Anisotropic conductivity tensor imaging in MREIT using directional diffusion rate of water molecules

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Abstract

Magnetic resonance electrical impedance tomography (MREIT) is an emerging method to visualize electrical conductivity and/or current density images at low frequencies (below 1 KHz). Injecting currents into an imaging object, one component of the induced magnetic flux density is acquired using an MRI scanner for isotropic conductivity image reconstructions. Diffusion tensor MRI (DT-MRI) measures the intrinsic three-dimensional diffusion property of water molecules within a tissue. It characterizes the anisotropic water transport by the effective diffusion tensor. Combining the DT-MRI and MREIT techniques, we propose a novel direct method for absolute conductivity tensor image reconstructions based on a linear relationship between the water diffusion tensor and the electrical conductivity tensor. We first recover the projected current density, which is the best approximation of the internal current density one can obtain from the measured single component of the induced magnetic flux density. This enables us to estimate a scale factor between the diffusion tensor and the conductivity tensor. Combining these values at all pixels with the acquired diffusion tensor map, we can quantitatively recover the anisotropic conductivity tensor map. From numerical simulations and experimental verifications using a biological tissue phantom, we found that the new method overcomes the limitations of each method and successfully...
reconstructs both the direction and magnitude of the conductivity tensor for both the anisotropic and isotropic regions.

Keywords: anisotropy, MREIT, DTI, conductivity tensor, diffusion tensor

(Some figures may appear in colour only in the online journal)

1. Introduction

The diffusion tensor MRI (DT-MRI) has been used to measure the diffusivity of water in tissues such as brain white matter and skeletal muscle by applying the diffusion-sensitizing magnetic field gradient (Cleveland et al 1976, Chenevert et al 1990, Moseley et al 1990, LeBihan 1991). The DT-MRI can determine the nerve fiber tract orientation within the brain white matter using the effective diffusion tensor. Adopting the effective macroscopic anisotropic tensor modeled by a two-phase anisotropic medium (Sen and Torquato 1989), the electrical conductivity tensor and the water diffusion tensor have been analyzed in terms of the intra- and extra-cellular transport coefficients with the same eigenvectors. Based on the model, Tuch et al (2001) derived a linear relationship between the eigenvalues of the conductivity tensor and those of the water diffusion tensor.

Using the linear relationship, a conductivity tensor map of the human brain has been investigated in several studies: independent estimation of the extra-cellular conductivity and diffusivity (Tuch et al 2001, Sekino et al 2003), use of the volume-constraint model (Wolters et al 2006), estimation of the signal attenuation in the cortex and the corpus callosum using the stimulated echo acquisition mode sequence (Sekino et al 2009) and estimation of the volume fraction in each compartment through a multi-compartment model (Wang et al 2008). There was also an attempt to experimentally find the cross-property relation among electrical conductivity, diffusion and $T_2$ (Oh et al 2006). However, these methods lack a reliable way of experimentally estimating the extra-cellular conductivity values needed to completely recover the conductivity tensor in terms of its direction and magnitude.

There have been several previous studies to produce conductivity images by using an MRI scanner as a tool to acquire the internal measurements of the current-induced magnetic field (Zhang 1992, Woo et al 1994, Ider and Birgul 1998, Kwon et al 2002, Seo et al 2003, Oh et al 2003, Muftuler et al 2004, Ozdemir et al 2004, Oh et al 2005). The externally injected low-frequency current produces the internal current density $\mathbf{J} = (J_x, J_y, J_z)$ and magnetic flux density $\mathbf{B} = (B_x, B_y, B_z)$ distributions, where the conductivity information is embedded. When the main field of the MRI scanner is in the $z$-direction, the induced $z$-component, $B_z$, causes changes in the MR phase image. Without rotating the object, therefore, one can extract an image of only $B_z$ from the MR phase image (Joy et al 1989). Magnetic resonance electrical impedance tomography (MREIT) can now produce images of the electrical conductivity distribution with injection currents of about 5 mA or less (Birgul et al 2006, Hamamura et al 2006, Woo and Seo 2008, Hamamura and Muftuler 2008, Hasanov et al 2008, Kim et al 2009, Seo and Woo 2011).

Since $B_z$ reflects $\mathbf{J}$ as its volume integral and the normal component of $\mathbf{J}$ is continuous at the interface of a conductivity change, most MREIT image reconstruction algorithms using only $B_z$ need at least two independent injection currents to produce isotropic conductivity images. However, biological tissues such as the white matter and skeletal muscle show anisotropy due to asymmetric cellular structures. Even though there have been a few studies for anisotropic conductivity image reconstructions in MREIT (Seo et al 2004, Pyo et al 2005,
Figure 1. (a) DT-MRI pulse sequence and (b) MREIT pulse sequence with low-frequency injection currents.

Degirmenci and Eyuboglu 2007, 2012, 2013, Nam and Kwon 2010b), there is no practically reliable method available yet. We, therefore, need a reliable experimental method to obtain additional information on the three-dimensional anisotropic conductivity tensor.

In this paper, we adopt the linear relation between the conductivity tensor \( \mathbf{C} \) and the water diffusion tensor \( \mathbf{D} \) (Tuch et al 2001) and propose a novel algorithm to reconstruct the anisotropic conductivity tensor by combining the DT-MRI and MREIT techniques without any referred extra-cellular conductivity and diffusivity information. This idea was first suggested by Ma et al (2013) as diffusion tensor current density impedance imaging (DT-CD-II), where DT-MRI is combined with current density impedance imaging (CDII) for anisotropic conductivity tensor imaging. Since they use CDII, measurements of the vector quantity \( \mathbf{B} \) are required. To obtain all the three components of \( \mathbf{B} = (B_x, B_y, B_z) \), the imaging object must be rotated twice inside the MRI scanner. In this paper, we perform the anisotropic conductivity image reconstruction using only \( B_z \) data without rotating the object.

To use the linear relation between the two tensors, we recover the projected current density \( \mathbf{J}_P \) from the measured \( B_z \) data as the best approximation of \( \mathbf{J} \). Using the reconstructed \( \mathbf{J}_P \) and the water diffusion tensor map, we determine the extra-cellular conductivity and diffusivity ratio (ECDR) denoted as \( \eta_{ext} \). This enables us to use a new direct algorithm to quantitatively visualize the anisotropic conductivity tensor map.

In the following sections, we will first investigate the relation between \( \mathbf{C} \) and \( \mathbf{D} \). Presenting a novel direct conductivity tensor reconstruction algorithm combining \( \mathbf{J}_P \) and \( \mathbf{D} \), we will evaluate its performance through numerical simulations and imaging experiments using a phantom including both isotropic and anisotropic objects.

2. Methods

2.1. Relation between conductivity and water diffusion tensors

The pulsed gradient spin echo (PGSE) in figure 1(a) excites the spin system by applying time-constant magnetic field gradients before and after the \( \pi \)-pulse and acquires the k-space data. Due to the dephasing of magnetization because of diffusion in the period \( \Delta \), the acquired signal intensity reflects the amount of diffusion that has occurred during the diffusion gradient pulses.
The effective water diffusion tensor \( \mathbf{D} \) can be written as a positive definite symmetric matrix:

\[
\mathbf{D} = \mathbf{S}_D \tilde{\mathbf{D}} \mathbf{S}_D^T \quad \text{with} \quad \tilde{\mathbf{D}} = \begin{pmatrix}
d_1 & 0 & 0 \\
0 & d_2 & 0 \\
0 & 0 & d_3 
\end{pmatrix}
\] (1)

where the column vectors of \( \mathbf{S}_D \) are the orthogonal eigenvectors of \( \mathbf{D} \), the superscript \( T \) denotes the transpose and \( d_i \) for \( i = 1, 2, 3 \) are the corresponding eigenvalues. The signal intensity \( \rho_D \) of diffusion MRI is given by

\[
\rho_D = \rho_0 \exp(-b \mathbf{g}^T \tilde{\mathbf{D}} \mathbf{g})
\] (2)

where \( \rho_0 \) is the signal obtained without diffusion-sensitizing gradient, \( \mathbf{g} \) is the normalized diffusion-sensitizing gradient vector and \( b \) denotes the diffusion-weighting factor depending on the gradient pulse used in the DT-MRI sequence. From figure 1(a),

\[
b = \frac{\gamma^2 \delta^2 G^2}{\Delta - \frac{\delta}{3}}
\] (3)

where \( \gamma = 26.75 \times 10^7 \text{rad Ts}^{-1} \) is the gyromagnetic ratio of hydrogen and \( \delta \) and \( G \) are the duration and amplitude, respectively, of the diffusion-sensitizing gradient pulse along a given direction. Diffusion in the \( x \)-, \( y \)- and \( z \)-directions can be measured by applying the gradient in the \( x \)-, \( y \)- and \( z \)-directions, respectively.

The eigenvalue \( c_i \) of the conductivity tensor \( \mathbf{C} \) can be represented as

\[
c_i = \frac{\sigma_{\text{ext}}}{d_{\text{ext}}} \left[ d_i \left( \frac{d_{\text{int}}}{3d_{\text{ext}}} + 1 \right) + \frac{d_i d_{\text{int}}}{d_{\text{ext}}} + \frac{2}{3} d_{\text{int}} \right] + O(d_{\text{int}}^2), \quad i = 1, 2, 3
\] (4)

where \( \sigma_{\text{ext}} \) is the extra-cellular conductivity, \( d_{\text{int}} \) and \( d_{\text{ext}} \) are the intra- and extra-cellular diffusion coefficients, respectively, and \( O(d_{\text{int}}^2) \) is bounded as \( d_{\text{int}} \) tends to infinity (Tuck et al 2001, Haueisen et al 2002). For small intra-cellular diffusion \( d_{\text{int}} \approx 0 \), the eigenvalue \( c_i \) satisfies

\[
c_i = \frac{\sigma_{\text{ext}}}{d_{\text{ext}}} d_i, \quad i = 1, 2, 3.
\] (5)

The eigenvalues \( c_i \) of \( \mathbf{C} \) and the eigenvectors of \( \mathbf{D} \) in \( \mathbf{S}_D \) can determine the conductivity tensor as

\[
\mathbf{C} = \mathbf{S}_D \tilde{\mathbf{C}} \mathbf{S}_D^T \quad \text{where} \quad \tilde{\mathbf{C}} = \begin{pmatrix}
c_1 & 0 & 0 \\
0 & c_2 & 0 \\
0 & 0 & c_3 
\end{pmatrix}
\] (6)

2.2. Measurement of current-induced magnetic flux density

In a conventional spin-echo MREIT pulse sequence, both positive and negative currents of the same amplitude and duration are injected. These injection currents with the pulse width of \( T_c \) accumulate extra phases. The corresponding k-space MR signals can be described as

\[
S^\pm(k_x, k_y) = \int_\Omega \rho(x, y) e^{i\phi(x,y)} e^{i\frac{k_y}{\gamma} T_c} e^{i2\pi(k_x, k_y) T_c} dx dy
\] (7)

where \( \rho \) is the \( T_2 \) weighted spin density, \( \phi \) is any systematic phase artifact and \( \Omega \) is a field-of-view (FOV). Here, the superscript of \( S^\pm \) denotes a brief notation for \( S^+ \) and \( S^- \). For the standard coverage of the k-space, we set

\[
k_x = \frac{\gamma}{2\pi} G_x (t - T_E) \quad \text{for} \quad |t - T_E| < T_c/2
\]

\[
k_x = \frac{\gamma}{2\pi} m \Delta G_x T_{pe} \quad \text{for} \quad m = -N_y/2, \ldots, N_y/2 - 1
\] (8)
where $G_x$ is the frequency encoding gradient strength, $T_E$ is the echo time, $\Delta G_y$ is the phase encoding step and $T_{pe}$ is the phase encoding time. The induced magnetic flux densities generated by the positive and negative injection currents $I^\pm$ are denoted as $\pm B_z$, respectively.

The standard two-dimensional inverse Fourier transform provides the complex MR images $M^\pm$ as

$$M^\pm(x, y) = \rho(x, y) e^{i\phi(x, y)} e^{\pm i \gamma B_z T_c}.$$  \hspace{1cm} (9)

From (9), the magnetic flux density $B_z$ can be recovered as

$$B_z(x, y) = \frac{1}{2y T_c} \tan^{-1} \left( \frac{\alpha(x, y)}{\beta(x, y)} \right)$$  \hspace{1cm} (10)

where $\alpha$ and $\beta$ are the imaginary and real part of $M^+ / M^-$, respectively. From the analysis by Scott et al (1992) and Sadleir et al (2005), the noise standard deviation $sd_{B_z}$ of the measured $B_z$ is given by

$$sd_{B_z} = \frac{1}{2y T_c \gamma M}$$  \hspace{1cm} (11)

where $T_c$ is the current injection duration and $\gamma M$ is the signal-to-noise ratio (SNR) of the MR magnitude image.

Using the property that the noise standard deviation is inversely proportional to $T_c$ and $|\rho|$, a multi-echo imaging sequence which acquires a series of echoes has been developed and optimized to reduce the noise level in the measured $B_z$ data (Nam and Kwon 2010a). Figure 1(b) shows a schematic diagram for the injection current nonlinear encoding (ICNE) gradient-multi-echo pulse sequence.

### 2.3. Computation of projected current density

Let $\Omega$ be a cylindrical domain with its boundary $\partial\Omega$. We may express $\Omega$ as a union of the slices perpendicular to the $z$-axis:

$$\Omega = \cup_{t \in (-H, H)} \Omega_t \quad \text{where} \quad \Omega_t = \Omega \cap \{(x, y, z) \in \mathbb{R}^3 | z = t \in (-H, H)\}.$$  \hspace{1cm} (12)

Here, $\Omega_0$ denotes the center slice. In this paper, we use the following two-dimensional estimations:

$$\hat{\nabla} f := \left( \frac{\partial f}{\partial x}, \frac{\partial f}{\partial y}, 0 \right), \quad \hat{\nabla}^\perp f := \left( \frac{\partial f}{\partial y}, -\frac{\partial f}{\partial x}, 0 \right).$$  \hspace{1cm} (13)

Since $B_z$ is the only measurable quantity without rotating the object inside the MRI scanner, we inject current in the orthogonal direction to the main magnetic field through a pair of attached electrodes to maximize $B_z$. According to the Helmholtz decomposition, Park et al (2007) decomposed the internal current density $J$ into curl-free and divergence-free components as

$$J = J_0 + \nabla \times \Psi.$$  \hspace{1cm} (14)

Here, $J_0 := -\nabla \alpha$ is the background current density determined by

$$\begin{cases}
\nabla^2 \alpha = 0 & \text{in } \Omega \\
\nabla \alpha \cdot n = g & \text{on } \partial\Omega
\end{cases}$$  \hspace{1cm} (15)

where $n$ is the outward unit normal vector on $\partial\Omega$ and $g$ denotes the Neumann boundary data subject to the injection current. The vector potential $\Psi$ satisfies

$$\begin{cases}
-\nabla^2 \Psi = \nabla \times J & \text{in } \Omega \\
\nabla \cdot \Psi = 0 & \text{in } \Omega \\
\n\nabla \times \Psi \cdot n = 0 & \text{on } \partial\Omega
\end{cases}$$  \hspace{1cm} (16)
We define the vector field \( \mathbf{J}_p \) as the projected current density, which can be directly calculated from any vector field \( \mathbf{J} \), with

\[
\mathbf{J}_p := \mathbf{J}_0 + \nabla \perp \psi \quad \text{in} \quad \Omega_t
\]

where the potential \( \psi \) solves

\[
\begin{cases}
\nabla^2 \psi = \frac{1}{\mu_0} \nabla^2 B_z \quad \text{in} \quad \Omega_t \\
\nabla \perp \psi \cdot \mathbf{n} = 0 \quad \text{on} \quad \partial \Omega_t.
\end{cases}
\]

Note that \( \mathbf{J}_p \) may not be identical to \( \mathbf{J} \) of which the \( z \)-component is not negligible. The projected current density \( \mathbf{J}_p \) is the quantity observable from the measured \( B_z \) data, which satisfies \( \nabla \cdot \mathbf{J}_p = 0 \) and the following stability condition (Park et al 2007):

\[
\| \mathbf{J} - \mathbf{J}_p \|_{\Omega_t} \leq C \left( \left\| \frac{\partial}{\partial z} (J_z - J_{0,z}) \right\|_{\Omega_t} + \left\| J_z - J_{0,z} \right\|_{\Omega_t} \right).
\]

Here, the constant \( C \) depends only on \( \Omega_t \) and not on \( \mathbf{J} \). The estimated stability between \( \mathbf{J} \) and \( \mathbf{J}_p \) implies that \( \mathbf{J}_p \) is close to the true current density \( \mathbf{J} \) depending on the \( z \)-component of \( \mathbf{J} - \mathbf{J}_p \).

2.4. Reconstruction of conductivity tensor

As described by Ma et al (2013), from (5) and (6), we can get

\[
\mathbf{C} = \mathbf{S}_0 \mathbf{\tilde{S}}_D^T = \left( \frac{\sigma_{\text{ext}}}{\eta_{\text{ext}}} \right) \mathbf{S}_0 \tilde{\mathbf{S}}_D^T = \frac{\sigma_{\text{ext}}}{\eta_{\text{ext}}} \mathbf{D}.
\]

The internal current densities \( \mathbf{J}_i \) for \( i = 1, 2 \) subject to two externally injected currents can be represented as

\[
\mathbf{J}_i = -\mathbf{C} \nabla u_i = -\eta_{\text{ext}} \mathbf{D} \nabla u_i
\]

where \( u_i \) is the voltage potential corresponding to the injection current \( g_i \) for \( i = 1, 2 \) and

\[
\eta_{\text{ext}} := \frac{\sigma_{\text{ext}}}{\eta_{\text{ext}}}
\]

is a scale factor called the ECDR.

Using the estimated diffusion tensor \( \mathbf{D} \), the current \( \mathbf{J}_i \) satisfies the following relation:

\[
\nabla \times (\mathbf{D}^{-1} \mathbf{J}_i) = -\nabla \times (\eta_{\text{ext}} \nabla u_i) = -\nabla \eta_{\text{ext}} \times \nabla u_i
\]

and it implies

\[
\nabla \times (\mathbf{D}^{-1} \mathbf{J}_i) = -\frac{\nabla \eta_{\text{ext}}}{\eta_{\text{ext}}} \times (\eta_{\text{ext}} \nabla u_i) = \nabla \log \eta_{\text{ext}} \times (\mathbf{D}^{-1} \mathbf{J}_i).
\]

The term \( \mathbf{D}^{-1} \mathbf{J}_i \) can be defined as the pseudo-current as suggested by Ma et al (2013). With a current density in place of \( \mathbf{D}^{-1} \mathbf{J}_i \), the relation (24) is also the basis to recover the isotropic conductivity from two internal current densities in CDII (Hasanov et al 2008).

Assuming that the reconstructed projected current density \( \mathbf{J}_{p,i} \approx \mathbf{J}_i = -\eta_{\text{ext}} \mathbf{D} \nabla u_i \) by injecting transversal currents, the unknown \( \eta_{\text{ext}} \) can be represented as

\[
\nabla \log \eta_{\text{ext}} \times (\mathbf{D}^{-1} \mathbf{J}_{p,i}) = \nabla \times (\mathbf{D}^{-1} \mathbf{J}_{p,i})
\]

where \( \mathbf{D} \) is known. Setting

\[
\mathbf{E}_i = \mathbf{D}^{-1} \mathbf{J}_{p,i},
\]
the identity (25) can be written as

$$\nabla \times (E_{i,x}, E_{i,y}) = -\nabla \eta_{\text{ext}} \times \nabla u_i = \hat{\nabla} \log \eta_{\text{ext}} \times (E_{i,x}, E_{i,y})$$

(27)

where $E_{i,x}$ and $E_{i,y}$ are the $x$- and $y$-components of $E_i$, respectively. Using (27), we have the following matrix equation:

$$Ax = b$$

(28)

where

$$A = \begin{pmatrix} E_{1,x} & E_{1,y} \\ E_{2,x} & E_{2,y} \end{pmatrix}, \quad b = \begin{pmatrix} -\nabla \times (E_{1,x}, E_{1,y}) \\ -\nabla \times (E_{2,x}, E_{2,y}) \end{pmatrix}$$

(29)

and the unknown variable $x = (\frac{\partial \log \eta_{\text{ext}}}{\partial x}, \frac{\partial \log \eta_{\text{ext}}}{\partial y})^T$. By solving (28), we get the transversal gradient vector $\hat{\nabla} \log \eta_{\text{ext}}$ in the imaging slice $\Omega_t$.

The log-scale $\log \eta_{\text{ext}}$ is recovered by

$$\log \eta_{\text{ext}}(r) = -\int_{\Omega_t} \hat{\nabla} \Phi_2(r - r') \cdot \hat{\nabla} \log \eta_{\text{ext}}(r') \, dr' + \int_{\partial \Omega_t} \frac{\partial \Phi_2(r - r')}{\partial n} \log \eta_{\text{ext}}(r') \, dl_r$$

(30)

where $\Phi_2(r - r') = \frac{1}{2\pi} \log |r - r'|$ is the two-dimensional fundamental solution of the Laplace equation. From a reference background value of $\eta_{\text{ext}}$, the log-scale $\log \eta_{\text{ext}}$ can be iteratively updated based on the equation (30). A similar formula to determine the isotropic conductivity from the measured $B_z$ data was introduced by Oh et al. (2003). To guarantee the uniqueness of the solution $\log \eta_{\text{ext}}$, we set $\log \eta_{\text{ext}} := \zeta + \varphi$ where

$$\zeta(r) = -\int_{\Omega_t} \hat{\nabla} \Phi_2(r - r') \cdot \hat{\nabla} \log \eta_{\text{ext}}(r') \, dr'$$

$$\varphi(r) = \int_{\partial \Omega_t} \frac{\partial \Phi_2(r - r')}{\partial n} \log \eta_{\text{ext}}(r') \, dl_r$$

(31)

The following two-dimensional harmonic equation in $\Omega_t$ is uniquely determined up to a constant:

$$\begin{cases} \hat{\nabla}^2 \varphi(r) = 0 & \text{in } \Omega_t \\ \hat{\nabla} \varphi(r) \cdot n(r) = \hat{\nabla} (\log \eta_{\text{ext}}(r) - \zeta(r)) \cdot n(r) & \text{on } \partial \Omega_t. \end{cases}$$

(32)

Therefore, the scale factor $\log \eta_{\text{ext}}$ is uniquely determined up to a constant in $\Omega_t$. The determination of the constant depends on a practical situation including a known background conductivity value or a reference region with a known conductivity value such as the hydrogel under the thin carbon electrode.

2.5. Numerical simulation

We built a three-dimensional numerical model using COMSOL (COMSOL Inc., USA). Figure 2(a) shows the cylindrical model with 100 mm diameter and 140 mm height. We attached two pairs of electrodes on its surface to inject currents. Figure 2(b) shows its finite element mesh with 264 020 tetrahedral and 19 130 triangular elements. As shown in figure 2(c), the model includes two types of anomalies: one is the isotropic agar gel object and the other is the anisotropic muscle tissue with different directional diffusion rates. The orientations of three muscle tissues were 0, $\pi/2$ and 0.6 radian as marked in figure 2(c). The background of the model was assumed to be saline.
To generate simulated data, we set $S_0$ as the signal obtained without the diffusion-sensitizing gradient:

$$S_0(r) = \rho(r) (1 - e^{-T_e/T_1(r)}) e^{-T_e/T_2(r)}.$$  

(33)

With the diffusion-sensitizing gradient, we calculated the echo signal intensity as

$$S_b = S_0 e^{-bg^TD_b}$$

(34)

where $g$ represents the normalized diffusion-sensitizing gradient vector and

$$D = \begin{pmatrix} \cos \alpha & \sin \alpha & 0 \\ -\sin \alpha & \cos \alpha & 0 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} d_1 \\ d_2 \\ d_3 \end{pmatrix} \begin{pmatrix} \cos \alpha & \sin \alpha & 0 \\ -\sin \alpha & \cos \alpha & 0 \\ 0 & 0 & 1 \end{pmatrix}^T$$

(35)

where $\alpha$ is the orientation specified in table 1. Figure 2(d) shows the echo signal intensities $S_b$ for the six direction gradients of

$$g = \left\{ (1, 0, 0), (0, 1, 0), (0, 0, 1), \left( \frac{1}{\sqrt{2}}, \frac{1}{\sqrt{2}}, 0 \right), \left( 0, \frac{1}{\sqrt{2}}, \frac{1}{\sqrt{2}} \right), \left( \frac{1}{\sqrt{2}}, 0, \frac{1}{\sqrt{2}} \right) \right\}$$

(36)

and the used parameters in table 1.
Table 1. Simulation parameters to generate the diffusion tensor map in figure 2.

| Parameter          | Saline | Muscle | Agar |
|--------------------|--------|--------|------|
| Proton density     | 1.0    | 0.7    | 0.5  |
| $T_1$ (ms)         | 3620   | 1420   | 883  |
| $T_2$ (ms)         | 767    | 31.7   | 70   |
| $d_1$ ($\times 10^{-3}$ mm$^2$ s$^{-1}$) | 1.70   | 1.17   | 2.10 |
| $d_2$ ($\times 10^{-3}$ mm$^2$ s$^{-1}$) | 1.70   | 0.84   | 2.10 |
| $d_3$ ($\times 10^{-3}$ mm$^2$ s$^{-1}$) | 1.70   | 0.70   | 2.10 |
| Orientation, $\alpha$ (rad) | 0      | 0, $\pi/2$, 0.6 | 0    |

The most commonly used measure to quantify the anisotropy is the fractional anisotropy (FA). We calculated the FA value as the normalized variance of the three eigenvalues of the water diffusion tensor:

$$FA = \sqrt{\frac{3}{2} \left( \frac{d_1 - \hat{d}}{d_2 + d_3} \right)^2 + \left( \frac{d_2 - \hat{d}}{d_1 + d_3} \right)^2 + \left( \frac{d_3 - \hat{d}}{d_1 + d_2} \right)^2}$$

(37)

where $\hat{d} := \frac{d_1 + d_2 + d_3}{3}$. Figure 2(e) shows the color-coded FA map of the numerical model to indicate diffusion along the $x$-axis (red), $y$-axis (green) and $z$-axis (blue). We computed the FA map by taking the projection of the FA value on to the principal eigenvector (Jiang et al. 2006). For the case of our numerical simulation, the principal eigenvector was $[-\cos \alpha, -\sin \alpha, 0]^T$ and, therefore, the color-coded FA map was computed as

$$[R, G, B] = [FA \cos \alpha, FA \sin \alpha, 0].$$

For the muscle anomaly oriented at 0.6 radian, the FA value was found to be 0.2610 using equation (37). The corresponding color was $[R, G, B] = [0.2154, 0.1474, 0]$, which is between the red and green. Since the FA value is zero for the isotropic object, the agar object is not visible in the FA map.

For the MREIT simulation, the isotropic conductivity values of the background saline and circular agar anomaly regions were 0.2 Sm$^{-1}$ and 0.5 Sm$^{-1}$, respectively. The orientations of the eigenvectors of the anisotropic muscle region were assumed to be the same as those of the diffusion eigenvectors and the eigenvalues were set to be $(c_1, c_2, c_3) = (1.00, 0.710, 0.675)$ Sm$^{-1}$.

### 2.6. Imaging experiment

Figures 3(a) and (b) illustrate the phantom design. Around the cylindrical phantom with 200 mm diameter and 140 mm height, we attached four carbon-hydrogel electrodes (HUREV Co. Ltd, Korea). We filled it with 1 S m$^{-1}$ saline and placed one cylindrical isotropic gel object of 2 S m$^{-1}$ conductivity. We also put three pieces of anisotropic biological tissue (chicken breast) with the dimension of $35 \times 35 \times 35$ mm$^3$. We placed the phantom inside the bore of the 3 T MRI scanner (Achieva, Philips) equipped with the 32-channel receiver RF coil (SENSE-Head-32ch, Philips).

We acquired the diffusion-weighted data using the single-shot spin-echo echo planar imaging sequence. We applied the diffusion-weighting gradients in 15 directions with $b$-value of 1000 s mm$^{-2}$. The imaging parameters were as follows: repetition time $T_R = 3000$ ms, echo time $T_E = 73$ ms, slice thickness = 5 mm, number of excitations (NEX) = 2, FOV = $180 \times 180$ mm$^2$ and acquisition matrix size = $64 \times 64$. The NEX means the number of repeated acquisitions to improve the SNR by averaging. Figure 3(c) shows the $T_2$ weighted MR magnitude image. Three images in figure 3(d) are the $b$-value diffusion-weighted MR
magnitude images with the applied gradients in the x-, y- and z-directions. Figure 3(e) shows the color-coded FA map. The left chicken breast object shows diffusion along the x-direction (red), the middle-top object shows diffusion along intermediate directions (red and green) and the right one shows diffusion along the y-direction (green).

We used a custom-designed MREIT current source to sequentially inject 10 mA currents for the horizontal and vertical directions (Kim et al. 2011). The current source was synchronized with the ICNE multi-gradient-echo pulse sequence to optimize the multiple $B_{z,l}$ data for $l = 1, \ldots, N_E$ by minimizing the noise effect (Nam and Kwon 2010a). The imaging parameters were as follows: repetition time $T_R = 35$ ms, first echo time $T_{E_1} = 1.88$ ms, echo space $E_s = 2.2$ ms, slice thickness = 5 mm, number of echoes $N_E = 15$, NEX = 50, flip angle = 6.65°, FOV = 260 × 260 mm², imaging matrix = 128 × 128. The imaging time ($T_R \times 128 \times NEX$) was 3.7 min. For each current injection direction, we acquired the k-space data twice, subject to the positive and negative injection currents to cancel out the systematic phase artifact. Therefore, to obtain the full data set for the horizontal and vertical directions, the total imaging time was 14.8 min. The multiple echoes corresponding to the different echo times $T_{E_l} = 1.88 + 2.2 \times (l - 1)$ ms for $l = 1, \ldots, 15$ were acquired by the alternating read-out gradients.

3. Results

3.1. Simulation results

Figure 4(a) shows the simulated data of $B_{z,1}$ and $B_{z,2}$ subject to the horizontal and vertical current injections, respectively. Figure 4(b) shows the x- and y-components of the recovered
Figure 4. (a) Simulated $B_z$ data and (b) computed projected current density $J_{P}$. Superscripts 1 and 2 denote the horizontal and vertical current injections, respectively. (c) Diffusion tensor map and (d) computed ECDR $\eta_{ext}$. (e) Reconstructed images of the anisotropic conductivity tensor $C$. 

\[ B_{z1} \quad B_{z2} \]
\[ J_{P1} \quad J_{P2} \]
\[ D_{xx} \quad D_{yy} \quad D_{zz} \]
\[ D_{xy} \quad D_{xz} \quad D_{yz} \]
\[ \eta_{ext} \]
\[ \sigma_{11} \quad \sigma_{22} \quad \sigma_{33} \]
\[ \sigma_{12} \quad \sigma_{13} \quad \sigma_{23} \]
projected current densities $J_{p1}$ and $J_{p2}$ for the horizontal and vertical injection currents, respectively.

Figure 4(c) shows the water diffusion tensor $D$. Since it is symmetric with six variables, we estimated them from the six diffusion-sensitizing gradient vectors and one reference $S_0$ by taking the logarithm on both sides of (34). From the estimated water diffusion tensor, we determined its three eigenvectors by diagonalizing it. Using $J_p$ in figure 4(b) and $D$ in (c), we solved the matrix equation (28) to compute the ECDR factor $\eta_{ext}$ using a regularization factor $\xi$ as

$$\tilde{\nabla} \log \eta_{ext} = (A^T A + \xi I)^{-1} A^T b$$

(38)

where $I$ is the $2 \times 2$ identity matrix. The value of $\xi$ was set to be inversely proportional to $|A|$ small and vice versa. Figures 4(d) and (e) show the computed ECDR $\eta_{ext}$ and the reconstructed conductivity tensor $C$, respectively.

We estimated the $L^2$-error of the reconstructed $C$ using the following formula:

$$E(C) = \sqrt{\frac{\sum_{(x_i, y_j) \in \Omega_i} (C(x_i, y_j) - C^*(x_i, y_j))^2}{N_{xy}}}$$

(39)

where $\Omega_i$ is the imaging region, $C^*$ denotes the true conductivity tensor and $N_{xy}$ is the number of pixels in $\Omega_i$. The $L^2$-error values were 0.0900, 0.0885, 0.0895, 0.0066, 0.000 and 0.000 for $\sigma_{11}, \sigma_{22}, \sigma_{33}, \sigma_{12}, \sigma_{13}$ and $\sigma_{23}$, respectively.

To evaluate the performance of the proposed method at different noise levels, we added the white Gaussian random noise to both the diffusion weighted signal and $B_z$ data assuming that the DT-MRI and MREIT experiments were conducted independently. For the DT-MRI experiment, we assumed that the SNR of $S_0$ in the background saline varied from 70 to 80 dB, in steps of 5 dB. Since the SNRs of the different regions depend on their relaxation properties, we used the following relation to compute the SNRs of the gel and tissue regions:

$$\Upsilon_{M,k} = \Upsilon_{M,0} \frac{(1 - e^{-T_{1,k}/T_1}) e^{-T_{2,k}/T_2}}{(1 - e^{-T_{1,0}/T_1}) e^{-T_{2,0}/T_2}}$$

(40)

where $T_{1,0}, T_{2,0}$ and $\Upsilon_{M,0}$ were the $T_1$ and $T_2$ relaxation values and the SNR of the background saline region, respectively. The subscript $k$ denotes either the gel or tissue regions and the $T_{1,k}$ and $T_{2,k}$ values are given in table 1. We chose $T_R$ and $T_E$ as 4000 and 40 ms, respectively, which were similar to those used in the typical experimental study. After computing the SNR in each region, we calculated the noise standard deviation $s_d$ of each region using the following relation:

$$s_d = 0.66 \frac{\langle S_{b,k} \rangle}{\Upsilon_{M,k}}$$

(41)

where $\langle S_{b,k} \rangle$ is the average signal amplitude in each region and the factor 0.66 accounts for Rayleigh statistics. We generated and added the complex white Gaussian noise with zero mean and the standard deviation given by (41).

For the MREIT experiment, we assumed that the SNR of the background saline region $\Upsilon_{M,0}$ varied from 70 to 100 dB, in steps of 15 dB. With $T_R = 1200$ and $T_E = 15$ ms, we computed the expected noise levels for the gel and tissue regions using (40). For the current pulse width, $T_c = 30$ ms, the expected noise standard deviation, $s_d_{B_z}$ of $B_z$, for each region, was

$$s_d_{B_z,k} = \frac{1}{2\gamma T_c \Upsilon_{M,k}}$$

(42)
Figure 5. Computed ECDR $\eta_{\text{ext}}$ and reconstructed images of the diagonal elements of $C$ for different noise levels of $(\Upsilon_{D M,0}, \Upsilon_{B z M,0})$: (a): $(70, \infty)$, (b): $(70, 100)$, (c): $(70, 85)$ and (d): $(70, 70)$ dB.

Table 2. $L^2$-errors of the reconstructed conductivity tensor for different noise levels.

| $\Upsilon_{B z M,0}$ (dB) | $\sigma_{11}$ | $\sigma_{22}$ | $\sigma_{33}$ | $\sigma_{12}$ | $\sigma_{13}$ | $\sigma_{23}$ |
|--------------------------|--------------|--------------|--------------|--------------|--------------|--------------|
| $\infty$                 | 0.0916       | 0.0909       | 0.0907       | 0.0221       | 0.0213       | 0.0220       |
| 100                      | 0.1097       | 0.1078       | 0.1052       | 0.0225       | 0.0216       | 0.0226       |
| 85                       | 0.1132       | 0.1109       | 0.1056       | 0.0235       | 0.0232       | 0.0243       |
| 70                       | 0.1240       | 0.1211       | 0.1186       | 0.0247       | 0.0242       | 0.0256       |

We tried four different noise levels of $(\Upsilon_{D M,0}^{(b)}, \Upsilon_{B z M,0}^{(b)}) = (70, \infty)$, $(70, 100)$, $(70, 85)$ and $(70, 70)$ dB where $\Upsilon_{D M,0}^{(b)}$ and $\Upsilon_{B z M,0}^{(b)}$ are the background region SNRs of the DT-MRI and MREIT experiments, respectively. Figure 5 shows images of the ECDR $\eta_{\text{ext}}$ and diagonal elements $\sigma_{11}, \sigma_{22}, \sigma_{33}$ of $C$ for the chosen noise levels. Table 2 summarizes the estimated $L^2$-errors showing that the proposed method stably reconstructed the conductivity tensor $C$ for the chosen noise levels.
Table 3. Conductivity values ($\sigma_{ij}$), eigenvalues ($\epsilon_i$) and FA values computed from the reconstructed conductivity tensor images of the phantom in figure 3.

|                | Saline     | Agar       | Left tissue | Right tissue | Top-middle tissue |
|----------------|------------|------------|-------------|--------------|-------------------|
| $\sigma_{11}$  | 1.0271 ± 0.0246 | 2.1771 ± 0.1444 | 0.2220 ± 0.0403 | 0.1587 ± 0.0227 | 0.1576 ± 0.0504 |
| $\sigma_{22}$  | 1.0335 ± 0.0209 | 2.1950 ± 0.1538 | 0.1745 ± 0.0295 | 0.1969 ± 0.0249 | 0.1503 ± 0.0449 |
| $\sigma_{33}$  | 1.0187 ± 0.0230 | 2.1978 ± 0.1637 | 0.1679 ± 0.0303 | 0.1541 ± 0.0221 | 0.1355 ± 0.0410 |
| $\sigma_{12}$  | -0.0177 ± 0.0062 | -0.0069 ± 0.0117 | -0.0089 ± 0.0023 | 0.0113 ± 0.0034 | 0.0192 ± 0.0057 |
| $\sigma_{13}$  | -0.0095 ± 0.0053 | 0.0011 ± 0.0193 | -0.0017 ± 0.0016 | 0.0010 ± 0.0031 | 0.0039 ± 0.0026 |
| $\sigma_{23}$  | -0.0039 ± 0.0052 | -0.0195 ± 0.0161 | -0.0007 ± 0.0040 | 0.0029 ± 0.0010 | 0.0023 ± 0.0020 |
| $c_1$          | 1.0525 ± 0.0240 | 2.2294 ± 0.1581 | 0.2241 ± 0.0391 | 0.1994 ± 0.0532 | 0.1745 ± 0.0532 |
| $c_2$          | 1.0202 ± 0.0239 | 2.1864 ± 0.1499 | 0.1745 ± 0.0308 | 0.1579 ± 0.0212 | 0.1364 ± 0.0422 |
| $c_3$          | 1.0065 ± 0.0209 | 2.1542 ± 0.1538 | 0.1658 ± 0.0302 | 0.1515 ± 0.0222 | 0.1326 ± 0.0408 |
| FA             | 0.0233 ± 0.0050 | 0.0178 ± 0.0049 | 0.1664 ± 0.0098 | 0.1535 ± 0.0161 | 0.1561 ± 0.0105 |

3.2. Experimental results

Figure 6(a) shows the measured $B_{z1}$ and $B_{z2}$ data from the phantom in figure 3 corresponding to the horizontal and vertical current injections, respectively. Figure 6(b) plots computed $J_{P1}$ and $J_{P2}$ for the horizontal and vertical injection currents, respectively. Figure 6(c) shows the diffusion tensor map $D$. In the three chicken breast regions with muscle fibers oriented in the $x$-, $y$- and $xy$-directions as shown in figure 3(e), the diffusion tensor map shows different diffusion anisotropy effects in each region. The cylindrical gel region shows the isotropic diffusion. Figure 6(d) and (e) show images of the ECDR $\eta_{ext}$ and the conductivity tensor $C$, respectively, reconstructed from the measured $D$ and $B_z$ data without using any referred or assumed extra-cellular and diffusivity values.

Figure 7 shows the color-coded FA and conductivity values in the three chicken breast tissue regions. The reconstructed conductivity values of the tissues exhibit their anisotropic characteristics depending on the muscle fiber orientation. We can see that $\sigma_{11}$ is relatively higher in the left tissue and $\sigma_{12}$ is higher in the top middle tissue.

Table 3 shows the conductivity values, eigenvalues and FA values of the reconstructed conductivity tensor $C$ at five different regions. The maximum eigenvalues of the background saline and the agar gel object were 1.05 and 2.22 $\text{S m}^{-1}$, respectively, which were close to the true values of 1 and 2 $\text{S m}^{-1}$. For the anisotropic muscle regions, the ratio between the maximum and minimum eigenvalues was 1.38.

4. Discussion

To compare the reconstructed conductivity tensor with the one without using the measured $B_z$ data, we estimated the extra-cellular diffusivity $d_{ext}$ in the background saline as

$$d_{ext} = \frac{D_{xx} + D_{yy} + D_{zz}}{3} = 2.3604 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}. \quad (43)$$

With the known background conductivity value of $\sigma_{ext} = 1 \text{ S m}^{-1}$, the extra-cellular conductivity to the diffusivity ratio was given as

$$\frac{\sigma_{ext}}{d_{ext}} = 0.4237 \text{ Ss mm}^{-3}. \quad (44)$$

Without using the measured $B_z$ data, we computed the eigenvalues of the conductivity tensor $C$ using the following relation:

$$\sigma_i = \frac{\sigma_{ext}}{d_{ext}} d_i. \quad (45)$$
Figure 6. (a) Measured $B_z$ data from the phantom in figure 3 and (b) computed projected current density $J_P$. Superscripts 1 and 2 denote the horizontal and vertical current injections, respectively. (c) Diffusion tensor map and (d) computed ECDR $\eta_{ext}$. (d) Reconstructed images of the anisotropic conductivity tensor $C$. 
Figure 7. (a) Color-coded FA map of three chicken breast tissue regions and (b) reconstructed images of the anisotropic conductivity tensor $C$ in the same regions.

Figure 8. Reconstructed images of the anisotropic conductivity tensor $C$ without using MREIT data. The images lack quantitative information regarding the absolute conductivity values.

Then, we reconstructed the conductivity tensor image shown in figure 8 by using the relation $C = S_D \tilde{C} S_D^T$. We note that the agar gel region is not distinguished from the background saline. Since the water diffusion tensor can provide only the direction information of the conductivity tensor, quantitative reconstructions of the conductivity tensor are not possible without using
the referred or assumed extra-cellular conductivity values at all pixels. Comparing the reconstructed images of C in figures 6(e) and 8, we can clearly see that the proposed method overcomes the limitations of the conventional DT-MRI and MREIT techniques.

Unlike the method by Ma et al (2013) where all the three components of $B = (B_x, B_y, B_z)$ are used, we are restricted to the $B_z$ data in this paper to avoid rotating the imaging object inside the MRI scanner. Instead of using $J = \frac{1}{\mu_0} \nabla \times B$, therefore, we computed the projected current density $J_P$ from the measured $B_z$ data subject to two injection currents. Though $J_P$ is the best approximation of $J$, it may have a relatively large error if $J_{P,z}$ is significantly different from $J_{0,z}$, which is the $z$-component of the current density $J_0$ for the isotropic homogeneous conductivity distribution. This undesirable situation may occur if the isotropic or anisotropic conductivity distribution changes a lot along the $z$-direction. To reduce the error, it would be advantageous to use long electrodes in the $z$-direction and choose the imaging slices around the middle of them.

Without measuring $B_x$ and $B_y$, we can reconstruct isotropic conductivity images by using two sets of the $B_z$ data subject to two linearly independent injection currents (Woo and Seo 2008, Seo and Woo 2011). In the proposed DT-MREIT method, we take advantage of the diffusion tensor acquired by using DT-MRI and transform the anisotropic conductivity tensor image reconstruction problem into the image reconstruction of the ECDR factor $\eta_{ext}$, which is a scalar quantity. Though we speculate that the error in $\eta_{ext}$ originated from $J_P$ instead of $J$ would be small for most cases, further study is needed to quantitatively investigate the effects of using $J_P$ on the errors in reconstructed anisotropic conductivity images.

Since the proposed method should utilize the measured $B_z$ data in addition to the water diffusion tensor map, we have to carefully deal with the measurement noise in $B_z$. In the procedure to estimate $J_P$, we solve the harmonic equation (18) with $\nabla^2 B_z$ as a source term. For those local regions of MR signal void or very short $T_2$ relaxation time, the amount of noise in measured $B_z$ data cannot be reduced. Future studies of in vivo animal and human experiments should adopt denoising techniques to effectively deal with these problematic regions and avoid the noise propagation to other regions (Jeon et al 2010, Lee et al 2011).

To probe the passive material property of the conductivity, we inject current into the imaging object in MREIT. The amount of the injection current must be lower than a certain level so that the generated internal current density does not stimulate the nerve and muscle. For example, the internal current density of 1 to 23 A m$^{-2}$ was estimated as the threshold to stimulate a nerve with 20 $\mu$m diameter (Reilly 1989). Injection of 5 mA through a uniform-current-density electrode with 25 cm$^2$ contact area will produce 2 A m$^{-2}$ current density underneath the electrode (Song et al 2011). We speculate that current injections of 1 to 5 mA through surface electrodes with a practical size will produce negligible side effects such as nerve or muscle stimulations since the injected current spreads to result in a local current density below a stimulation threshold. However, there must be further studies of carefully designed in vivo animal and human experiments to find the maximum allowed imaging current.

Electrical property tomography (EPT) is another MR-based method to produce conductivity and permittivity images at the Larmor frequency using the B1 mapping technique (Katscher et al 2009, van Lier et al 2013, Zhang et al 2013). Local Maxwell tomography (LMT) also produces conductivity images at the Larmor frequency (Sodickson et al 2013). Noting that the anisotropy is mostly observable at low frequencies and also, that most physiological events occur at relatively low frequencies, MREIT, especially when combined with DT-MRI, seems to be more advantageous for functional imaging applications since it provides conductivity images at low frequencies below 1 KHz. EPT and LMT, which do not require current injection, may find important clinical applications to determine different tissue pathologies and values of local specific absorption rate.
In this study, current density imaging was done as part of the anisotropic conductivity image reconstruction. The projected current density $J_p$ may find useful clinical applications in deep brain stimulation (DBS) and transcranial direct current stimulation (tDCS). We suggest further experimental studies where the anisotropic conductivity tensor imaging together with the projected current density is utilized to better understand the underlying mechanisms of DBS and tDCS. Once we obtain the anisotropic conductivity tensor image, we may also perform various numerical analyses for any electrode configuration and stimulation pattern.

5. Conclusion

We proposed the novel method called DT-MREIT to reconstruct the anisotropic conductivity tensor image. By combining the DT-MRI and MREIT techniques, the new method quantitatively recovers the direction and magnitude of the anisotropic conductivity tensor as well as the isotropic conductivity value. Results of the numerical simulations and phantom experiments clearly show the feasibility of the new method.

The DT-MREIT technique suggested in this paper can provide quantitative anisotropic and also isotropic conductivity images together with diffusion tensor images. There could be numerous potential applications for the brain and muscle including ischemia, inflammation, bleeding and tumor (Woo and Seo 2008, Seo and Woo 2011). There is also an attempt to detect local conductivity changes accompanied by neural activities using MREIT (Sadleir et al 2010). EEG and MEG source imaging is to provide non-invasive fast imaging of the brain activity by solving the associated forward and inverse problems (Baillet et al 2001). We expect that quantitative anisotropic conductivity information will be valuable in these source imaging methods to improve their performance (Haueisen et al 2002, Gao et al 2006).

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