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Magnetoacoustic Tomography with Magnetic Induction (MAT-MI) for Imaging Electrical Conductivity of Biological Tissue: A Tutorial Review

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Abstract

Magnetoacoustic tomography with magnetic induction (MAT-MI) is a noninvasive imaging method developed to map electrical conductivity of biological tissue with millimeter level spatial resolution. In MAT-MI, a time-varying magnetic stimulation is applied to induce eddy current inside the conductive tissue sample. With the existence of a static magnetic field, the Lorentz force acting on the induced eddy current drives mechanical vibrations producing detectable ultrasound signals. These ultrasound signals can then be acquired to reconstruct a map related to the sample's electrical conductivity contrast. This work reviews fundamental ideas of MAT-MI and major techniques developed in these years. First, the physical mechanisms underlying MAT-MI imaging are described including the magnetic induction and Lorentz force induced acoustic wave propagation. Second, experimental setups and various imaging strategies for MAT-MI are reviewed and compared together with the corresponding experimental results. In addition, as a recently developed reverse mode of MAT-MI, magneto-acousto-electrical tomography with magnetic induction (MAET-MI) is briefly reviewed in terms of its theory and experimental studies. Finally, we give our opinions on existing challenges and future directions for MAT-MI research. With all the reported and future technical advancement, MAT-MI has the potential to become an important noninvasive modality for electrical conductivity imaging of biological tissue.

Keywords

magnetoacoustic tomography with magnetic induction; MAT-MI; MAET-MI; Lorentz force; conductivity; bioimpedance; imaging

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1. Introduction

Electrical properties of biological tissue including electrical conductivity σ and permittivity γ are important biophysical parameters in the studies of electrophysiology and electromagnetic therapies such as transcranial direct current stimulation (tDCS) (Malmivuo *et al.*, 1995; Sadleir *et al.*, 2010). In addition, due to their changes under physiological and pathological conditions, tissue electrical properties may serve as an imaging contrast for possible diagnosis and research use (Geddes and Baker, 1967). Previous studies have shown that cancerous breast tumor tissue has significantly different electrical properties than normal breast tissue or benign tumors (Surowiec *et al.*, 1988; Jossinet, 1996, 1998). Significant electrical conductivity difference has also been found between liver tumors and normal liver tissue (Haemmerich *et al.*, 2003). Generally such kind of differences between carcinoma and normal tissue are attributed to different cellular water content, amount of extracellular fluid, membrane permeability, packing density and orientation of the malignant cells (Zou and Guo, 2003). Other than carcinomas, tissues under conditions of ischemia, hemorrhage or edema are expected to exhibit different electrical properties as blood and most body fluid have quite different conductivity and permittivity than most other soft tissues (Fallert *et al.*, 1993; Cinca *et al.*, 1997). Therefore, noninvasive imaging methods measuring tissue electrical properties with good accuracy and high spatial resolution are of great research and clinical interest.

Over decades, different electromagnetic imaging methods have been developed to measure electrical properties of biological tissue, including electrical impedance tomography (EIT) (Barber and Brown, 1984; Cheney *et al.*, 1999), magnetic induction tomography (MIT) (Griffiths *et al.*, 1999) and magnetic resonance electrical impedance tomography (MREIT) (Khang *et al.*, 2002; Woo and Seo, 2008). Among these techniques, EIT maps tissue electrical properties using acquired surface voltage measurements in response to different current injections. Though EIT has advantages in its low cost, real-time speed and safety, major limitations including its low spatial resolution and degraded sensitivity in the center of an object still hinder its broad applications. In addition, due to its use of current injection through surface electrodes, EIT may be limited by the “shielding effect” (Wen, 2000) caused by an insulating or low conductive region in the object, such as bone or adipose tissue. In comparison, MIT uses dynamic magnetic field to induce current in conductive tissue and measures the second magnetic field generated by the induced eddy current using noncontact sensing coils. Yet, because of the ill-posed inverse problem similar to EIT, the spatial resolution of current MIT techniques is still quite limited. In order to achieve high spatial resolution in imaging electrical conductivity, MREIT has been developed by combining EIT and magnetic resonance current density imaging (MRCDI) (Joy *et al.*, 1989). With current injection through surface electrodes similar as EIT while measuring the corresponding magnetic field disturbance generated by injected current in tissue through magnetic resonance imaging (MRI), MREIT made it possible to map electrical conductivity in *ex vivo* and *in vivo* tissues with high spatial resolution (Woo *et al.*, 2008; Seo and Woo, 2014). However, a relatively high level of current injection (on the level of mA) is generally required in MREIT to obtain sufficient signal-to-noise ratio (SNR) level and the use of MRI machine makes the cost of MREIT higher than other methods.

Alternative approaches utilizing the coupling between electromagnetic field and acoustic field have also been developed to image electrical properties of tissue or bioelectrical current (Roth, 2011). Such kind of coupling was first demonstrated in magnetoacoustic tomography (MAT) (Towe and Islam, 1988; Roth *et al.*, 1994) and Hall effect imaging (HEI) (Wen *et al.*, 1998). In MAT and HEI, the imaging object is placed in a static magnetic field. Spontaneous or injected current flow, which is associated with ion movement in biological tissue, is then coupled to acoustic vibrations through Lorentz force acting on these moving ions. Such vibrations can be sensitively detected by ultrasound transducers and used for possible mapping of the bioelectric current or tissue electrical properties with spatial resolution close to ultrasound imaging. Using similar coupling mechanism in a reverse mode, one can apply ultrasonic energy to the imaging object and record voltage/current signals to obtain the sample's conductivity information (Montalibet *et al.*, 2001b; Montalibet *et al.*, 2001a; Roth and Schalte, 2009). Such technique was also called magneto-acousto-electrical tomography (MAET) (Haider *et al.*, 2008; Renzhiglova *et al.*, 2010; Kunyansky, 2012) or Lorentz force electrical impedance tomography (LFEIT) (Grasland-Mongrain *et al.*, 2015; Grasland-Mongrain *et al.*, 2013). Of course, the problem of the "shielding effect" associated with the use of surface electrodes for current injection or voltage measurement, i.e. regions surrounded by low-conductive tissue become invisible, still exists in these methods. Such problem has then led to the development of magnetoacoustic tomography with magnetic induction (MAT-MI) (He, 2005; Xu and He, 2005). MAT-MI utilizes magnetic induction to induce eddy current in the conductive sample and generates acoustic vibrations through the same Lorentz force coupling mechanism as in MAT or HEI. Ultrasound waves are then sensed to reconstruct the electrical conductivity related image. Ever since the MAT-MI method was proposed, there have been many numerical studies (Li *et al.*, 2007; Ma and He, 2007; Li *et al.*, 2009; Zhou *et al.*, 2011) and experimental studies using physical phantoms (Li *et al.*, 2006; Xia *et al.*, 2007; Sun *et al.*, 2013) or biological tissues (Hu *et al.*, 2011; Hu and He, 2011) demonstrating the feasibility and performance of MAT-MI. Advancement on experimental system design (Hu *et al.*, 2010; Li and He, 2010) and image reconstruction algorithms (Li and He, 2010; Mariappan and He, 2013) has also been achieved in recent years. In addition, similar to the reverse mode of HEI or MAET, i.e. applying ultrasound transmission and measuring the Lorentz force induced current or voltage for imaging electrical conductivity, the reverse mode of MAT-MI named magneto-acousto-electrical tomography with magnetic induction (MAET-MI) has also been developed recently (Guo *et al.*, 2015b), which uses ultrasound stimulation and coil measurement of the dynamic magnetic field generated by Lorentz force induced current in conductive imaging objects.

In this review, we first go over the basic theories and physical mechanisms underlying the MAT-MI imaging methodology. Different experimental systems and imaging strategies that have been developed during these years are then discussed and compared. At last we give our opinions on the challenges and possible future directions on MAT-MI research.

2. Theories and Physical Mechanisms

The schematic diagram of the imaging principle of MAT-MI is shown in Fig. 1. In MAT-MI, a conductive object with electrical conductivity $\sigma(\mathbf{r})$ is placed in a static magnetic field $\mathbf{B}_0$ and a time-varying magnetic stimulation with magnetic flux density $\mathbf{B}_1$ is applied to induce

eddy current $\mathbf{J}$ inside the object volume Ω . Note that the induced eddy current is determined by the $\mathbf{B}_1$ field and the conductivity distribution $\sigma(\mathbf{r})$, where $\mathbf{r}$ is the position vector. Also note here that in MAT-MI we are considering around MHz system frequency (central frequency of magnetic stimulation and ultrasound transducer) and conduction current is much larger than displacement current (Xu and He, 2005). Therefore tissue capacitance effect related to permittivity is ignored here and only conductivity of the tissue needs to be considered. Within the static magnetic field, the Lorentz force $\mathbf{F} = \mathbf{J} \times \mathbf{B}_0$ moves those charged ions forming the eddy current and leads to detectable ultrasound pressure signals. These ultrasound signals can be acquired by ultrasound probes and used to estimate the object's electrical conductivity map. In the following, theories of the two major physical mechanisms in MAT-MI, i.e. magnetic induction in conductive tissue sample and Lorentz force induced acoustic wave propagation are described.

2.1 Magnetic induction in conductive tissue sample

As in MAT-MI we are considering magnetic stimulation centered around MHz (usually pulsed magnetic stimulation with microsecond pulse duration), the corresponding skin depth of magnetic induction in general biological tissue (assuming conductivity of 0.2 S/m and relative permeability of 1) is at the level of meters and much larger than most organ size. Therefore the magnetic induction problem in MAT-MI can be considered quasi-static and magnetic diffusion can be ignored (Li and He, 2010). The quasi-static condition allows us to separate the spatial and temporal functions of the time-varying magnetic field, i.e. $\mathbf{B}_1(\mathbf{r}, t) = \mathbf{B}_1(\mathbf{r})f(t)$. This condition also indicates that the magnetic field in the tissue can be very well approximated by the field produced by the coil in the absence of the tissue and can be estimated with the known coil geometry (Wang and Eisenberg, 1994).

Using the magnetic vector potential $\mathbf{A}(\mathbf{r}, t)$ as $\mathbf{B}_1 = \nabla \times \mathbf{A}$. According to Faraday's law, we have

$$\nabla \times \left(\mathbf{E} + \frac{\partial \mathbf{A}}{\partial t} \right) = 0 \quad (1)$$

where $\mathbf{E}(\mathbf{r}, t)$ is the electrical field intensity. Therefore the electrical field intensity $\mathbf{E}(\mathbf{r}, t)$ can be written as:

$$\mathbf{E} = -\nabla \phi - \frac{\partial \mathbf{A}}{\partial t} \quad (2)$$

where $\phi(\mathbf{r}, t)$ is the electrical scalar potential. According to Ampere's law and because we ignore the displacement current, the current density $\mathbf{J}(\mathbf{r}, t)$ is solenoidal as:

$$\nabla \cdot \mathbf{J} = 0 \quad (3)$$

In addition, according to Ohm's law, the current density is related to the electrical field through conductivity as:

$$\mathbf{J} = \sigma \mathbf{E} \quad (4)$$

Combining Eqs. (2)-(4), we can have:

$$\nabla \cdot (\sigma \nabla \phi) = - \nabla \cdot \left(\sigma \frac{\partial \mathbf{A}}{\partial t} \right) \quad (5)$$

According to the quasi-static condition and Faraday's Law and Ohm's Law, the similar spatial and temporal separation holds for the magnetic vector potential, induced electrical field and eddy current density, i.e. $\mathbf{A}(\mathbf{r}, t) = \mathbf{A}(\mathbf{r})f(t)$, $\phi(\mathbf{r}, t) = \phi(\mathbf{r})f'(t)$, $\mathbf{E}(\mathbf{r}, t) = \mathbf{E}(\mathbf{r})f'(t)$ and $\mathbf{J}(\mathbf{r}, t) = \mathbf{J}(\mathbf{r})f'(t)$ where the prime denotes the first order time derivative. Assuming a uniform magnetic stimulation over space, Eq. (5) has an analytical solution in a two layer concentric spherical model (Li *et al.*, 2007), yet for arbitrary geometry, Eq. (5) must be solved in the whole conductive sample domain Ω with a Neumann boundary condition on the current density at the outer boundary surface as $\mathbf{J} \cdot \mathbf{n} = 0$, where $\mathbf{n}$ is the unit vector norm of the outer boundary Ω . This boundary condition requires the current density component that is normal to the bounding surface to vanish. With such boundary condition, the final equation describing the magnetic induction problem in MAT-MI (in spatial domain) can be written as

$$\begin{cases} \nabla \cdot (\sigma(\mathbf{r}) \nabla \phi(\mathbf{r})) = - \nabla \cdot (\sigma(\mathbf{r}) \mathbf{A}(\mathbf{r})) & \text{in } \Omega \\ (\nabla \phi(\mathbf{r}) + \mathbf{A}(\mathbf{r})) \cdot \mathbf{n} = 0 & \text{at } \partial\Omega \end{cases} \quad (6)$$

If the electrical conductivity is known in the whole tissue volume, a unique solution for the electrical potential ϕ inside the conductive domain Ω can be determined up to a reference point. This solution can generally be obtained in arbitrary geometry by using numerical method such as finite element method (FEM) (Wang and Eisenberg, 1994). With the solution of electrical potential, electrical field and eddy current can be calculated accordingly using Eqs. (2) and (4).

2.2 Lorentz force induced acoustic wave propagation

With the magnetically induced eddy current $\mathbf{J}$ and the static magnetic field $\mathbf{B}_0$, the Lorentz force acting on the eddy current over unit volume can be written as $\mathbf{F} = \mathbf{J} \times \mathbf{B}_0$. Note here that we assumed $B_1 \ll B_0$ as the strength of the dynamic field for magnetic induction is much smaller than that of the static field in most of the MAT-MI experiment systems. According to Newton's second law of motion and assuming the particle velocity $\mathbf{v}$ caused by the Lorentz force is small, we have the following Eq. (7) (Roth *et al.*, 1994; Xu and He, 2005):

$$\frac{\partial (\rho_0 \mathbf{v})}{\partial t} = - \nabla p + \mathbf{J} \times \mathbf{B}_0 \quad (7)$$

where ρ_0 is the density of the material at rest and p is acoustic pressure. Taking the divergence of both sides of Eq. (7), we have Eq. (8):

$$\frac{\partial (\nabla \cdot (\rho_0 \mathbf{v}))}{\partial t} = -\nabla^2 p + \nabla \cdot (\mathbf{J} \times \mathbf{B}_0) \quad (8)$$

In addition, we have the conservation of mass as in Eq. (9) and the definition of the adiabatic compressibility of the medium β_s as in Eq. (10):

$$\nabla \cdot (\rho_0 \mathbf{v}) = -\frac{\partial \rho}{\partial t} \quad (9)$$

$$\beta_s p = \frac{\rho}{\rho_0} \quad (10)$$

where ρ is the density variation. Combining Eqs. (8)-(10) and using the relationship

$c_s = \frac{1}{\sqrt{\rho_0 \beta_s}}$ where c_s is the acoustic speed in the medium, we can derive the wave equation with the Lorentz force induced acoustic source (Roth *et al.*, 1994; Xu and He, 2005):

$$\nabla^2 p - \frac{1}{c_s^2} \frac{\partial^2 p}{\partial t^2} = \nabla \cdot (\mathbf{J} \times \mathbf{B}_0) \quad (11)$$

Note here that in MAT-MI the static magnetic field is generally generated from some external sources such as permanent magnets placed outside the imaging object volume, thus $\nabla \times \mathbf{B}_0 = 0$ inside the imaging object volume (Xu and He, 2005). The MAT-MI acoustic source, i.e. the right hand side of the wave equation (11), can be written as $AS(\mathbf{r}) = \nabla \cdot (\mathbf{J} \times \mathbf{B}_0) = (\nabla \times \mathbf{J}) \cdot \mathbf{B}_0$. Note here that since the MAT-MI acoustic source is related directly to the curl of the eddy current density, the irrotational part of the current density does not contribute to MAT-MI acoustic sources (Mariappan and He, 2013). According to both Ohm's law and Faraday's law and by using the quasi-static condition to separate the spatial and temporal functions, the MAT-MI acoustic source $AS(\mathbf{r}, t)$ can be further expanded as

$$AS(\mathbf{r}, t) = AS(\mathbf{r}) f'(t) = (\sigma (\nabla \times \mathbf{E}) + \nabla \sigma \times \mathbf{E}) \cdot \mathbf{B}_0 = \left(-\sigma \frac{\partial \mathbf{B}_1}{\partial t} + \nabla \sigma \times \mathbf{E} \right) \cdot \mathbf{B}_0 = (-\sigma \mathbf{B}_1(\mathbf{r}) + \nabla \sigma \times \mathbf{E}(\mathbf{r})) \cdot \mathbf{B}_0 f'(t) \quad (12)$$

As shown in Eq. (12), besides the static and dynamic magnetic fields, the MAT-MI acoustic source is related to both the conductivity and its spatial gradient. Assuming the medium is

acoustically homogeneous and the acoustic speed c_s is a constant over space, using the 3D Green's function, the solution to Eq. (11) can be written as (Xu and He, 2005):

$$p(\mathbf{r}_0, t) = -\frac{1}{4\pi} \int \int \int_v d\mathbf{r} \cdot AS(\mathbf{r}) \cdot \frac{\delta(t - |\mathbf{r}_0 - \mathbf{r}|/c_s)}{|\mathbf{r}_0 - \mathbf{r}|} \quad (13)$$

where $\mathbf{r}_0$ is a position located on certain ultrasound detection aperture.

In Eq. (13) we assumed the Lorentz force induced acoustic source does not have specific propagation direction. In comparison, some previous studies modeled such Lorentz force induced acoustic source as acoustic dipole radiations (Ma and He, 2008; Sun *et al.*, 2012; Sun *et al.*, 2013; Wang *et al.*, 2014), i.e. acoustic sources with specific propagation direction that is aligned with the Lorentz force. Such dipole acoustic radiation have been modeled using Eq. (13) with an extra spatial derivative on the acoustic source term in the direction of the Lorentz force (Ma and He, 2008; Sun *et al.*, 2012) or with an extra projection term i.e. $\cos\theta$, where θ represents the angel between the direction of the Lorentz force $\mathbf{F}$ and the transmission line between acoustic source position and the plane transducer $\mathbf{r}_0 - \mathbf{r}$ (Sun *et al.*, 2013; Wang *et al.*, 2014). The directional acoustic source in MAT-MI has been previously demonstrated in experiment with line-shape objects (Wang *et al.*, 2014), yet due to the directional nature of most piston transducer, similar directional behavior may also been observed with non-dipole acoustic radiations (Mariappan *et al.*, 2011), i.e. acoustic sources residing on tissue boundaries that are perpendicular to the transducer's surface cannot be effectively detected. Therefore, further experimental validation may be needed to prove that in MAT-MI the Lorentz force does induce acoustic dipole radiations.

2.3 Reverse mode - MAET-MI

As a reverse model of MAT-MI, magneto-acousto-electrical tomography with magnetic induction MAET-MI (Guo *et al.*, 2015a) was recently developed to map electrical conductivity using ultrasound stimulation and coil detection of the magnetic field generated by the Lorentz force induced current.

In the forward problem of MAET-MI, two sources that contribute to the coil-detectable magnetic field $\mathbf{H}_I$ are the source current density $\mathbf{J}_{eI}$ and the corresponding electric field $\mathbf{E}_I$. If the object Ω has a conductivity distribution σ , the relations among these fields can be described as a first governing equation set:

$$\begin{cases} \nabla \times \mathbf{H}_I = \mathbf{J}_{eI} + \sigma \mathbf{E}_I \\ \nabla \times \mathbf{E}_I = -\mu \frac{\partial \mathbf{H}_I}{\partial t} \\ \mathbf{J}_{eI} = \sigma (\mathbf{v} \times \mathbf{B}_0) \end{cases} \quad (14)$$

in which μ is the permeability of the medium and $\mathbf{v}$ is the velocity of local conductive particles driven by ultrasound field. In order to determine the induced voltage u across the detection coil, reciprocal theorem was applied to obtain a second equation set:

$$\begin{cases} \nabla \times \mathbf{H}_2 = \mathbf{J}_{e2} + \sigma \mathbf{E}_2 \\ \nabla \times \mathbf{E}_2 = -\mu \frac{\partial \mathbf{H}_2}{\partial t} \\ \mathbf{J}_2 = \sigma \mathbf{E}_2 \end{cases} \quad (15)$$

when an external current $\mathbf{J}_{e2}$ is injected into the coil, inducing eddy current $\mathbf{J}_2$ within Ω . In fact, such reciprocal process of MAET-MI is similar to the actual working process of MAT-MI discussed above, in which magnetic induction is applied to produce an electric field $\mathbf{E}_2$ over the object. Then, both $\mathbf{J}_{e2}$ and $\mathbf{E}_2$ contribute together and relate to the magnetic field $\mathbf{H}_2$.

Based on Eqs. (14) and (15), one can solve for the voltage u by taking the assumptions of infinite boundary condition and non-conductive property at the boundaries of Ω . This mathematical procedure can be simplified to equation (16), as long as the spectral content of $\mathbf{J}_{e2}$ is non-zero within the spectrum range of the measured voltage u :

$$u(t) = \int \int \int_{r \in \Omega} \frac{B_0}{\rho} \cdot \nabla \times \mathbf{J}_2(\mathbf{r}) \varphi(\mathbf{r}, t) d\mathbf{r} \quad (16)$$

in which ρ is the mass density, and $\varphi(\mathbf{r}, t)$ is the velocity potential due to the ultrasound vibration. This velocity potential satisfies $\nabla \varphi = \rho \mathbf{v}$, and can be further determined from the wave equation and the corresponding Green's function by taking acoustic far-field assumption. Another unknown variable needed to solve equation (16) is $\mathbf{J}_2(\mathbf{r})$, the spatial component of the induced eddy current $\mathbf{J}_2$. The approaches of calculating such a vector field have been proposed in MAT-MI (Li and He, 2010; Mariappan and He, 2013; Li et al., 2007), and an appropriate method can be chosen depending on the specific geometric feature and conductivity distribution of the object Ω .

3. Experimental Setups

According to the involved physical processes, a MAT-MI experimental system has three major components, a static magnetic field, a dynamic magnetic field for current induction, and a scanning system with ultrasound transducer for acquiring ultrasound signals. Common experimental setup for MAT-MI imaging system is illustrated in Fig. 2. Each component of the MAT-MI experimental system is discussed below.

The static magnetic field in MAT-MI is usually generated by permanent magnets, which can give field strength of 0.1-0.3 Tesla around the sample in z direction (Xia *et al.*, 2007; Hu *et al.*, 2011). In a recent study, MAT-MI system using superconducting magnet in a 9.4T MRI scanner have also been explored (Mariappan *et al.*, 2014) with a slightly different scanning framework, i.e. due to the limited space in the MRI bore, the transducer and coil were fixed while rotation of the imaging sample was performed.

To generate dynamic magnetic stimulations, computer controlled magnetic stimulators are used to drive coil load arranged around the imaging sample. For MAT-MI with pulsed

magnetic stimulations, the magnetic stimulators usually use high voltage and high current switches to control capacitor discharge through connected coil load. Depending on the hardware design, high voltage capacitors that charge to 600V (Xia *et al.*, 2007) and to as high as 24 kV have been used in previous MAT-MI systems (Hu *et al.*, 2010). The corresponding maximum dynamic magnetic field, which can be measured by small sensing coils around the imaging object, ranged from 0.00125 T to 0.07 T (Xu and He, 2005; Li and He, 2010; Hu *et al.*, 2010). Magnetic stimulations sent through different coils in MAT-MI have also been explored in the past. Most MAT-MI systems use a single magnetic stimulation generated through one coil set, such as a Helmholtz coil pair, which produces a region with a nearly uniform magnetic field (Xia *et al.*, 2007; Mariappan and He, 2013). In addition, MAT-MI systems using different coil sets to generate different magnetic stimulations and consequently different eddy current pattern in the conductive tissue sample have also been developed in the so-called multi-excitation MAT-MI system (Li and He, 2010).

Ultrasound transducer mounted to certain scanning system that can either rotate the transducer or the imaging sample can be used to acquire MAT-MI signals around the imaging sample. Usually both the sample and transducer are submerged in acoustic coupling media with very low electrical conductivity e.g. distilled water. Data acquisition is synchronized with the magnetic stimulation. Signal detected by the transducer are then filtered, amplified and fed to the data acquisition system. In MAT-MI, the magnetic induced eddy current in conductive tissues and the Lorentz force induced acoustic source are intrinsically distributed in the three-dimensional (3D) tissue volume. Thus 3D scanning and mapping of the Lorentz force induced acoustic source is needed to map the 3D electrical conductivity distribution. Three-dimensional MAT-MI systems have been previously developed based on ultrasound focusing and cylindrical scanning (Xia *et al.*, 2007; Li *et al.*, 2010). As shown in Fig. 2, through ultrasound focusing in the Z direction, we can localize the MAT-MI acoustic sources in a specific XY plane. A 2-dimensional (2D) MAT-MI image can be obtained at each cross section of the 3D object and vertical scans in the Z direction can provide a stack of 2D images, thus forming a 3D volume image of the object. With such a circular scan, the spatial resolution of the MAT-MI image in each slice is mainly determined by the central frequency and bandwidth of the transducer, while the resolution in Z direction is determined by the focusing beam width. For imaging objects that are uniform in the Z direction and with homogeneous static and dynamic magnetic field, the whole MAT-MI system can be simplified as a 2D system, in which only 2D ultrasound scan is needed (Li *et al.*, 2006; Hu *et al.*, 2010). For 2D ultrasound scans, besides the circular scan mode with large scanning radius around the objects using unfocused transducer, scanning in B-mode scan using focused transducer may also be used (Mariappan *et al.*, 2011).

As the reverse mode of MAT-MI, MAET-MI also includes three major components, a static magnetic field, an ultrasound stimulation system with waveform control, and a detecting system using detection coils close to the object. The static magnetic fields in MAET-MI systems are also created by permanent magnets, and the applied field strength ranges from 0.2-0.3 Tesla around the imaged object along z direction (Guo *et al.*, 2015a). Depending on different system designs, the ultrasound stimulations may employ transducers working at different center frequencies, e.g. 500 kHz with a pulse repetition frequency (PRF) of 2 kHz

(Guo *et al.*, 2015a). Similar to the high voltage used to instantaneously excite the radio-frequency coil in MAT-MI, a 80-ns pulsed, 1200-V amplitude voltage was applied in a recent MAET-MI study (Guo *et al.*, 2015a) to drive the ultrasound transducer. It is believed that optimized ultrasonic parameters could lead to a sufficient acoustic pressure onto the region of interest (ROI), thus producing significant mechanical vibrations (the velocity) to potentially achieve a good SNR for the acquired MAET-MI data. In addition, higher center frequencies and smaller oscillation numbers of the transmitted ultrasound can result in better spatial resolutions. In that study, two 150-turn coils connected in series were arranged and fixed at top and bottom sides of the object. The acquired signals were then fed to a low noise amplifier, and were further averaged 1024 times to improve SNR (Guo *et al.*, 2015a). MAET-MI confronts a practical challenge that the ultrasonic wave may also vibrate the sensing coils in detection, thus raising significant artifacts in the reconstructed image. Therefore, the distance between the sensing elements and the ultrasound targeted ROI needs to be optimized, such that the artifacts in the collected signal can be suppressed, while the detecting sensitivity will not be sacrificed too much (Guo *et al.*, 2015a). Such problem is of course mainly due to the whole experimental setup immersing in nonconductive oil in that study, which potentially provides acoustic pathways between the coil and ultrasound transducer. One good practice from MAET-MI experiment is its shielding design using an aluminum tank, which is believed to improve the signal quality. To our best knowledge, current MAET-MI images are 2D based, and 3D implementation of MAET-MI with focused ultrasound technique may be developed in the future.

4. Imaging Strategies and Experimental Results

The goal of MAT-MI is to reconstruct the electrical conductivity distribution $\sigma(\mathbf{r})$ inside the tissue volume, with the knowledge of the static magnetic field $\mathbf{B}_0(\mathbf{r})$, the dynamic magnetic stimulation $\mathbf{B}_1(\mathbf{r}, t)$ or its vector potential $\mathbf{A}(\mathbf{r}, t)$ and the measured MAT-MI acoustic signals $p(\mathbf{r}_0, t)$. As discussed before, the signal generation mechanism of MAT-MI includes both the processes of magnetic induction and acoustic wave propagation with the Lorentz force induced acoustic vibrations. Accordingly solving the inverse problem of MAT-MI often involves two steps. In the first step, we reconstruct certain intermediate variable related to the volume conductivity from the measured acoustic signals. It may be the Lorentz force induced acoustic sources (Xu and He, 2005; Li *et al.*, 2007; Li and He, 2010), the Lorentz force (Xia *et al.*, 2009, 2010) or the eddy current (Mariappan and He, 2013; Mariappan *et al.*, 2014). In the second step, we then reconstruct the conductivity distribution from the intermediate variable we get from the first step. It should be noted that the inverse problem of MAT-MI is not as ill-posed as in EIT or MIT techniques because the ultrasound measurements collected around the sample can be used to estimate the selected intermediate variable in each pixel/voxel in the whole imaging volume. This is because the acoustic sources over space are time resolved in the measured acoustic signal due to their acoustic time of flight difference. In comparison, the electromagnetic measurements used in EIT or MIT at each location are always a volume integration of the product between the current density and the lead field of the probes, e.g. surface electrode or coil.

4.1 Mapping conductivity through mapping MAT-MI acoustic source

For simplicity, we often assume a pulsed magnetic stimulation and letting $f'(t) = \delta(t)$ and assume the medium is acoustically homogeneous, i.e. the acoustic speed c_s is a constant in the tissue volume. Applying the time reversal method in MAT-MI (Xu and Wang, 2004; Xu and He, 2005), the MAT-MI acoustic source can be estimated as

$$AS(\mathbf{r}) \approx \frac{-1}{2\pi c_s^3} \iint_{S_0} dS_0 \frac{\mathbf{n}_0 \cdot (\mathbf{r} - \mathbf{r}_0)}{|\mathbf{r} - \mathbf{r}_0|^2} \frac{\partial^2 p(\mathbf{r}_0, t)}{\partial t^2} \bigg|_{t=|\mathbf{r}-\mathbf{r}_0|/c_s} \quad (17)$$

where $\mathbf{r}_0$ is a point on the detection surface S_0 and $\mathbf{n}_0$ is a unit vector normal to the surface S_0 at $\mathbf{r}_0$.

This is the most commonly used method for reconstructing MAT-MI acoustic sources. Experimentally, the MAT-MI acoustics sources have been shown to be strongest at tissue boundaries with large electrical conductivity change (Li *et al.*, 2006) and proportional to the magnitude of conductivity gradient (Li *et al.*, 2006; Hu *et al.*, 2010), i.e. the higher the gradient magnitude the higher the detected ultrasound signal and reconstructed MAT-MI acoustic source. This is not totally unexpected because theoretically the MAT-MI acoustic source is related with both the conductivity and its spatial gradient as shown in Eq. (12). Recent simulations have shown that the conductivity gradient related acoustic source ($\nabla \sigma \times \mathbf{E}(\mathbf{r}) \cdot \mathbf{B}_0$) will be at least 5 times larger than its counterpart related to conductivity itself, i.e. $\sigma \mathbf{B}_1(\mathbf{r}) \cdot \mathbf{B}_0$, unless the transition zone between pieces with different conductivity values is wider than 10% of the piece size (Wang *et al.*, 2015). In addition, the bandwidth limitation of most transducers used in MAT-MI experiments will further filter the acoustic signals generated by these two sources, most possibly favoring the gradient source which is a wide-band source in piecewise homogeneous samples (Li and He, 2010).

Though it is not a direct measure of tissue electrical conductivity, the MAT-MI acoustic source itself reconstructed using Eq. (17) can give some valuable information in regards to the boundaries between different tissue types with different electrical conductivities, e.g. muscle versus fat tissue. In recent MAT-MI studies using a static magnetic field of 0.2-0.3T, magnetic stimulator equipped with high voltage discharging system (with capacitors charged up to 24 kV that can give maximum magnetic field strength $\mathbf{B}_1$ of 0.07T around the imaging object), it has been demonstrated that MAT-MI acoustic sources can be detected between *ex vivo* fat tissue (with conductivity of 0.02-0.03 S/m) and muscle tissue (with conductivity of 0.55-0.62 S/m) (Fig. 3a and 3b) (Hu *et al.*, 2010). As shown in Fig. 3c and 3d, such system has also been shown able to detect MAT-MI acoustic sources generated at the tissue boundary between liver tumor (with conductivity of 0.65-0.7 S/m) and normal liver tissue (with conductivity of 0.25-0.28 S/m) (Hu *et al.*, 2011).

With the reconstructed MAT-MI acoustic sources, there are several ways to further calculate the electrical conductivity. Early approaches assumed piecewise homogeneous conductivity distribution and ignored the conductivity gradient sources (Xu and He, 2005; Li *et al.*, 2007). Though demonstrated in computer simulation, such simplified approach can be hardly

applied on experimentally collected MAT-MI signal, which is dominated by conductivity gradient sources. As mentioned in some later theoretical studies (Kunyansky, 2012; Zhou *et al.*, 2014), if it is possible to rotate the static magnetic field $\mathbf{B}_0$, e.g. setting it to three orthogonal directions, while keeping the magnetically induced eddy current in the conductive tissue sample the same, one may be able to get a good estimation of the curl of the eddy current $\nabla \times \mathbf{J}$ and further estimate the electrical conductivity. However, rotation of the static magnetic field is usually hard to manage in practice, especially when acoustic pathway and ultrasound transducers need to be arranged around the imaging sample. Reconstructing the electrical conductivity from the estimated MAT-MI acoustic sources without rotating the static magnetic field is possible using the so-called multi-excitation MAT-MI method (Li and He, 2010; Li *et al.*, 2010). The basic idea is to combine MAT-MI acoustic sources under different magnetic inductions thus different eddy current patterns. In the form of Eq. (12), this is equivalent to measuring MAT-MI acoustic sources with different $\mathbf{B}_1$ and $\mathbf{E}$ field. Let the static magnetic field sit in the Z direction i.e. $\mathbf{B}_0 = B_{0z} \hat{z}$ and note that $\mathbf{B}_1^j(\mathbf{r}, t) = \mathbf{B}_1^j(\mathbf{r}) f_j(t)$ and $\mathbf{E}^j(\mathbf{r}, t) = \mathbf{E}^j(\mathbf{r}) f_j'(t)$ where the subscript j corresponds to the j th of the N magnetic excitations. Equation (12) can then be rewritten as Eq. (18):

$$AS^j = \left(\sigma \left(-B_{1z}^j \right) + \left(\frac{\partial \sigma}{\partial x}, \frac{\partial \sigma}{\partial y} \right) \cdot \left(E_y^j - E_x^j \right) \right) B_{0z} f_j'(t) \quad j=1, \dots, N \quad (18)$$

where E_x^j and E_y^j are the x and y components of the induced electrical field vector $\mathbf{E}^j$, respectively. B_{1z}^j is the z component of $\mathbf{B}_1^j(\mathbf{r})$. With MAT-MI acoustic measurements under N different magnetic excitations with appropriately chosen coil setups, we can then

reconstruct the conductivity gradient $\nabla \sigma = \left(\frac{\partial \sigma}{\partial x}, \frac{\partial \sigma}{\partial y} \right)$ in x and y directions by solving a matrix equation as

$$\mathbf{U}\mathbf{x} = \mathbf{b} \quad (19)$$

where

$$\mathbf{U} = \begin{bmatrix} E_y^1 & -E_x^1 \\ \vdots & \vdots \\ E_y^N & -E_x^N \end{bmatrix}, \quad \mathbf{x} = \begin{bmatrix} \frac{\partial \sigma}{\partial x} \\ \frac{\partial \sigma}{\partial y} \end{bmatrix} \quad \text{and} \quad \mathbf{b} = \begin{bmatrix} \frac{AS^1(\mathbf{r})}{B_{0z}} + \sigma B_{1z}^1 \\ \vdots \\ \frac{AS^N(\mathbf{r})}{B_{0z}} + \sigma B_{1z}^N \end{bmatrix}$$

Such matrix equation however needs to be solved in an iterative way, as the electrical field component in $\mathbf{U}$ depends on the unknown conductivity distribution $\sigma(\mathbf{r})$ and the vector $\mathbf{b}$ contains a term related to the conductivity distribution. In order to compute σ from

$\nabla \sigma = \left(\frac{\partial \sigma}{\partial x}, \frac{\partial \sigma}{\partial y} \right)$ in all the imaging slices, a 2D layer potential integration technique can be used as (Oh et al., 2003)

$$\sigma(\mathbf{r}) = - \int_S \nabla_{\mathbf{r}'} \Phi(\mathbf{r} - \mathbf{r}') \cdot \nabla \sigma(\mathbf{r}') d\mathbf{r}' + \int_{\partial S} \mathbf{n}_{\mathbf{r}'} \cdot \nabla_{\mathbf{r}'} \Phi(\mathbf{r} - \mathbf{r}') \sigma_{\partial S}(\mathbf{r}') dl_{\mathbf{r}'} \quad (20)$$

where $\Phi(\mathbf{r} - \mathbf{r}') = \frac{1}{2\pi} \log|\mathbf{r} - \mathbf{r}'|$ is the two dimensional Green's function of the Laplacian operator and $\nabla_{\mathbf{r}'} \Phi(\mathbf{r} - \mathbf{r}') = -\frac{1}{2\pi} \frac{\mathbf{r} - \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|^2}$. S denotes the 2D imaging ROI in the imaging slice where $\nabla \sigma$ is obtained and ∂S denotes its boundary. Σ_S is the conductivity value restricted at the boundary ∂S . The 2D integration as in Eq. (20) can be applied in a whole 3D volume slice by slice. In addition, modifications can be made on Eqs. (18) and (19), i.e. removing the terms related to conductivity σ while keeping those terms related to conductivity gradient $\nabla \sigma$, to account for the bandwidth limitation in the ultrasound measurement (Li and He, 2010). Such modification was based on the fact that with limited bandwidth acoustic measurements, the reconstructed acoustic source is mainly determined by the conductivity gradient term. Similar iterative procedure can be used to solve the inverse problem. However, as shown in both computer simulation and experiment studies, using the multi-excitation MAT-MI approach with limited bandwidth acoustic measurements, we are only able to reconstruct the relative conductivity contrast (Li and He, 2010; Li *et al.*, 2010).

Some example results acquired in a phantom using a 2D multi-excitation MAT-MI system are shown in Fig. 4. In that experiment, the static magnetic field was measured to be 0.26 Tesla (Gaussmeter, Alpha Lab) at the coordinate center where the object was located. Three coil sets were used to send three different magnetic excitation patterns, including a Helmholtz coil pair (group C in Fig. 4a) and two figure-eight coil pairs (group A and B in Fig. 4a). The distance between the upper coils and lower coils in each group was around 5 cm. The coils were driven by 1 μ s current pulse. The estimated maximum dynamic magnetic field strength B_{1z} was around 0.007 T at the coordinate center. A 500 kHz flat ultrasound transducer (Panametrics V301) with around 60% bandwidth was used to scan around the sample with 330 degrees view angle and 2.5 degrees step size. The scanning radius, i.e. the distance between the transducer and the scanning center was 22.8 cm. A 3 cm thick gel phantom (Fig. 4b), which was uniform in Z direction was submerged in 3 cm thick deionized water media for acoustic coupling. The phantom contained a background region made from 5% salinity gel (~ 8 S/m). Two cylindrical columns with diameter of 12 mm were embedded in the gel. Marked by the red and blue circles in the photo were two high conductive regions filled with 20% (~ 22 S/m) and 10% (~ 13 S/m) salinity gels, respectively. These two regions had diameter of 8 mm. The two annular areas sitting between the two high conductive regions and the background were made from beef suet (~ 0.03 S/m). The acoustic signal collected using the transducer was fed into preamplifiers with 90 dB gain and digitized by a 5 MHz data acquisition card.

The acoustic source images reconstructed using Eq. (17) corresponding to the three different magnetic excitations (group A, B and C in Fig. 4a) were shown in Fig. 4c-4e, respectively. Different acoustic source distributions under different magnetic stimulations were observed,

which agrees with the predicted pattern using computer simulation (Li and He, 2010). Using the modified multi-excitation algorithm, the conductivity image of the gel phantom was reconstructed as shown in Fig. 4f. From this image, we can clearly see the relative conductivity contrast, while the fat layer shows lower conductivity than the surrounding background, the 10% salinity gel shows higher conductivity value and the 20% salinity gel shows the highest conductivity. A conductivity profile at $y = 0.01$ m is given in Fig. 4g showing the comparison between the target and reconstructed conductivity values.

4.2 Mapping conductivity through reconstructing vector sources

Previous theoretical studies have shown that if MAT-MI ultrasound signal can be collected at specific acoustic apertures, e.g. spherical aperture or cylindrical aperture, at large distance to the source field (far field assumption), the Lorentz force vector $\mathbf{F} = \mathbf{J} \times \mathbf{B}_0$ may be reconstructed by time reversing a vectorized acoustic pressure measurements (Xia *et al.*, 2009, 2010). Electrical conductivity may be further estimated given the knowledge of both the static and the dynamic magnetic fields, i.e. $\mathbf{B}_0$ and $\mathbf{B}_1$. Though such methods have been demonstrated theoretically using computer simulations, it is hard to validate them in experiments due to the requirement of acoustic measurements on special 3D acoustic apertures. Nevertheless, they gave some new thoughts about how to estimate the electrical conductivity in MAT-MI.

Inspired by the Lorentz force mapping method, recently an ultrasound beam forming method has been developed for MAT-MI to map the electrical conductivity through the estimation of magnetic induced eddy current vector (Mariappan and He, 2013; Mariappan *et al.*, 2014). We call it current density vector source method here. The basic idea is to design certain point spread function (psf) of the ultrasound imaging system to extract the orthogonal components of the current density. The beam-forming algorithm comprises of summing up the weighted and time delayed pressure signal at all the receiver locations to synthesize certain signal source at the source location $\mathbf{r}_s$ as

$$V(\mathbf{r}_s) = \sum_n W_a p(\mathbf{r}_0, t - t_a) \quad (21)$$

where W_a is the weight and t_a is the time delay applied to the signal; n is the number of ultrasound receiver used in the beam formation process. Substituting Eqs. (12) and (13) in Eq. (21) and applying the fact that the MAT-MI acoustic source vanishes outside the conductive region (Xia *et al.*, 2009; Mariappan and He, 2013), we get

$$V(\mathbf{r}_s) = \sum_n W_a \int \int \int_v d\mathbf{r} \cdot (\mathbf{J} \times \mathbf{B}_0) \cdot \nabla_{\mathbf{r}} G(\mathbf{r}_0, \mathbf{r}, t - t_a) \quad (22)$$

where G is the Green's function for the wave equation, i.e. $G(\mathbf{r}_0, \mathbf{r}, t) = \frac{\delta(t - |\mathbf{r}_0 - \mathbf{r}|/c_s)}{|\mathbf{r}_0 - \mathbf{r}|}$. Switching the integration over space and the summation in beam forming process and using the vector identity for the triple vector product, Eq. (22) can be rewritten as

$$V(\mathbf{r}_s) = \int \int \int_v d\mathbf{r} \cdot \mathbf{J} \cdot \left(\mathbf{B}_0 \times \sum_n W_n \nabla_{\mathbf{r}} G(\mathbf{r}_0, \mathbf{r}, t - t_n) \right) \quad (23)$$

With appropriately designed weights and time delays, the vector point spread function in Eq. (23), i.e. $S(\mathbf{r}) = \mathbf{B}_0 \times \sum_n W_n \nabla_{\mathbf{r}} G(\mathbf{r}_0, \mathbf{r}, t - t_n)$ can be constructed to be spatial impulse vector pointing to one of the orthogonal directions, e.g. making $S(\mathbf{r}) = \delta(\mathbf{r}) \hat{x}$ or $S(\mathbf{r}) = \delta(\mathbf{r}) \hat{y}$ assuming $\mathbf{B}_0 = B_0 \hat{z}$, and corresponding components of the current density $\mathbf{J}_x$ and $\mathbf{J}_y$ can then be estimated. Since the irrotational part of eddy current does not contribute to MAT-MI acoustic source, in a piecewise homogenous sample, the conductivity in any homogeneous piece can be estimated by (Mariappan and He, 2013)

$$\sigma \approx -\mathbf{J}_c / \left(\frac{\partial \mathbf{A}}{\partial t} \right) \quad (24)$$

where $\mathbf{J}_c$ is the rotational part of the induced eddy current in homogeneous regions. Note here that Eq. (24) does not apply at conductivity boundaries. Inside each homogeneous region, the conductivity value can be robustly estimated using a least square fit (Mariappan and He, 2013). In recent studies on this vector source reconstruction method (Mariappan and He, 2013; Mariappan *et al.*, 2014), the bandwidth limitation of ultrasound measurement were handled with inverse filtering and least square fitting over space in homogeneous regions, while the conductivity values at or near conductivity boundaries were calculated by interpolation. Computer simulations and experimental studies have been conducted to demonstrate the validity of this method.

Some experimental results acquired in a gel phantom using this method are demonstrated in Fig. 5. In such experiment, static magnetic field was measured to be 0.2 T and a Helmholtz coil pair was used to generate pulsed magnetic field (a bipolar single cycle sinusoid with 2μs pulse width) around 0.006 T at the coordinate center. The MAT-MI acoustic signal measurement was conducted using a circular scanning scheme with a 500 kHz flat transducer (Panametrics V301) and around 60% bandwidth. Again because of the uniform conductivity distribution of the imaging sample and the relatively uniform magnetic field in Z direction, the corresponding MAT-MI problem can be simplified as 2D problem. The acoustic signals collected were pre-amplified with 90 dB gain and digitized at 5 MHz sampling. Band-pass filtering with passband of 100 k to 900 kHz were applied to remove electromagnetic interference (EMI) noises. After each experiment, the conductivity of the sample was measured using a four-electrode probe (Hu *et al.*, 2010). The reconstructed conductivity distribution using the current density vector source method was then normalized to the expected range of values using a calibration factor to account for various gains in the system. The phantom was made with a 0.4% salinity gel (0.67 S/m) in the background and a 2.5-cm-diameter cylindrical column with 1.2% salinity gel (2.01 S/m) in the center (the black part in Fig. 5a). The reconstructed acoustic source distribution is shown in Fig. 5b. As expected, with limited bandwidth measurement the MAT-MI acoustic source

was mainly distributed around the conductivity boundaries in the sample. The rotational nature of the induced current was observed in the two components of the reconstructed current density, i.e. J_x and J_y (Fig. 5c and 5d). The estimated conductivity distribution (Fig. 5e) and quantitative values (as shown in the profile in Fig. 5f) agreed well with the expected values in the phantom.

4.3 Inverse problem of MAET-MI

To solve the inverse problem in MAET-MI (Guo *et al.*, 2015a), a compressed sensing method was introduced to solve an intermediate variable $D(\mathbf{r})$, which is a distributed source function for a constructed wave. Further, a matrix form of equation (16), i.e. $U = \Phi D$ (a constructed vector of $D(\mathbf{r}_j)$), and empirical observations of the sparsity of D in certain functional basis Ψ , i.e. $D = \Psi \theta$ enables one to transform the problem of reconstructing $D(\mathbf{r})$ to a l_1 norm minimization problem:

$$\begin{cases} \min \|\theta\|_{l_1} \\ \text{subject to } \|U - \Phi \Psi \theta\|_{l_2} < \varepsilon \end{cases} \quad (25)$$

in which U is a vector of the voltage signal detected using the coil in the forward problem, and Φ is a known matrix composed of time derivatives of $\varphi(\mathbf{r}, t)$ at discretized time points and spatial locations. However, to use equation (25), MAET-MI requires $\Phi \Psi$ to be a compressed-sensing matrix, which needs $\varphi(\mathbf{r}, t)$ to be a linear independent function. This condition implies that ultrasound transmissions, i.e. the distance between a transducer and the imaged object and the angular step of the transducer in scan, need to be carefully designed.

The next step is reconstructing the conductivity distribution σ from the calculated $D(\mathbf{r})$. Based on the assumption of uniform B_0 and ρ the spatial component of $\nabla \times J_2(\mathbf{r})$ along the same direction of B_0 can thus be determined from the distributed source function $D(\mathbf{r})$ which is denoted as P . By further using the hypothesis that the conductivity at the boundaries of Ω

vanishes, i.e. $\sigma|_{r \in \partial\Omega} = 0$, a discretized matrix form can be constructed as:

$$C\sigma = -P \quad (26)$$

in which C is a coefficients matrix varying with σ , and thus the reconstruction of σ is a iterative process. The Levenberg-Marquardt algorithm can be used to solve this non-linear least squares problem, thus obtaining the correction value for σ in each iterative step while keeping update both matrices C and σ .

5. Challenges and Future Directions

In spite of many technical advances achieved in these years on MAT-MI, limitations still exist in currently available MAT-MI methods in the aspects of sensitivity, instrumentation

and reconstruction algorithms and further improvement is necessary to make it useful and applicable in clinic.

As discussed before, the strength of MAT-MI acoustic source is related to the static magnetic field $\mathbf{B}_0$, the dynamic magnetic stimulation $\mathbf{B}_1$ and electrical conductivity of the imaging sample. For the ultimate application goal of MAT-MI, e.g. for tumor detection, a sensitivity of detecting electrical conductivity contrast on the level of 0.01 S/m is necessary. Current MAT-MI imaging systems are getting close to have such sensitivity, but further improvement may be achieved by pushing the static magnetic field strength and dynamic stimulation. First, in most MAT-MI experimental systems developed in previous studies, due to cost and simplicity, permanent magnets were used to give the static magnetic field up to 0.2 to 0.3 Tesla around the imaging sample. Obviously the strength of the static magnetic field in MAT-MI has large space of improvement, e.g. the signal strength may increase more than 10 times in clinically available 3T or even ultrahigh field (7T and above) MRI scanners. The increase of MAT-MI signal at higher static magnetic field has been recently observed at 9.4T (about 14 times increase in signal strength and SNR) (Mariappan *et al.*, 2014), yet technical challenges in terms of developing a MAT-MI system that works in MRI machine has also been observed. Such challenges partly come from the need to use magnetic stimulations with short pulses and relatively low central frequency (around MHz) in MAT-MI as compared to the Larmor frequency in MRI (400MHz at 9.4T), thus MRI coils cannot be used directly for MAT-MI. In addition, to comply with MRI safety regulations, long cables (~7 m) had to be used to connect the coils and transducers with the magnetic stimulators and amplifiers outside the MRI shielding room, thus energy loss and noise pickup in the long cable were not trivial and partly cancelled out the SNR gains obtained by using the high field (Mariappan *et al.*, 2014). Better-designed instrumentation will have to be developed in the future to fully appreciate the SNR gains obtained by doing MAT-MI in high field MRI. Second, with the use of solid-state high voltage and high current switch, the dynamic magnetic stimulation used in MAT-MI system has been substantially improved to about 0.07T in its maximum dynamic range, which corresponds to a stimulating electric field of about 550 V/m (Hu *et al.*, 2010; Hu *et al.*, 2011). This is comparable to the magnetic stimulation strength used in transcranial magnetic stimulation (TMS) but still lower than the nerve stimulation threshold of 2×10^{-3} Vs/m given the μ s pulse duration (Wen *et al.*, 1998). So there may be some space of improvement in terms of the magnetic stimulations. Using the magnetic stimulation strength of latest MAT-MI system (0.07T) and about 0.2-0.3 T static magnetic field, previous studies have shown that MAT-MI signals can be detected at tissue boundaries with conductivity contrast at about 0.03 S/m (Hu *et al.*, 2010; Hu *et al.*, 2011) between tumorous tissue and normal tissue. Note here that with the increased magnetic stimulation strength, the assumption $B_1 \ll B_0$ for Eq. (7) may need to be modified to include the contribution of $\mathbf{J} \times \mathbf{B}_1$ in the induced Lorentz Force. With improved field strength and stimulation, sensitivity to detect 0.01 S/m conductivity contrast using MAT-MI is believed to be feasible. In addition, the improved sensitivity and SNR gain would also allow much less signal averaging and speed up the MAT-MI scan. MAT-MI imaging speed may be further improved by using electrically controlled ultrasound phased array instead of single element transducer and mechanical scanning.

Another technical challenge in MAT-MI instrumentation is the electromagnetic interference (EMI) caused by the time varying magnetic field on the ultrasound transducer. Related to the turn off transients in the stimulator and the impulse response of the transducer, such EMI usually contaminates the MAT-MI signal for substantial long period (tens of μs) and have been observed to have some low frequency variations (Mariappan *et al.*, 2014). Therefore, further band-pass filtering is usually needed before MAT-MI image reconstruction. Better ways to avoid the EM contamination to the ultrasound transducer, such as better EM shielding or the use of optical fiber based transducers may be further explored to allow acquiring ultrasound signals in a closer distance (e.g. when using transducer with shorter focus) and further improve the MAT-MI signal quality.

In terms of reconstruction algorithms, for electrical conductivity reconstruction through mapping MAT-MI acoustic sources such as the multi-excitation MAT-MI method, more sophisticated coil pattern designs may help better improve the inverse conditions and the final image quality. On the other hand, the recently developed beam-forming current density vector source method has shown great potential for electrical conductivity reconstruction with the use of only single magnetic excitation. Ultrasound bandwidth limitations have been successfully tackled using inverse filtering in that method. Further improvement may be achieved by considering the conductivity gradient term using iterative process when calculating the electrical conductivity from the estimated current density vector.

In most previous MAT-MI studies, homogeneous acoustic properties and isotropic electrical conductivity in the imaging sample have been assumed. This is however not always true in biological tissues (Duck, 1990; Gabriel *et al.*, 1996). Small variations in acoustic properties including acoustic speed and tissue density or acoustic impedance (though less than 10%) in soft tissue is an important source for ultrasound speckle patterns and have been observed in Lorentz force electrical impedance imaging (Grasland-Mongrain *et al.*, 2015). Such inhomogeneity may also partly explain some textures observed in previous MAT-MI images acquired in tissue samples, e.g. in the tumor tissue in Fig. 3d. In addition, such heterogeneity may cause imaging artifacts, as it was not accurately modeled in most current MAT-MI theory. Acoustic reflections due to the acoustic impedance heterogeneity will also create extra “noisy” acoustic sources that are not related to the electrical properties of the imaging objects and may provide extra information of the mechanical properties if modeled correctly in the future. Some recent studies have started to tackle this problem, and initial theoretical and computer simulation studies have demonstrated the feasibility to better quantify electrical conductivity in MAT-MI by mapping the inhomogeneous acoustic speed from ultrasound transmission tomography (Zhou *et al.*, 2014). In addition, MAT-MI image reconstruction algorithms that can take into account the conductivity anisotropy need to be developed in the future, as electrical conductivity anisotropy in certain tissue types such as muscles and neural fibers has been suggested to change the MAT-MI signal significantly (Brinker and Roth, 2008; Li *et al.*, 2013).

Theoretically it is also possible to image the Lorentz force induced MAT-MI acoustic sources using the corresponding signal due to shear wave propagation which would include extra useful information related to tissue shear modulus and stiffness etc. Yet, due to the much larger attenuation of shear wave than acoustic longitudinal wave in normal soft tissue

(several orders of magnitude difference), sensitivity is an issue when measuring the shear wave directly. In a recent study (Grasland-Mongrain *et al.*, 2014), Lorentz force induced tissue displacement on the order of 1 micrometer was successfully detected by ultrasound speckle tracking. This provides another possible path for imaging both the electrical and elastic properties of tissue using shear wave, which may be a potential research direction for MAT-MI.

Finally, after all the technical improvement, *in vitro* or *in vivo* animal experiments need be further conducted to assess the MAT-MI method for high-resolution conductivity imaging. Different types of soft tissues, organs or the whole body may be explored in the future imaging studies. The most possible clinical application of MAT-MI is believed to be tumor detection especially in cancer screening and detection. A recent work on magneto acoustic tomography with the aid of magnetic nanoparticles suggested such possibility; employing the magnetomotive force, magneto acoustic tomography in a MAT-MI compatible setup was demonstrated as a high-spatial-resolution approach to reconstruct the *in vivo* distributions of nanoparticles, and to further highlight tumor by a high contrast (Mariappan *et al.*, 2016). This study sheds light on the possibility of improving magnetoacoustic imaging by harnessing the versatility of nanoparticles. Without using the contrast agents, a high-frequency MAT-MI technique has been developed lately (Yu *et al.*, 2016). This study has demonstrated the first *in vivo* tumor image by the MAT-MI, and the improved spatial resolution to detect not only the muscle-tumor interface but also the internal conductivity variations of the tumor. As reported, the MAT-MI has also been demonstrated to track the tumor growth on a tumor-bearing mouse model, which shows the feasibility of applying this imaging technique for early cancer detection (Yu *et al.*, 2016).

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Figure 1.
Schematic diagram of the imaging principle of magnetoacoustic tomography with magnetic induction (MAT-MI).

Figure 2.

Diagram of an example setup of a MAT-MI experiment system. This figure was reprinted with permission from reference (Xia *et al.*, 2007).

Figure 3.

(a) A phantom made from *ex vivo* pork tissue sample with both fat and muscle tissue. (b) The corresponding MAT-MI image obtained with a single excitation MAT-MI system showing the MAT-MI acoustic source mainly generated from tissue boundaries with different electrical conductivity. (c) An *ex vivo* human liver tumor sample showing both the tumor (left) and the normal liver tissue (right). (d) The corresponding MAT-MI acoustic source image demonstrating the sensitivity to detect tissue boundary between normal and

tumorous tissue using MAT-MI. This figure was reproduced with permission using sources from reference (Hu *et al.*, 2010) and (Hu *et al.*, 2011).

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Figure 4.

(a) Diagram of three different coil setups, i.e. group A, B and C, used in the multi-excitation MAT-MI system. Different coil setups were designed to induce different eddy-current patterns in the imaging object. (b) A gel phantom used to test the multi-excitation MAT-MI method. The red circle marks a region containing 20% salinity gel and the blue circle marks a region containing 10% salinity gel. (c)–(e) Reconstructed MAT-MI acoustic source images under magnetic excitations delivered through the coil groups of A, B and C, respectively. (f) Reconstructed conductivity image showing the relative conductivity contrast. (g)

Conductivity profile along $y = 0.01$ m showing the comparison between the target and reconstructed conductivity values. This figure was reproduced with permission using sources from reference (Li and He, 2010).

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Figure 5.

(a) A gel phantom used to test MAT-MI with beam forming vector source reconstruction. (b) The MAT-MI acoustic source image of the phantom. (c-d) The reconstructed x and y components of the induced eddy current in the conductive sample, respectively. (e) The reconstructed conductivity image of the phantom. (f) A line profile at $x = -1$ mm showing the comparison between the target and reconstructed conductivity values. This figure was reprinted with permission from reference (Mariappan and He, 2013)