Lorentz force distribution can be rewritten as follows: $\mathbf{F} = \mathbf{J} \times \mathbf{B}_0 = \mathbf{J}_c \times \mathbf{B}_0 - \nabla \times (\theta \mathbf{B}_0)$. As the acoustic source is the divergence of the Lorentz force and the term $\nabla \times (\theta \mathbf{B}_0)$ is a purely rotational vector, it does not contribute to the source of the pressure waves. So the acoustic pressure source can be further simplified as $As(\mathbf{r}, t) = \nabla \cdot \mathbf{F}_d$, where $\mathbf{F}_d = \mathbf{J}_c \times \mathbf{B}_0$ is the part of the Lorentz force giving rise to the MAT-MI acoustic signal and is dependent fully on the rotational part of the induced current.

The detected acoustic pressure $p(\mathbf{r}, t)$ signal at any point on the scanning aperture can be obtained using Green's function solution to the wave equation, which consists of volume integration of the source distribution weighted by the appropriate Green's function. Now, suppose the induced eddy currents are confined to the object space Ω , the acoustic source is then zero outside the conductive object, the Green function solution can be described as follows.^{18,30}

$$p(\mathbf{r}, t) = \frac{1}{4\pi} \iiint d^3r' \mathbf{F}_d(\mathbf{r}') \cdot \nabla_{r'} G(\mathbf{r}, \mathbf{r}', t), \quad (3)$$

where $\mathbf{r}'$ is the location of the acoustic source, $\mathbf{r}$ is the location of detectors, $\nabla_{r'}$ implies derivative with respect to source space $\mathbf{r}'$, the Green function for this solution is

$$G(\mathbf{r}, \mathbf{r}', t) = \frac{\delta(t - \frac{R}{c_s})}{R}, \quad (4)$$

where $R = |\mathbf{r} - \mathbf{r}'|$. The volume integration is carried out over the acoustic source distribution in the object space Ω . This equation gives the observed pressure for an impulse source which is a source with its time function as $\delta(t)$. An induced acoustic source field with time dependence $h(t)$ and the transducer impulse response $r(t)$ gives rise to an observed pressure $p(\mathbf{r}, t) \otimes h(t) \otimes r(t)$, where $\otimes$ is the convolution operator. The Green function for this time dependence can be written as $G(\mathbf{r}, \mathbf{r}', t) = \frac{hr(t - \frac{R}{c_s})}{R}$, where $hr(t) = h(t) \otimes r(t)$.

2.B. Inverse problem description

For the MAT-MI tomographic reconstruction, ultrasound transducers are placed around the object to measure the induced acoustic pressure waves, which are used to reconstruct the source distribution of the acoustic signal. A beamformer algorithm can be applied by combining the signals obtained from all the transducer locations from around the object to perform the ultrasound image reconstruction. The desired PSF to image the ultrasound pressure distribution is ideally a spatial delta function. Under limited bandwidth reconstruction, the obtained PSF is an approximation of the delta func-

tion with the spread of the function in space corresponding to the spatial resolution in various directions. In the present work, we use the beamformer algorithm to design a vector point spread function which can extract the individual orthogonal vector components of the Lorentz force, $\mathbf{F}_d$, which gives rise to the acoustic waves. The conductivity distribution in the object can then be estimated from the reconstructed vector source distribution. The beamformer algorithm comprises of summing up the magnitude weighted and time delayed signal at all the receiver locations. Using the ultrasound transfer function, which is obtained as the system response to a point source at the scanning aperture, the weights and time delay for the beamformer algorithm can be designed by utilizing a linear algebra formulation of the least squared error between the system PSF and the desired PSF. For a point receiver the system spatial response is $hr(\mathbf{r}, \mathbf{r}', t)$, which can be obtained by simulation or experiments.^{24,27,36}

By applying the beamformer algorithm³⁶ to the signal obtained from the discrete number of transducer locations on the scanning aperture, the resultant signal can be described by the following equation:

$$V(\mathbf{r}_s) = \sum_n W_n p(\mathbf{r}, t - t_a), \quad (5)$$

where W_n is the weight applied to the ultrasound signal, t_a is the time delay applied to the signal to obtain the source at $\mathbf{r}_s$ the weights and time delay in ultrasound beamformation depends on the transducer and the source location, n is the number of ultrasound receiver signals used in the beamformation process and V is the resultant signal obtained at source location $\mathbf{r}_s$ from the beamformation process. By substituting for the pressure $p(\mathbf{r}, t)$ using Eqs. (3) in (5) we get

$$V(\mathbf{r}_s) = \iiint d^3r' \mathbf{J}_c \cdot \left(\mathbf{B}_0 \times \sum_n \left(\frac{1}{4\pi} \right) W_n \nabla_{r'} G(\mathbf{r}, \mathbf{r}', t - t_a) \right). \quad (6)$$

If the vector term $\mathbf{S}(\mathbf{r}') = \mathbf{B}_0 \times \sum_n \left(\frac{1}{4\pi} \right) W_n \nabla_{r'} G(\mathbf{r}, \mathbf{r}', t - t_a) \approx \delta(\mathbf{r}') \hat{i} + 0\hat{j}$ would lead to reconstructing the x component of the source vector, $J_{cx}(\mathbf{r}') = \mathbf{J}_c(\mathbf{r}') \cdot \hat{i}$ and $\mathbf{S}(\mathbf{r}') \approx 0\hat{i} + \delta(\mathbf{r}') \hat{j}$ would lead to reconstructing the y component of the source vector, $J_{cy}(\mathbf{r}') = \mathbf{J}_c(\mathbf{r}') \cdot \hat{j}$. This term $\mathbf{S}(\mathbf{r}')$ is the PSF of the ultrasound imaging system reconstructing the orthogonal components of the vector source. The weights and time delay to generate such a vector point spread function can be computed by forming a set of linear equations with the known Green's function distribution as follows:

$$Ux = b, \quad (7)$$

where $U = \frac{B_0}{4\pi} \left(\frac{-\nabla_{r'} G(\mathbf{r}, \mathbf{r}', t - t_a)}{\nabla_{r'} G(\mathbf{r}, \mathbf{r}', t - t_a)} \right)$ when $\mathbf{B}_0 = B_0 \hat{k}$, $x = W_n$, and $b = \begin{pmatrix} \delta(\mathbf{r}') \\ 0 \end{pmatrix}$ or $\begin{pmatrix} 0 \\ \delta(\mathbf{r}') \end{pmatrix}$ corresponding to the two desired point spread functions reconstructing the x and y components of the current source, respectively, and $t = \frac{|\mathbf{r} - \mathbf{r}_s|}{c_s}$ to obtain the source at location $\mathbf{r}_s$. The reconstructed vector source is uniformly present in the object and can be used to

estimate the conductivity in an object with piecewise homogeneous conductivity distribution. The induced current density $\mathbf{J}$ is given by³⁰

$$\mathbf{J} = -\sigma \frac{\partial \mathbf{A}}{\partial t} + \phi \nabla \sigma - \nabla (\sigma \phi). \quad (8)$$

For an object with piecewise homogeneous conductivity distribution, $\nabla \sigma \approx 0$ at points other than at the conductivity boundaries. So in regions away from the boundary the induced current can be approximated as follows:

$$\mathbf{J} \approx -\sigma \frac{\partial \mathbf{A}}{\partial t} - \nabla (\sigma \phi). \quad (9)$$

In this region, the term $-\sigma \frac{\partial \mathbf{A}}{\partial t}$ is a purely rotational vector due to the design of the magnetic vector potential $\mathbf{A}$ and is the only contributor to the MAT-MI acoustic pressure source in the homogeneous region given by $-\sigma \nabla \times \frac{\partial \mathbf{A}}{\partial t}$. So the vector source $\mathbf{J}_c$, which is the rotational part of the induced current giving rise to the MAT-MI source, under a piecewise homogeneous conductivity distribution at points away from the boundary can be represented as follows:

$$\mathbf{J}_c \approx -\sigma \frac{\partial \mathbf{A}}{\partial t}. \quad (10)$$

Under limited bandwidth reconstruction encountered in ultrasound imaging systems,^{25,30} the point spread function acts as a bandpass filter removing the dc to low frequency components of the generated signal. The resultant point spread function of the imaging system is a nonideal pulse and to get a more complete reconstruction of the current source, the estimated point spread function of the imaging system can be used to filter the reconstructed image. Further, in the presence of noise, there is a tradeoff between the completeness of the inverse filtering process and noise amplification. When a uniform pulsed field, $\mathbf{B}_1 = \nabla \times \mathbf{A}$, is applied over the object space, the induced MAT-MI current source, which is proportional to the vector potential, increases with the radius inside the homogeneous conductive region,²³ and the curl of the current source is approximately constant away from the conductivity boundaries.²⁰

Under the imaging conditions leading to inaccuracies in the low frequency portion of the estimated acoustic source reconstruction, the conductivity can be better reconstructed from a modification with discrete derivatives of the above vector equation as follows:

$$\sigma \approx S_1 \setminus S_2, \quad (11)$$

where

$$S_1 = (\mathbf{J}_c(\mathbf{r}'_1, \mathbf{r}'_2 \dots \mathbf{r}'_n) \cdot \hat{i} - \mathbf{J}_c(\mathbf{r}'_{1\Delta y}, \mathbf{r}'_{2\Delta y} \dots \mathbf{r}'_{n\Delta y}) \cdot \hat{i})$$

$$- (\mathbf{J}_c(\mathbf{r}'_1, \mathbf{r}'_2 \dots \mathbf{r}'_n) \cdot \hat{j} - \mathbf{J}_c(\mathbf{r}'_{1\Delta x}, \mathbf{r}'_{2\Delta x} \dots \mathbf{r}'_{n\Delta x}) \cdot \hat{j})$$

$$S_2 = (\mathbf{A}'(\mathbf{r}'_1, \mathbf{r}'_2 \dots \mathbf{r}'_n) \cdot \hat{i} - \mathbf{A}'(\mathbf{r}'_{1\Delta y}, \mathbf{r}'_{2\Delta y} \dots \mathbf{r}'_{n\Delta y}) \cdot \hat{i})$$

$$- (\mathbf{A}'(\mathbf{r}'_1, \mathbf{r}'_2 \dots \mathbf{r}'_n) \cdot \hat{j} - \mathbf{A}'(\mathbf{r}'_{1\Delta x}, \mathbf{r}'_{2\Delta x} \dots \mathbf{r}'_{n\Delta x}) \cdot \hat{j}),$$

where $\mathbf{A}' = \frac{\partial \mathbf{A}}{\partial t}$, $\setminus$ operator is the least square fit, $\mathbf{r}'_1, \mathbf{r}'_2 \dots \mathbf{r}'_n, \mathbf{r}'_{1\Delta y}, \mathbf{r}'_{2\Delta y} \dots \mathbf{r}'_{n\Delta y}, \mathbf{r}'_{1\Delta x}, \mathbf{r}'_{2\Delta x} \dots \mathbf{r}'_{n\Delta x}$ are points within a

region of uniform conductivity in the object, subscript Δy and Δx indicates change in y and x direction, respectively, around points $\mathbf{r}'_1, \mathbf{r}'_2 \dots \mathbf{r}'_n$. S_1, S_2 are a collection of estimates of the curl of the current source and the vector potential, respectively, in a homogeneous conductivity region. The boundaries of such a region can be determined from the MAT-MI acoustic source distribution, which is the strongest at the location of conductivity change in the object.^{20,25,30} The conductivity estimation around the boundaries of a homogeneous region, where the error is maximum over one imaging resolution, is determined by interpolating the values around the region.

2.C. Computer simulation method

Figure 1(a) shows the diagram of the MAT-MI imaging setup, and Fig. 1(b) shows the design of the point spread function for the scalar and vector source reconstruction. In the computer simulation setup as seen in Fig. 1(a), the static magnetic field $\mathbf{B}_0$ points in the Z direction with a uniform strength of 1 Tesla, and the pulsed magnetic field is applied with a coil arrangement as seen in the figure. For the simulation, a coil pair with a 16 cm diameter separated by 3 cm is used to build a uniform magnetic field over the object space, which has a dimension of 10 cm diameter by 2 cm height and it is placed symmetric to the center of the coils. A current pulse applied to the coil generates the magnetic field and the maximum rate of change of the current is fixed at 10^7 A/s. The electric potential ϕ induced in the object space is computed using FEM simulations with COMSOL (Ref. 30) in the forward problem. The induced electric field can be then determined using the computed electric potential ϕ , from which the induced current density is determined as $\mathbf{J} = \sigma \mathbf{E}$. This current density $\mathbf{J}$ is then interpolated to a square mesh of size 10×10 cm with a grid size of 0.15 mm from which the induced MAT-MI acoustic source distribution is then computed according to $\mathbf{A}_s = \nabla \cdot \mathbf{F} = (\nabla \times \mathbf{J}) \cdot \mathbf{B}_0$.

The acoustic pressure measured by the ultrasound scanning setup is determined according to the Green function solution to wave equation as given in Eq. (5). The piston transducers used in the simulation are assumed to have a receive bandwidth of 100% around the central frequency which corresponds to $\sim 70\%$ bandwidth in a pulse echo system consisting of limited transmit and receive bandwidth. The transducers are placed on a circular scanning geometry 30 cm away from the center of the object on $Z = 0$ plane. The 30 cm scanning radius leads to an approximately uniform sensitivity over the object space. Thus the piston transducer can be assumed to be acting as a point receiver. The large scanning radius also ensures that the spherical acoustic waves from the MAT-MI source can be approximated as plane waves at the transducer, which allows the signals from the limited Z direction in the object to add up, so the ultrasound imaging setup can be also approximated as a 2D system. The weightings and time delay for the beamformation are determined according to Eq. (7). The time delays with a discretized pressure signal can be applied as $t_a = n\Delta T$, where n is an integer with $n = -\frac{N}{2} \text{ to } \frac{N}{2}$, $\left| \frac{N}{2} \right| \Delta T$ is the maximum delay applied to the

FIG. 1. (a) Schematic diagram of MAT-MI imaging method. (b) Schematic representation of the point spread function for scalar and vector reconstruction.

signal, N is an integer determining the maximum delay, and ΔT is the time between samples. This set of weightings and the corresponding time delay applied to each line of transducer signals, prior to the summation of the signals from all the transducer location, can be considered as an $N+1$ tap finite impulse response (FIR) filter acting on the received pressure signal which is combined in the beamformation algorithm to reconstruct the acoustic source distribution. Under limited bandwidth data collection in the presence of noise, to obtain an ideal spatial impulse $\delta(\mathbf{r}')$ as the point spread function, such a filter would act as an inverse filter increasing the signal bandwidth and could amplify the noise. So in the design of the beamformer, $N = 0$ is used which would lead to the design of point spread function with nonideal spatial pulse (denoting it as $D(\mathbf{r}')$) approximating the desired spatial impulse response $\delta(\mathbf{r}')$. In the study, the function $D(\mathbf{r}')$ is set to the imaging point spread function obtained for the pressure source reconstruction with the backprojection algorithm for the given scanning setup. For determining the beamformation design, a source region $\mathbf{r}'$ of 18×18 mm with a spacing of 0.15 mm is considered. A least square truncated singular value decomposition (TSVD) solution to Eq. (7) is used to solve for the weights. Inverse filtering is performed on the reconstructed vector source image, which has improved signal-to-noise ratio (SNR) compared to the 1D signal obtained at the transducer due to the summation process in the beamformation algorithm. The filtered image gives a more complete estimation of the source distribution and the conductivity is then determined from this source image according to the description in Sec. 2.B.

2.D. Experiment methods

Figure 2 shows the hardware setup for MAT-MI experiments under a MRI environment. The MRI scanner (Magnet, Oxford, UK) had a maximum 9.4 T static magnetic field in horizontal Z direction and 65 cm inner diameter bore, which has already been used for preliminary human subject study.³⁷ Our sample and a 25 mm-diameter unfocused transducer (V301, Olympus, MA) with nominal peak frequency of 500 kHz were immersed under distilled water filled in a plastic tank which was vertically sitting on a wooden bed placed in the MRI scanner bore. The sample has uniform conductivity along the Z direction and the transducer is ~ 270 mm away from the sample similar to the simulation setup. A customized nonmagnetic linear motor (N-310K128, PhysikInstrumente, Germany) was mounted on the top of the tank. This motor had a 125 mm travel range, 7 m control cable and it could provide up to 10 N push or pull force. We designed a gear system to convert the motor's linear motion into rotary motion using three gears with a diameter of 32 mm cascaded to realize 360° rotation of the sample for full-angle signal measurements. In experiments, the sample was fixed well to the bottom gear through a plastic sample holder. A customized magnetic stimulator was employed to deliver magnetic stimulation to the sample to induce eddy currents. The three-turn magnetic coil with an outer diameter of 70 mm was vertically placed very close to the tank wall to maximize the stimulation. The coil driver was equipped with an adjustable high-voltage source (0–24 kV), a capacitor and a solid state switch for handling large currents. For charging voltage at 24 kV,

FIG. 2. Schematic diagram of MAT-MI experiment setup in MR system. A coil is placed close to the sample to deliver short-duration pulse magnetic stimulation. The sample is rotated by a nonmagnetic motor for 360° ultrasound measurements by a transducer. Both the sample and transducer are immersed under distilled water.

the induced electrical field applied to the sample was around 550 V/m, which is comparable to the stimulating strength in transcranial magnetic stimulation (TMS). However, the total energy applied to the samples in MAT-MI is much lower than TMS as the MAT-MI pulse duration is at the microsecond level instead of hundreds of microseconds in TMS.³⁸ Piezo-electric signals collected by the transducer were amplified with low-noise ultrasound amplifiers (5660 B, Olympus, MA and VP2000, Reson, Denmark) before entering the data acquisition system which acquired 2048 data points for each channel with a 5 MHz sampling rate. To comply with MRI compatibility rules, all electrical devices were put outside of the shielded magnet room except for the transducer and MRI-compatible linear motor. We used 7 m cables for electrical connections to the coil, the transducer and the motor as seen from the side view in Fig. 2. The object is rotated in 3° steps over 360° to acquire the ultrasound signals for the image reconstruction. The data acquisition time is around 12 min. The limited bandwidth system point spread function is estimated with ultrasound imaging simulation by using the estimated transducer impulse response and the measured magnetic pulse waveform.^{24,30,34}

The strong magnetic pulse used to generate the MAT-MI signal induces electromagnetic interference (EMI) in the ultrasound imaging system. This continues for a certain time duration due to the turn-off transients associated with the magnetic stimulator and the impulse response of the transducer. The observed EMI signal in the experiment data is seen

to have significant low frequency variations which could interfere with the estimation of low spatial frequency conductivity distribution, and a bandpass filter is used to suppress this noise. In the reconstructed image, additional artifacts in the form of concentric rings are observed as a result of coherent addition of weak background signal. The strength of the artifacts is comparable to that of MAT-MI sources. However, the circular nature of the artifacts can be used to filter out the rings by use of a high pass filter along the azimuthal direction at each radial location on the image. The useful MAT-MI source, present strongly at the conductivity boundary in the limited bandwidth setup, is further filtered to obtain a more complete estimate of the vector current sources, and the conductivity is then determined using this source according to the method in Sec. 2. The conductivity distribution reconstructed in experiments was normalized to the expected range of values using a scaling factor to account for the various gains in the system. The scaling factor was determined by estimating the conductivity of a 50 mm diameter test sample of 0.7% salinity whose conductivity was measured to be ~ 1.20 S/m using a four electrodes probe.²⁴

3. RESULTS

3.A. Numerical study

The results of the vector source reconstruction, with the designed PSF, and the conductivity estimation for an object

FIG. 3. (a) Simulated target conductivity distribution (b), (c) Orthogonal components of the induced current source. (d) Reconstructed conductivity distribution, (e), (f) Reconstructed orthogonal components of current source. (g), (h) Line profiles of conductivity and current source J_x at $x = 0$.

is shown in Fig. 3. Figure 3(a) shows the conductivity distribution of the simulated object, and the normalized current density corresponding to the induced current source due to the applied magnetic pulse is shown in Figs. 3(b) and 3(c). As the induced eddy currents are cyclic in nature, the individual vector components have phase inversions about the orthogonal axis as seen in the figure. The estimated conductivity distribution and the reconstructed vector current source are shown in Figs. 3(d)–3(f), respectively. Figures 3(g) and 3(h) show a line profile of the reconstructed conductivity and the current source, respectively, at $x = 0$. As seen in the line profile of the current source, due to the limited bandwidth of the imaging system, spatial smoothing is observed in the reconstructed current density especially at the conductivity boundaries where a sharp change in the current density occurs. This smoothing effect in the reconstruction of the current density leads to the estimated conductivity to have maximum error around the boundaries of the object. To reduce this error, the conductivity in this region of over 3 mm corresponding to the boundary spread, is estimated by extrapolating the conductivity at the neighboring points which leads to reliably reproducing the target conductivity as seen in the line profile of the reconstructed conductivity.³⁰

The resolution of the imaging system determines the size of the object that can be reconstructed reliably. We have simulated the ability of MAT-MI to reconstruct the conductivity distribution of objects with different sizes under various system frequencies as seen in Fig. 4. The resolution of the imaging system, as determined by the point spread function, increases with frequency bandwidth of the imaging system as seen in Fig. 4(a), which shows the line profiles of the PSF for imaging system frequencies of 300 kHz, 500 kHz, and 2.5 MHz with the half width half maximum (HWHM) marked in the plot. The HWHM is half the resolution of the imaging system, and the resolutions at these frequencies are obtained as ~ 2.5 , 1.5, and 0.3 mm, respectively. The target object imaged in this simulation, as shown in Fig. 4(b), consists of conductive circular objects with diameters of 4.5, 3.0, 1.5, 0.5 mm in a nonconductive background. The reconstructed conductivity images at different system frequencies are shown in Figs. 4(c)–4(e) corresponding to 2.5 MHz, 500 kHz, and 300 kHz, respectively. As seen in the reconstructed image objects larger than the resolution of the imaging system are reliably reconstructed. However, even for smaller objects, if the boundary spread is limited a conductivity estimate can be obtained in the homogeneous region with some errors. This is

FIG. 4. (a) Line profiles of the PSF at 2.5 MHz, 500 kHz, and 300 KHz center frequency with the HWHM of the PSF marked. (b) Target conductivity distribution. (c), (d), and (e) Reconstructed conductivity distribution with ultrasound frequency at 2.5 MHz, 500 kHz, and 300 KHz, respectively.

then extrapolated as the estimate of the conductivity of the object as seen in Figs. 4(d) and 4(e).

3.B. Experiment study

We have conducted MAT-MI experiments using the proposed system under the static field of a MRI magnet. We have used a well-controlled gel phantom to check the intensity of the induced MAT-MI ultrasound signal. In this experiment, two 50 mm-diameter, 25 mm-thickness single layer uniform phantoms built with a cooled gelatin solution were used. The phantoms had salinities of 0.7% and 1.0% for the comparison with the data obtained from the previous imaging experiments.²⁸ Five different charging voltages, i.e., 8, 12, 16, 20, 24 kV were chosen in the magnetic stimulator. The ultrasound signals were acquired with 20 times averaging to improve signal-to-noise ratio. The testing results are shown in Fig. 5(a). It can be seen that around 14 times improvement in induced MAT-MI ultrasound signals was observed, which mainly attributes to the use of the high 9.4 T static field in the MRI scanner. However, the energy losses in the long cable to the excitation coil and the detection transducer significantly decrease the expected gain from high B_0 field. Experiments were also performed on biological tissues. A piece of fresh

FIG. 5. (a) Comparison of the induced MAT-MI ultrasound signal intensity produced by the previous experiment and present experiment in a 9.4 T MRI scanner. Single layer uniform phantoms with salinity of 0.7% and 1.0% were tested with different charging voltage setting. (b) A recorded temporal MAT-MI ultrasound wave shows the bipolar-structure signals reflecting the electrical conductivity contrast at muscle-fat interfaces in a piece of pork tissue.

pork tissue purchased from a local grocery store was cut into a size of $18 \times 15 \times 15$ mm for the experiment. This sample had a natural fat-muscle-fat structure implying detectable electrical conductivity contrasts for measurements. We put this tissue sample into a thin-wall plastic container, which had a diameter of 50 mm. The container was then filled with cooled gelatin solution with a salinity of 1.0% to finalize the sample as shown in the photograph in Fig. 5(b). The charging voltage was set at 16 kV and the ultrasound signal was acquired with 20 times data averaging. The collected single channel ultrasound data plotted in Fig. 5(a) clearly shows bipolar-structure signals, which correspond well to the locations where electrical conductivity interfaces exist. The tissue signals appearing roughly at time points from 175.8 μ s to 186.2 μ s are in agreement with the approximate tissue thickness of 15 mm when

FIG. 6. (a) Photograph of the imaged saline phantom, (b) Simulated conductivity distribution similar to the experiment phantom, (c) Experiment pressure source reconstruction with the ring artifacts removed, (d) Reconstructed conductivity distribution with the experiment phantom. (e) and (f) Pressure source and conductivity reconstruction in simulation without added MR noise. (g) Filtered simulation pressure source reconstruction with background MR environment noise added to the data (h) conductivity reconstruction of the simulated phantom.

FIG. 7. Goat tissue phantom conductivity reconstruction. (a) Photograph of a tissue phantom with muscle conductivity of 0.65 S/m, fat conductivity of 0.01 S/m. (b) Reconstruction of the conductivity distribution. (c) Line profiles of target and reconstructed conductivity at $x = 0$.

considering an averaged acoustic speed of $1.5 \text{ mm}/\mu\text{s}$ for soft tissues. The fat-muscle-fat tissue structure is also reflected in the recorded ultrasound data, demonstrating the capability of MAT-MI under a MRI scanner to resolve small conductivity contrasts in tissues even with a single channel ultrasound measurement.

We have performed imaging experiments on a well-controlled saline phantom as shown in Fig. 6. As seen in Fig. 6(a), the phantom consists of 0.7% cooled saline gel with a nonconductive gel structure embedded in it. A dark dye is applied to the surface of the nonconductive gel after the experiment for improving photograph contrast. Also for better comparison with the experiment result, a simulation has been performed with the target conductivity similar to the experiment phantom as seen in Fig. 6(b). In Fig. 6(c), the reconstructed acoustic source, from the experiment, can be seen and the ring artifacts induced by the background noise are filtered as described in Sec. 2.D, which suppresses the circular noise. Some artifacts are induced in the boundary signals due to this filtering and these errors in the boundary signal reconstruction propagate to the conductivity estimation. The conductivity distribution of the object estimated from the reconstructed vector sources is shown in Fig. 6(d). The simulation reconstruction under no MR environment artifact is shown in Fig. 6(e) and the corresponding conductivity estimation is shown in Fig. 6(f). Under such conditions there is no ring artifact in the reconstruction and the conductivity

estimate is more reliable. In the simulation reconstruction shown in Fig. 6(g), common background signal measured in the MRI environment is added to each channel of the simulated pressure data and this leads to ring artifacts which are removed with the filter. The effect of the artifacts from the filtering, which is similar to the experiment reconstruction, is seen in the estimated conductivity distribution in Fig. 6(h).

We have further imaged phantoms consisting of biological tissue. Figure 7 shows the conductivity reconstruction result with a phantom consisting of goat muscle tissue pressed against a piece of fresh pork fat with a saline gel of 0.8% salinity placed around the sample. The tiny mechanical discontinuities at the muscle-to-fat tissue interface will not contribute much to the induced MAT-MI ultrasound signals.²⁹ The conductivity of the gel, the goat tissue and the pork fat is 1.40, 0.65, and 0.02 S/m, respectively, and the reconstructed average conductivity values are 1.30, 0.81, 0 S/m. As seen from the experiment reconstructions, due to the additional ring noise, there is around 25% error in the estimated conductivity for the objects placed in the background gel, which is the conductive structure, used to determine the scaling factor for the reconstruction. However, the relative conductivities of the objects are reliably imaged.

4. DISCUSSION AND CONCLUSION

We have applied the vector beamformation algorithm to MAT-MI and from the reconstructed vector sources estimated the conductivity of the object using a high field MRI scanner. In the conductivity estimation a piecewise homogeneous assumption is used, and at the conductivity boundaries the error in the estimation is maximum. However, the MAT-MI acoustic source is also the strongest at such boundaries, due to the contribution of sharp conductivity change.^{20,25,30} This is used to determine these boundary regions³³ where the conductivity is then estimated by extrapolating the values from the surrounding uniform conductivity regions. It can be seen from the computer simulation and experiments that the conductivity distribution can be estimated reliably with this method. In order to improve the accuracy of the reconstruction in regions of variable conductivity, the dependence of the vector source on the conductivity gradient and electric potential would have to be taken into account. The electric potential is a term that depends on the magnetic stimulation and the conductivity distribution of the object. *A priori* knowledge of this term is not possible for all objects, so an iterative reconstruction algorithm would have to be implemented.¹⁰ The conductivity anisotropy of biological tissue is another factor that would have to be taken into account for accurate imaging.²² In this case, a multiexcitation method can be used to estimate the directionally dependent components of conductivity.²⁵

The frequency bandwidth of the imaging system determines the spatial resolution of the reconstructed vector source distribution, and the spatial resolution can be estimated from the FWHM of the imaging system which determines the smallest size of the object that can be reliably imaged with the system. At 500 kHz center frequency, which is also the operating frequency of our current imaging system, objects with a

size greater than 1.5 mm can be reliably imaged as seen in the imaging result.

In the simulation and experiment study, the objects imaged had a short uniform profile along the vertical Z direction. The applied magnetic fields and the spatial response of the ultrasound receiver were also uniform along the Z direction. To image under such simplified profiles a circular scanning aperture placed on the horizontal center plane is sufficient for the reconstruction of the cross section profile of the object. However, the proposed reconstruction algorithm can also be applied for 3D MAT-MI imaging using a 3D acoustic receiver aperture.²³ This setup can be used to image the distribution of MAT-MI vector sources in the object and the conductivity can then be estimated using the proposed method.

The acoustic homogeneity assumption used in the theoretical derivation in this study restricts the proposed imaging method to primarily soft tissue imaging. The acoustic heterogeneity of soft tissue is less than 10% and its effect can be negligible for those imaging techniques which are based on the acoustic measurements of induced ultrasound signals.^{39,40}

In this study, we have observed technical challenges when conducting MAT-MI experiments in a high field MRI system environment. The long coil cable (7 m) with redundant capacitance and inductance brings significant ringing and noise to the system due to the strong differential effects produced by $d\mathbf{B}_1/dt$ inducing eddy currents. Also, the energy loss in this cable is not negligible and the long cable for ultrasound detection picks up more environmental noise which pollutes the MAT-MI signals. In addition, the power line noise in the MRI center cannot be ignored, and it will be picked up by our MAT-MI hardware system, which may degrade the final image quality. So to fully realize the benefits of using a higher strength static magnetic field in MAT-MI, careful instrumentation would have to be developed to avoid these additional noise sources.

In conclusion, the results presented in this study indicate that the vector reconstruction algorithm with MAT-MI imaging experiments in a MRI scanner is able to distinguish the small electrical conductivity contrast in biological tissues with a spatial resolution at millimeter level.

ACKNOWLEDGMENTS

This work was supported in part by NIH EB014353, EB017069, EB006433, and P30 NS057091. The authors would also like to thank Dr. Pierre-Francois Van de Moortele and Dr. Kamil Ugurbil for useful discussions and support in developing the experiment system and Dr. Xiaotong Zhang for useful discussions with the computer simulation.

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¹L. A. Geddes and L. E. Baker, "The specific resistance of biological materials: A compendium of data for the biomedical engineer and physiologist," *Med. Biol. Eng.* **5**, 271–293 (1967).

²J. Surowiec, S. S. Stuchly, J. R. Barr, and A. Swarup, "Dielectric properties of breast carcinoma and the surrounding tissues," *IEEE Trans. Biomed. Eng.* **35**, 257–263 (1988).

- ³C. L. Carter, C. Allen, and D. E. Hensen, "Relation of tumor size, lymph node status, and survival in 24740 breast cancer cases," *Cancer* **63**, 181–187 (1989).
- ⁴B. He, *Modeling and Imaging of Bioelectrical Activity—Principles and Applications* (Kluwer Academic Publishers, New York, 2004).
- ⁵X. Zhang, S. Schmitter, P. F. Van de Moortele, J. Liu, and B. He, "From complex B_1 mapping to local SAR estimation or human brain MR imaging using multi-channel transceiver coil at 7T," *IEEE Trans. Med. Imaging* **32**, 1058–1067 (2013).
- ⁶U. Katscher, T. Voigt, C. Findekle, P. Vernickel, K. Nehrke, and O. Dossel, "Determination of electric conductivity and local SAR via B_1 mapping," *IEEE Trans. Med. Imaging* **28**, 1365–1374 (2009).
- ⁷P. Metherall, D. C. Barber, R. H. Smallwood, and B. H. Brown, "Three-dimensional electrical impedance tomography," *Nature (London)* **380**, 509–512 (1996).
- ⁸M. Cheney, D. Isaacson, and J. C. Newell, "Electrical impedance tomography," *SIAM Rev.* **41**, 85–101 (1999).
- ⁹K. Paulson, W. Lionheart, and M. Pidcock, "Optimal experiments in electrical-impedance tomography," *IEEE Trans. Med. Imaging* **12**, 681–686 (1993).
- ¹⁰E. J. Woo and J. K. Seo, "Magnetic resonance electrical impedance tomography (MREIT) for high-resolution conductivity imaging," *Physiol. Meas.* **29**, R1–R26 (2008).
- ¹¹M. Joy, G. Scott, and M. Henkelman, "In vivo detection of applied electric currents by magnetic resonance imaging," *Magn. Reson. Imaging* **7**, 89–94 (1989).
- ¹²H. Wen, "Feasibility of biomedical application of Hall effect imaging," *Ultrason. Imaging* **22**, 123–136 (2000).
- ¹³H. Griffiths, "Magnetic induction tomography," *Meas. Sci. Technol.* **12**, 1126–1131 (2001).
- ¹⁴C. Towe and M. R. Islam, "A magneto acoustic method for the noninvasive measurement of bioelectric currents," *IEEE Trans. Biomed. Eng.* **35**, 892–894 (1988).
- ¹⁵J. Roth, P. J. Basser, and J. P. Wikswo, Jr., "A theoretical model for magneto-acoustic imaging of bioelectric currents," *IEEE Trans. Biomed. Eng.* **41**, 723–728 (1994).
- ¹⁶H. Wen, J. Shah, and S. Balaban, "Hall effect imaging," *IEEE Trans. Biomed. Eng.* **45**, 119–124 (1998).
- ¹⁷B. He, "High-resolution functional source and impedance imaging," *Proc. Annu. Int. Conf. IEEE-EMBS* **2005**, 4178–4182.
- ¹⁸Y. Xu and B. He, "Magnetoacoustic tomography with magnetic induction," *Phys. Med. Biol.* **50**, 5175–5187 (2005).
- ¹⁹X. Li, Y. Xu, and B. He, "Magnetoacoustic tomography with magnetic induction for imaging electrical impedance of biological tissue," *J. Appl. Phys.* **99**, 066112 (2006).
- ²⁰X. Li, Y. Xu, and B. He, "Imaging electrical impedance from acoustic measurements by means of magnetoacoustic tomography with magnetic induction (MAT-MI)," *IEEE Trans. Biomed. Eng.* **54**, 323–330 (2007).
- ²¹Q. Ma and B. He, "Investigation on magnetoacoustic signal generation with magnetic induction and its application to electrical conductivity reconstruction," *Phys. Med. Biol.* **52**, 5085–5099 (2007).
- ²²K. Brinker and B. J. Roth, "The effect of electrical anisotropy during magnetoacoustic tomography with magnetic induction," *IEEE Trans. Biomed. Eng.* **55**, 1637–1639 (2008).
- ²³R. Xia, X. Li, and B. He, "Reconstruction of vectorial acoustic sources in time-domain tomography," *IEEE Trans. Med. Imaging* **28**, 669–675 (2009).
- ²⁴G. Hu and B. He, "Magnetoacoustic imaging of electrical conductivity of biological tissues with magnetic induction at a spatial resolution better than 2 mm," *PLoS ONE* **6**, e23421 (2011).
- ²⁵X. Li and B. He, "Multi-excitation magnetoacoustic tomography with magnetic induction for bioimpedance imaging," *IEEE Trans. Med. Imaging* **29**, 1759–1767 (2010).
- ²⁶X. Li, L. Mariappan, and B. He, "Three-dimensional multi-excitation magnetoacoustic tomography with magnetic induction," *J. Appl. Phys.* **108**, 124702 (2010).
- ²⁷L. Mariappan, X. Li, and B. He, "B-scan based acoustic source reconstruction for magnetoacoustic tomography with magnetic induction (MAT-MI)," *IEEE Trans. Biomed. Eng.* **58**, 713–720 (2011).
- ²⁸G. Hu, X. Li, and B. He, "Imaging biological tissues with electrical conductivity contrast below 1 S m⁻¹ by means of magnetoacoustic tomography with magnetic induction," *Appl. Phys. Lett.* **97**, 103705 (2010).
- ²⁹G. Hu and B. He, "Magnetoacoustic imaging of human liver tumor with magnetic induction," *Appl. Phys. Lett.* **98**, 023703 (2011).
- ³⁰L. Mariappan and B. He, "Magneto acoustic tomography with magnetic induction: Bioimpedance reconstruction through vector source imaging," *IEEE Trans. Med. Imaging* **32**, 619–627 (2013).
- ³¹B. J. Roth, "The role of magnetic forces in biology and medicine," *Exp. Biol. Med.* **236**, 132–137 (2011).
- ³²H. Ammari, Y. Capdeboscq, H. Kang, and A. Kozhemyak, "Mathematical models and reconstruction methods in magneto-acoustic imaging," *Euro J. Appl. Math.* **20**, 303–317 (2009).
- ³³X. Sun, F. Zhang, Q. Ma, J. Tu, and D. Zhang, "Acoustic dipole radiation based conductivity image reconstruction for magnetoacoustic tomography with magnetic induction," *Appl. Phys. Lett.* **100**, 024105 (2012).
- ³⁴X. Sun, D. Fang, D. Zhang, and Q. Ma, "Acoustic dipole radiation based electrical impedance contrast imaging approach of magnetoacoustic tomography with magnetic induction," *Med. Phys.* **40**, 052902 (12pp.) (2013).
- ³⁵W. Wang and S. R. Eisenberg, "A three-dimensional finite element method for computing magnetically induced currents in tissues," *IEEE Trans. Magn.* **30**, 5015–5023 (1994).
- ³⁶K. Ranganathan and W. F. Walker, "A novel beamformer design method for medical ultrasound. Part I: Theory," *IEEE Trans. Ultrason. Ferroelec. Freq. Control* **50**, 15–24 (2003).
- ³⁷T. Vaughan, L. DelaBarre, C. Snyder, J. Tian, C. Akgun, D. Shrivastava, W. Liu, C. Olson, G. Adrian, J. Strupp, P. Andersen, A. Gopinath, P. Moortele, M. Garwood, and K. Ugurbil, "9.4T human MRI: Preliminary results," *Magn. Reson. Med.* **56**, 1274–1282 (2006).
- ³⁸V. Walsh and A. Cowey, "Transcranial magnetic stimulation and cognitive neuroscience," *Nature Rev. Neurosci.* **1**, 73–80 (2000).
- ³⁹Y. Xu and L. V. Wang, "Effects of acoustic heterogeneity on thermoacoustic tomography in the breast," *IEEE Trans. Ultrason. Ferro. Frequency Contr.* **50**, 1134–1146 (2003).
- ⁴⁰X. Wang, Y. Pang, G. Ku, X. Xie, G. Stoica, and L. V. Wang, "Noninvasive laser-induced photoacoustic tomography for structural and functional *in vivo* imaging of the brain," *Nat. Biotechnol.* **21**, 803–806 (2003).