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Magnetoacoustic microscopic imaging of conductive objects and nanoparticles distribution

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Magnetoacoustic tomography has been demonstrated as a powerful and low-cost multi-wave imaging modality. However, due to limited spatial resolution and detection efficiency of magnetoacoustic signal, full potential of the magnetoacoustic imaging remains to be tapped. Here we report a high-resolution magnetoacoustic microscopy method, where magnetic stimulation is provided by a compact solenoid resonance coil connected with a matching network, and acoustic reception is realized by using a high-frequency focused ultrasound transducer. Scanning the magnetoacoustic microscopy system perpendicularly to the acoustic axis of the focused transducer would generate a two-dimensional microscopic image with acoustically determined lateral resolution. It is analyzed theoretically and demonstrated experimentally that magnetoacoustic generation in this microscopic system depends on the conductivity profile of conductive objects and localized distribution of superparamagnetic iron magnetic nanoparticles, based on two different but related implementations. The lateral resolution is characterized. Directional nature of magnetoacoustic vibration and imaging sensitivity for mapping magnetic nanoparticles are also discussed. The proposed microscopy system offers a high-resolution method that could potentially map intrinsic conductivity distribution in biological tissue and extraneous magnetic nanoparticles. *Published by AIP Publishing.*
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I. INTRODUCTION

In recent decades, magnetoacoustic imaging has attracted tremendous research interest for biomedical applications.¹ By integrating coil-based magnetic stimulation and ultrasonic detection, magnetoacoustic tomography (MAT) is capable of detecting conductive objects (CO) (called magnetoacoustic tomography with magnetic induction—MAT-MI),² as well as extraneous nanoparticles.³ In MAT-MI, a time-varying magnetic stimulation (usually pulsed magnetic excitation with microsecond duration) is applied to induce eddy current on the conductive objects. In the presence of a static magnetic field, the induced Lorentz force would lead to localized mechanical vibrations and produce detectable ultrasound signals. Such acoustic signals then can be acquired to reconstruct to map the electrical conductivity of imaging objects.⁴ Imaging magnetic nanoparticles is another attractive capability of the magnetoacoustic tomography, in which the magnetoacoustic wave is induced by the magnetic force acted on superparamagnetic iron oxide nanoparticles (SPIONs). Compared to other multi-wave imaging modalities (e.g., photoacoustic imaging and thermoacoustic imaging), magnetoacoustic imaging provides a more efficient solution in terms of energy transfer due to the non-magnetic nature of human body,⁵ which enables a superior penetration depth with no magnetic loss. For both applications, generated magnetoacoustic signals are normally collected by a scanning ultrasound detector that is rotated in either a circular or a cylindrical geometry—followed by algorithm based image reconstruction.

In terms of imaging performance, spatial resolution is one of the most important parameters in magnetoacoustic reconstruction. However, among all reported MAT, a spatial resolution of several millimeters (e.g., 3.0 mm in-plane resolution and 7.0 mm elevation resolution in Ref. 2) is achieved, and recently published high-frequency magnetoacoustic tomography (hfMAT-MI) obtained a spatial resolution of 1.0 mm resolution,⁶ which impedes its application for high-resolution imaging. The low in-plane and elevation resolution are partly due to the long duration of magnetic excitation (normally μ s pulse width), partly due to the limited bandwidth of the acoustic system adopted in previously report MAT.⁷ Higher frequency transducer with wider bandwidth can be employed to push the resolution limits; however, increased acoustic attenuation (0.5–1.5 dB/MHz/cm in biological tissue)⁸ along the long acoustic path (scanning radius of hundreds of millimeters)⁶ would greatly reduce the signal noise ratio (SNR) and imaging sensitivity. Though the low spatial resolution can be further improved by employing ultrashort stimulation with narrower pulse duration (e.g., optic-based nanosecond magnetic stimulator),⁹ induced bulky magnetic system and increased cost will make the magnetoacoustic technique less cost effective to apply in clinical examinations.

On the other hand, detection sensitivity is another key performance feature for any imaging system. For one of the most important applications of magnetoacoustics—MAT sensing of nanoparticles, magnetoacoustic detection suffers relative low efficiency due to inefficient acoustic receiving.¹⁰ In MAT, to render a homogeneous and circular-symmetrical magnetic stimulation, the coil based magnetic stimulator is always vertically placed along the rotation axis. In such a

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way, magnetoacoustic vibration and propagation are dominant along this axial direction,^{3,10} whereas the ultrasound transducer is horizontally placed in the tomographic plane for signal collection. Therefore, the detection efficiency of the magnetoacoustic wave and imaging sensitivity are highly limited.

In the present study, we have developed a novel high-resolution magnetoacoustic microscopy (MAM) system that is able to map both electrical conductivity profile and SPIONs distribution with a high lateral resolution of finer than 200 μm . Our imaging method differs significantly from the prior arts in magnetoacoustic tomography with magnetic induction. A compact and low-cost resonance coil and a matching network that is typically adopted in MRI are employed to form the magnetic stimulator.^{11,12} Acoustic signals are collected by a raster-scanning focused transducer (FTR) with a large numerical aperture (NA). Magnetoacoustic images were acquired directly without resorting to image reconstruction. For MAM imaging conductive objects, magnetoacoustic generation relies on eddy current induced Lorentz force, whereas imaging SPIONs distribution is based on magnetic translational force under the alternating magnetic field (AMF). Such two applications of the proposed MAM system can be achieved by two slightly different configurations.

II. THOERIES AND METHODS

A. Magnetic induction based magnetoacoustics

To generate the dynamic magnetic field, a radio-frequency coil is employed as the magnetic stimulator. Such magnetic coil is always driven by a short-time current burst $I(t) = I_0 f(t)$, where I_0 is the current amplitude and $f(t)$ is the unit temporal profile of the transient current. By the law of Biot and Savart, the stimulated time-varying magnetic field $\mathbf{B}(\mathbf{r}, t)$ can be computed as¹³

$$\mathbf{B}(\mathbf{r}, t) = \frac{\mu_0 N I(t)}{4\pi} \int \frac{\mathbf{e} \times (\mathbf{R} - \mathbf{R}')}{|\mathbf{R} - \mathbf{R}'|^3} dl' = \frac{\mu_0 N I_0}{4\pi} \mathbf{S}(\mathbf{r}) f(t), \quad (1)$$

where μ_0 is the permeability of free space, $\mathbf{R}$ is the position vector on coil, and $\mathbf{S}(\mathbf{r}) = \int \frac{\mathbf{e} \times (\mathbf{R} - \mathbf{R}')}{|\mathbf{R} - \mathbf{R}'|^3} dl'$ is an integral term that is only determined by the geometry of solenoid coil. Therefore, the generated time-varying magnetic field $\mathbf{B}(\mathbf{r}, t)$ can be expressed as the product of the temporal function $f(t)$ and a spatial term $\mathbf{B}(\mathbf{r})$, i.e., $\mathbf{B}(\mathbf{r}, t) = \mathbf{B}(\mathbf{r}) f(t)$. Simultaneously, the eddy current $\mathbf{J}(\mathbf{r}, t)$ will be generated with the intensity being proportional to the regional conductivity $\sigma(\mathbf{r})$: $\mathbf{J}(\mathbf{r}, t) = \sigma(\mathbf{r}) \mathbf{E}(\mathbf{r}, t)$, where $\nabla \cdot \mathbf{E}(\mathbf{r}, t) = -\frac{\partial \mathbf{B}(\mathbf{r}, t)}{\partial t}$. Under a static magnetic field $\mathbf{B}_0(\mathbf{r})$, induced Lorentz force $\mathbf{F}_L(\mathbf{r}, t) = \mathbf{J}(\mathbf{r}, t) \times \mathbf{B}_0(\mathbf{r})$ would consequently lead to localized mechanical vibration and subsequent acoustic propagation:

$$\nabla^2 p(\mathbf{r}, t) - \frac{1}{c^2} \frac{\partial^2 p(\mathbf{r}, t)}{\partial t^2} = \nabla \cdot [\mathbf{J}(\mathbf{r}, t) \times \mathbf{B}_0(\mathbf{r})], \quad (2)$$

where $p(\mathbf{r}, t)$ is the acoustic wave and c is the sound speed in surrounding medium. Since $\nabla \times \mathbf{B}_0(\mathbf{r}) = 0$ always holds for

the static magnetic field, $\nabla \cdot [\mathbf{J}(\mathbf{r}, t) \times \mathbf{B}_0(\mathbf{r})]$ can be further derived to be $\nabla \times \mathbf{J}(\mathbf{r}, t) \cdot \mathbf{B}_0(\mathbf{r})$. Solved by the Green function method with the zero-initial-value condition ($p(\mathbf{r}, t = 0) = 0$, $\frac{\partial p}{\partial t}(\mathbf{r}, t = 0) = 0$),¹⁴ the acoustic pressure at $\mathbf{r}$ can be derived to be⁷

$$p(\mathbf{r}, t) = -\frac{1}{4\pi} \iiint \frac{\nabla \times \mathbf{J}(\mathbf{r}, t') \cdot \mathbf{B}_0(\mathbf{r})}{|\mathbf{r} - \mathbf{r}'|} dV \bigg|_{t'=t-\frac{|\mathbf{r}-\mathbf{r}'|}{c}}. \quad (3)$$

Above volume integral is calculated inside a sphere with the radius of ct centered at $\mathbf{r}$, and integration variable $\mathbf{r}'$ is the position inside the sphere where the magnetoacoustic wave generated. The acoustic source term is not taken at time t but at an earlier time $t' = t - |\mathbf{r} - \mathbf{r}'|/c$; therefore, such an integration function is also called retarded potential.¹⁵ According to Faraday's Law and Ohm's Law,⁷ the separation of temporal term and spatial term also holds for induced electrical field and eddy current density, i.e., $\mathbf{E}(\mathbf{r}, t) = \mathbf{E}(\mathbf{r}) f'(t)$ and $\mathbf{J}(\mathbf{r}, t) = \mathbf{J}(\mathbf{r}) f'(t)$, where the prime denotes the first order time derivative. Hence, the acoustic pressure can be expressed as⁷

$$p(\mathbf{r}, t) = -\frac{1}{4\pi} \iiint \frac{AS(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} f' \left(t - \frac{|\mathbf{r} - \mathbf{r}'|}{c} \right) dV, \quad (4)$$

where $AS(\mathbf{r}') = -\mathbf{B}_0(\mathbf{r}') \cdot \mathbf{B}(\mathbf{r}') \sigma(\mathbf{r}') - \mathbf{B}_0(\mathbf{r}') \times \mathbf{E}(\mathbf{r}') \cdot \nabla \sigma(\mathbf{r}')$ is the acoustic source term in spatial domain. Given such a magnetoacoustic source term, the acoustic pressure field can be solved by integrating the product of the acoustic source and the corresponding Green's function for all the positions within the object volume. Equation (4) provides the basic formula to calculate the magnetoacoustic pressure generated by an arbitrary conductive objects, which suggests that magnetoacoustic vibration is related to the distribution of both conductivity $\sigma(\mathbf{r})$ and its gradient $\nabla \sigma(\mathbf{r})$.

The analytic solution of a magnetoacoustic problem is not available unless for some simple geometric structures such as an infinite layer, a sphere, or a cylinder.¹⁶ We now consider an infinite conductive layer with a thickness of d under an ideal impulse magnetic excitation $[\mathbf{B}(\mathbf{r}, t) = \mathbf{B}(\mathbf{r}) \delta(t)]$. As in Ref. 17, by assuming that the localized electromagnetic field and other physical quantities are sufficiently uniform in the lateral plane, such an acoustic problem can be treated as a one-dimensional problem in the z -axis;¹⁷ with the conductivity boundary at the $z = z_0$ plane^{15,18}

$$p(z, t) = -\frac{c}{2} \int AS(z') \cdot \delta \left(t - \frac{z - z'}{c} \right) dz'. \quad (5)$$

Accordingly, the acoustic source term is changed to be $AS(z) = B_0(z) B(z) \sigma(z) + B_0(z) E_y(z) \frac{\partial \sigma(z)}{\partial z}$, where $E_y(z)$ is the induced electrical field along the y direction in space. Integrating such an acoustic source term along the conductive layer where magnetoacoustic vibrations are generated, we obtain¹⁸

$$p(z, t) = -\frac{c^2}{2} AS(z - ct), \quad (6)$$

in which the acoustic source term $AS(z - ct)$ exists only in the range $z_0 \leq z - ct \leq z_0 + d$ and is zero otherwise. Similar

derivation of the analytical solution is also provided in Ref. 18. If a metal plate is employed as the conductive material, the magnetoacoustic vibration is only effectively generated within its skin depth (several tens of micrometer)¹⁹ around $z = z_0$. When an ultrasound transducer with an ideal infinitesimal focal spot and the focal distance of F is vertically placed and focused on the conductive boundary ($z = z_0$), the magnetoacoustic signal would occur at time $t = \frac{F}{c}$, corresponding to the time of flight from the focal point to the transducer aperture. On substitution of above acoustic source term $AS(z - ct)$ and the magnetic flux density $B(z)$ in Eq. (1) into Eq. (6), the received magnetoacoustic amplitude can be expressed as

$$p\left(z_t, t = \frac{F}{c}\right) = A_0(z_0)\sigma(z_0) + A_1(z_0) \cdot \frac{\partial\sigma(z_0)}{\partial z}, \quad (7)$$

$$\left\{ \begin{array}{l} A_0(z_0) = \frac{\mu_0 c^2 N I_0}{8\pi} S(z_0) B_0(z_0) \\ A_1(z_0) = \frac{c^2}{2} B_0(z_0) E_y(z_0) \end{array} \right\},$$

where z_t and z_0 , respectively, denote the position of focused transducer and its focal spot. The coefficient $A_0(z_0)$ becomes a constant if $S(z_0)$ and $B_0(z_0)$ keeps unchanged at different positions in the lateral plane, whereas $A_1(z_0)$ is related to the $B_0(z_0)$ and $E_y(z_0)$ at the focal spot. Noted that magnetoacoustic generation from conductive objects is spatially related to both electrical conductivity $\sigma(z_0)$ and its gradient $\frac{\partial\sigma(z_0)}{\partial z}$, which provides the imaging contrast mechanism for the magnetoacoustic system to image conductive objects. Noticed that the conductivity gradient is singular at the conductive boundaries, such singularity term is always replaced by a linear approximation or avoided by using an integral method for simple numerical calculation.^{17,20}

In the three-dimensional case, lateral resolution is provided by the diffraction limited focal spot of the focused ultrasound transducer. Since the magnetoacoustic wave only within the focal spot can be effectively collected by the focused transducer, the amplitude of the received magnetoacoustic signal actually reflects the averaged information of conductivity distribution around the focal point.²¹

B. Magnetic translational force based magnetoacoustics

Another application of the magnetoacoustics is imaging extraneous magnetic nanoparticles. Being different from magnetic induction based magnetoacoustics, where acoustic vibration is induced by Lorentz force, magnetoacoustic sensing of SPIONs relies on the magnetic translation force.³ When an external magnetic field is applied to the magnetic nanoparticles, magnetically motivated translational force $\mathbf{F}_m$ per unit volume can be expressed as

$$\mathbf{F}_m(\mathbf{r}, t) = \frac{v_m \chi_m \phi_m}{\mu_0} (\mathbf{B}(\mathbf{r}, t) \cdot \nabla) \mathbf{B}(\mathbf{r}, t), \quad (8)$$

where χ_m is the initial susceptibility of nanoparticles, v_m is the volume of the overall nanoparticles, and $\phi_m(\mathbf{r})$ describes the localized volume fraction of the nanoparticles, which indicates

the localized concentration of nanoparticles. With $(\mathbf{B}(\mathbf{r}, t) \cdot \nabla) \mathbf{B}(\mathbf{r}, t) = \frac{1}{2} \nabla(B^2(\mathbf{r})) \delta(t)$, such magnetically motivated force would act on surrounding biological medium and lead to subsequent magnetoacoustic emission^{3,22}

$$\nabla^2 p(\mathbf{r}, t) - \frac{1}{c^2} \frac{\partial^2}{\partial t^2} p(\mathbf{r}, t) = \frac{v_m \chi_m \phi_m(\mathbf{r})}{2\mu_0} \nabla^2(B^2(\mathbf{r})) \delta(t). \quad (9)$$

Like the divergence of Lorentz force in (2), the divergence of the magnetic translational force acts as the acoustic source term. This gives the induced acoustic pressure

$$p(\mathbf{r}, t) = -\frac{v_m \chi_m}{8\pi\mu_0} \iiint \phi_m(\mathbf{r}') \nabla^2(B^2(\mathbf{r}')) \frac{\delta\left(t - \frac{|\mathbf{r} - \mathbf{r}'|}{c}\right)}{|\mathbf{r} - \mathbf{r}'|} dV. \quad (10)$$

Equation (10) provides the basic formula to calculate the magnetoacoustic signal generated by the SPIONs ferrofluid, which suggests that magnetoacoustic vibration is related to the susceptibility of the nanoparticles and its volume fraction in SPIONs ferrofluid.

The analytic solution can be obtained by analyzing the magnetoacoustic generation from a thin ferrofluid layer with a thickness of d . Similarly, by assuming that magnetic field and nanoparticle distribution are sufficiently uniform in the lateral plane, this problem can be simplified as a one-dimensional problem in the z -axis¹⁵

$$p(z, t) = -\frac{cv_m \chi_m}{4\mu_0} \int \frac{\partial^2 B^2(z')}{\partial z'^2} \phi_m(z') \delta\left(t - \frac{z - z'}{c}\right) dz'. \quad (11)$$

Integrating the acoustic source term along the z axis from, the acoustic pressure distribution can be given as¹⁸

$$p(z, t) = \frac{c^2 v_m \chi_m}{4\mu_0} \frac{\partial^2 B^2(z - ct)}{\partial z^2} \phi_m(z - ct), \quad (12)$$

where ϕ_m are positive values only in the range $z_0 \leq z - ct \leq z_0 + d$ and zero otherwise. When such thin ferrofluid layer is placed within the focal range (depth of focus) of a focused ultrasound transducer (at $z = z_t$), the magnetoacoustic amplitude would be extracted at $t = \frac{F}{c}$, which corresponding to the distance from the focal point to the actual acoustic aperture surface. On substitution of $B(z)$ into Eq. (12), the final expression of the magnetoacoustic amplitude received at the focal spot can be expressed as

$$p\left(z_t, t = \frac{F}{c}\right) = A(z_0) \phi_m(z_0),$$

$$A(z_0) = \frac{c^2 N^2 I_0^2 \mu_0 v_m \chi_m}{64\pi^2} \frac{\partial^2 S^2(z_0)}{\partial z^2}. \quad (13)$$

It can be observed that the magnetoacoustic amplitude linearly depends on the localized nanoparticle concentration $\phi_m(z_0)$ at the focal spot. The coefficient $A(z_0)$ becomes a constant if the term $\frac{\partial^2 S^2(z)}{\partial z^2}$ is approximately homogeneous around z_0 within the thin ferrofluid layer.

In above derivations of analytical solution, an ideal impulse magnetic field with delta temporal function $\delta(t)$ is

the alternating magnetic field. In this way, the oscillating translation force is maximized without significant physical rotation and friction force in the imaging process.²⁶ The second reason is to suppress the thermoacoustic effect of SPIONs. Once weak static magnet is positioned, a unidirectional oscillating magnetic field, instead of an AMF, is applied to magnetic nanoparticles. Hence, an effective hysteresis loop for magnetic heating cannot be established, leading to suppressive thermoacoustic generation.²⁷ Therefore, by applying such weak magnet, the received ultrasound signals in the experiment can be maximized and only from magnetoacoustic vibration.

III. RESULTS AND DISCUSSION

A. MAM imaging of conductive objects

Experimental demonstration of magnetic induction based MAM system is performed on two closely-positioned aluminum sheet with a thickness of 1 mm. Figure 3(a) depicts the time domain acoustic waveform received by the focused ultrasonic transducer. Although we wrap aluminum foil on ultrasonic transducer and the wire for electromagnetic shielding, strong interference saturates the detection for a period of $3\ \mu\text{s}$. Considering an acoustic velocity of $1500\ \text{m/s}$ in water, such electromagnetic interference produces a $4.5\ \text{mm}$ dead zone from the transducer's active surface. Since such a distance is much shorter than the focal length of the focused transducer, this contamination will not bring severe distortion to the generated magnetoacoustic signals. To prevent the interference of static surface charge induced

electromagnetic acoustic,²⁸ the acoustic signal without the placement of the permanent magnets is recorded additionally [red waveform in Fig. 3(a)], which is at least 10 times smaller than the magnetoacoustic signal at where it is generated, and thus can be neglected. The later peak at around $16\ \mu\text{s}$ represents the reflected acoustic wave, which is emitted by the ultrasound transducer itself under strong radio frequency excitation.

The MAM image of two parallel metal sheets separated by $2.7\ \text{mm}$ is first displayed in Fig. 3(b). For explicit visualization, averaged amplitude profile along the x direction is plotted in Fig. 3(d). The well-bedded amplitude profile can be divided into five parts (separated by the black line): conductive zone ($0\text{--}0.9\ \text{mm}$ and $3.9\text{--}5.0\ \text{mm}$ in the x axis), non-conductive zone ($1.4\text{--}3.4\ \text{mm}$), and partial-conductive zone ($0\text{--}0.9\ \text{mm}$ and $3.9\text{--}5.0\ \text{mm}$) in which only part of conductive edge is in the scope of focused transducer, caused by the diffraction-limited acoustic resolution. Specifically, it is observed that the strongest magnetoacoustic wave is emitted from the conductive edge, which corresponds to the brightest zone in the MAM image. Such phenomenon can be well explained that both conductivity and its spatial gradient contribute to the acoustic generation, as stated in (5). Like in MAT,²⁹ it was also demonstrated that the higher gradient magnitude yields the higher magnetoacoustic signal and reconstructed intensity. Though it is not a direct measure of electrical conductivity, such magnetoacoustic signal can give some valuable information about conductivity distribution.

Here, two different methods are adopted to characterize the lateral resolution of MAM system. First, edge spread

FIG. 3. (a) Time domain acoustic signal received by the focused ultrasonic transducer with (blue) and without (red) the placement of static magnet pair; (b) MAM imaging of two metal sheets separated by $2.7\ \text{mm}$; (c) MAM imaging of two metal sheets separated by $200\ \mu\text{m}$; (d) amplitude profile of (b) along the x direction; (e) edge spread function (ESF), line spread function (LSF) along the conductive edge and corresponding full-width-half-maximum (FWHM); (f) amplitude profile of (c) along the x direction.

function (ESF) and corresponding line spread function [LSF, Fig. 3(e)] of the conductive edge are statistically analyzed and presented. Lateral resolutions, defined as full-width-half-maximum (FWHM) of the averaged LSF, is about $191\ \mu\text{m}$, which is in line with the theoretical diffraction-limited focal diameter of the used focused transducer ($0.62 \frac{c}{f_c \cdot \text{NA}} = 183\ \mu\text{m}$, where f_c is the cut off frequency of transducer).²¹ Lateral resolution gets further confirmed by imaging two metal sheets separated by $200\ \mu\text{m}$, which is regulated and measured by an optical reflective microscope. As expected, two nearby conductive edges can be clearly resolved, which demonstrates that a lateral resolution of better than $200\ \mu\text{m}$ can be achieved in the current MAM platform.

In this work, a 20 MHz 0.25 NA focused transducer is employed for magnetoacoustic signal acquisition. In biological tissues, assuming a normal acoustic attenuation of 1.0 dB/MHz/cm, there will be a moderate signal attenuation of 25.4 dB from the magnetoacoustic source to the transducer surface, which is slightly larger than that of 24.0 dB in MAT with a 1.5 MHz acoustic transducer and 160 mm scanning radius.⁶ In addition, on account of frequency dependent eddy current generation and magnetoacoustic vibration while

imaging conductive objects, above high attenuation can be, to some extent, neutralized. Therefore, MAM with high acoustic frequency is still preferred.

B. MAM imaging of nanoparticles distribution

To demonstrate the validity of MAM for imaging SPIONs distribution, phantom experiments on ferrofluid (3327NG, 20 mg/ml, Skyspring Nanomaterials) are conducted. As shown in Fig. 1, making slight changes on the use of static magnet, the MAM system can be seamlessly switched to imaging nanoparticles distribution. First, Fig. 4(a) records a sample magnetoacoustic waveform from a ferrofluid-filled plastic tube (PVC, $\varnothing = 2\ \text{mm}$) located at the focal plane of scanning ultrasound transducer. The magnetoacoustic wave generation is received in a $2\ \mu\text{s}$ time duration with the amplitude peak occurring at around $9\ \mu\text{s}$. Envelop of the received acoustic signal is also provided to present the explicit magnetoacoustic amplitude, from which an increasing tendency of magnetoacoustic emission can be roughly observed from about 8 to $9\ \mu\text{s}$.

The tomographic image of MAM at different depths [$z' = 0.5, 1.0$, and $1.5\ \text{mm}$. The location of the upper surface

FIG. 4. (a) Time domain acoustic signal received by the focused ultrasonic transducer; (b) Schematic of MAM imaging of a SPIONs ferrofluid tube; (c)–(e) MAM imaging of SPIONs at different depths (1.5, 1.0, and 0.5 mm below the top of the tube).

of plastic tube is set to be the origin of the z' axis, as shown in Fig. 4(b)] inside the ferrofluid tube are further presented in Figs. 4(c)–4(e). Serving as the contrast agent, SPIONs ferrofluid enables the outline of the plastic tube to be clearly visualized with a width of about 2 mm. Notably, from bottom to top in the ferrofluid tube, a significant decrease of magnetoacoustic amplitude (represented by brightness) can be clearly observed, which coincides with amplitude tendency in the time-resolved magnetoacoustic signal, as shown in Fig. 4(a). These results can be well explained by the axial distribution of ferrofluid inside the tube. Owing to the presence of gravity and magnetic attraction induced by the weak static magnet, a portion of SPIONs will settle to the bottom of the tube, leading to higher concentration of SPIONs and stronger magnetoacoustic emission around tube bottom. It has been reported that the reconstructed magnetoacoustic tomographic image is always dominated by the prominent boundary information.^{3,4,30} For example, in Ref. 3, only the boundary of the SPIONs ferrofluid can be clearly imaged though SPIONs is homogeneously dispersed inside the ferrofluid. Such absence of the internal information is mainly caused by the speckle free nature³¹ under the limited-view tomographic scenarios,³² in which magnetoacoustic response cancel out for equivalent neighboring particles, whereas builds up the constructive interference at the boundary. In this work, internal SPIONs distribution instead of the only boundary information is obtained, as shown in Figs. 4(c)–4(e). This is partly due to the fact that the nanoparticles in this work are not distributed uniformly along the axial direction and is partly due to the different scanning mechanisms compared to MAT. Therefore, the speckle free nature shows less influence on the imaging performance in MAM.

The directivity of magnetoacoustic vibration and imaging sensitivity are also analyzed here. Different acoustic sources have different propagation properties and acoustic field distributions. In photoacoustics/thermoacoustics, the acoustic source is the heating induced time-variant thermal expansion, which has the isotropic propagation properties. In these cases, acoustic radiation shows no directivity and can be modelled as an acoustic monopole source.³³ By contrast, in magnetoacoustics, acoustic vibration is induced by the directional magnetic force, which just makes the spread of acoustic vibration has directivity. And this type of vibration propagation can be represented by an acoustic dipole source model³⁴ with an extra projection term $\cos \theta_R$, where θ_R describes the propagation direction of the magnetoacoustic wave. Therefore, the placement of ultrasound transducer and the scanning method should be carefully considered for a high detection efficiency of magnetoacoustic wave.

In the well-known configuration of magnetoacoustic imaging, to render a homogenous magnetic stimulation, the coil is always vertically placed below the SPIONs, as shown in Fig. 4(b). In this scenario, the alternative magnetic field and its gradient at the location of ferrofluid would be mainly oriented in the z direction.³ Consequently, magnetoacoustic vibration would show the strongest propagation in the z direction. Correspondingly, the vertically placed ultrasound transducer in the method of MAM ($\cos \theta_R = 1$) would theoretically receive the strongest magnetoacoustic wave. However,

the horizontally placed transducer in MAT ($\cos \theta_R = 0$) would show lowest detection sensitivity in principle.

To demonstrate the directional nature of magnetoacoustic vibration and superior detection sensitivity in MAM, further experiments on SPIONs along different receiving directions are performed, as shown in Fig. 5. To avoid the

FIG. 5. Time domain acoustic signal received by a planar ultrasonic transducer at different receiving angles: (a) 0°; (b) 45°; and (c) 90°. Insets show the direction of ultrasound transducer and the direction of magnetic force. (d) Normalized magnetoacoustic amplitude versus receiving angle of ultrasound transducer.

misalignment between the transducer focal spot and magnetoacoustic vibration, another 20 MHz planar ultrasound transducer with much wider beam width is employed, which is mounted on a continuous rotation stage (CR1/M-27) for direction regulation. When the ultrasound transducer is positioned rightly above the SPIONs ferrofluid along the z direction (same as the MAM configuration with $\theta_R = 0$), the magnetoacoustic signal with an amplitude of 9 mV is observed from Fig. 5(a). When the ultrasound transducer is horizontally positioned (same as the MAT configuration with $\theta_R = 90^\circ$), the magnetoacoustic amplitude is about 2.8 mV [Fig. 5(b)], which is at least three times smaller than that shown in Fig. 5(a). For comparison, Fig. 5(c) also depicts the acoustic signal measured at $\theta_R = 45^\circ$, which shows a compromised amplitude. Figure 5(d) summarizes the magnetoacoustic amplitude obtained at 7 different receiving angles with a 15° step size. In line with the form of the directional term $\cos \theta_R$, the maximum and minimum of the magnetoacoustic amplitude are obtained, respectively, at $\theta_R = 0^\circ$ and $\theta_R = 90^\circ$, which suggests an improved detection sensitivity in the method of MAM.

In the current MAM system, for explicit image rendering, a relatively high concentration of SPIONs (20 mg/ml) is necessary. However, there is still much room to further improve the imaging sensitivity for lower nanoparticle concentration. First, sensitivity improvement can be realized by using a higher-power magnetic stimulator. Compared with normal hundreds of milli-Tesla magnetic stimulation adopted in transcranial magnetic stimulation (TMS),³⁵ the 5 mT magnetic field used in the current MAM system is much smaller, suggesting an at least 20-fold improvement of sensitivity to be potentially obtained. On the other hand, system contrast and imaging sensitivity may be further improved by using more efficient magnetic nanoparticles.³⁶ Compared to the SPIONs with a relative-low susceptibility χ_m of about 0.1 in this work, utilization of ferromagnetic nanoparticle^{37,38} with large susceptibility up to several hundred would greatly enhance the available sensitivity, which makes it possible to utilize magnetic nanoparticles with clinically acceptable concentrations (sub-mg/ml level) for in-vivo MAM imaging.

IV. CONCLUSION

In this work, we report a novel magnetoacoustic microscopy system that can map both electrical conductivity and magnetic nanoparticles distribution with a high lateral resolution. Our study demonstrates several attractive capabilities of the proposed MAM, compared to state of art MAT. The first is the greatly improved in-plane resolution. Determined by numerical aperture of the high frequency ultrasound transducer, a high resolution of better than $200 \mu\text{m}$ is obtained in this work. The second is the superior detection sensitivity of magnetoacoustic wave for imaging nanoparticles, which is attributed to the alignment of magnetoacoustic vibration directivity and the transducer position. Third, MAM enables a direct image rendering after a two-dimensional raster scanning, without resorting to computationally expensive reconstruction process. With currently

demonstrated capabilities and traceable technical advancements, MAM has the potential to become an important non-invasive imaging modality for biomedical applications. Future works will aim to customize and improve the MAM system to demonstrate the validity of high resolution magnetoacoustic microscopic imaging in human tissues *in vivo*.

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