Functional Brain Imaging using MREIT and EIT: Requirements and Feasibility

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Abstract—**We may consider the electrical conductivity of a head tissue as a passive material property affecting the volume conduction process inside the head. The electrophysiology and bioelectromagnetism of neural activities suggest that the conductivity could be also a direct and instantaneous biomarker of a neural activity. In this paper, we review two conductivity imaging methods of Electrical Impedance Tomography (EIT) and Magnetic Resonance Electrical Impedance Tomography (MREIT) in the context of neuro-imaging. EIT produces cross-sectional images of a conductivity distribution inside the human body with a high temporal resolution and a low spatial resolution, whereas MREIT visualizes the conductivity distribution with a high spatial resolution and a low temporal resolution. EIT is based on boundary measurements of induced voltages subject to externally injected currents from 10 Hz to 500 kHz, for example. MREIT utilizes internal measurements of induced magnetic flux density distributions subject to externally injected currents at frequencies below 1 kHz. MREIT requires an MRI scanner as a tool to acquire induced magnetic flux density data, whereas one may implement EIT as an inexpensive portable electronic device. The state of the art in EIT and MREIT indicates that neither of them is readily available for direct fast functional neuro-imaging of the brain. We summarize what kinds of technical breakthroughs are needed for EIT and/or MREIT to be a clinically useful direct functional neuro-imaging method. We also propose a multi-modal approach including EIT, EEG, MREIT and MRI.**

Keywords-EIT, MREIT, EEG, MRI, conductivity, neuro-imaging

I. INTRODUCTION

It is much desirable to quantitatively visualize neural activities inside the brain in a fast and direct way. Such a functional brain imaging method will have a high impact on neuroscience as a key research tool. Functional MRI (fMRI) has been applied to a wide range of neuroscience researches to indirectly visualize neural activities inside the brain. However, it still suffers from a low signal-to-noise ratio (SNR), a slow temporal resolution and certain ambiguity in terms of its interpretation [1]. Source imaging methods using EEG and MEG are gaining more interests since they produce real-time images of neural current sources, which enable direct monitoring of fast neural activities in the brain. Most EEG and MEG source imaging methods, however, lack of the uniqueness in solutions of the corresponding inverse problems and therefore require *a priori* information embedded in their solution methods. Though these direct methods have successfully been applied to numerous clinically important problems, there still exist technical difficulties including low SNRs in EEG and MEG measurements, global mixing of individual signals of internal neural current sources through the volume conduction process, uncertainty in the conductivity distribution inside the head and geometrical modeling errors [2]. Other functional brain imaging methods including PET, numerous MRI techniques, optical imaging methods and so on also suffer from their own technical limitations [1].

We consider the following endogenous bioelectromagnetic phenomena inside the head:

$$\begin{cases} \nabla \cdot \left(\sigma(\mathbf{r}) \nabla u(\mathbf{r}) \right) = f\left(\mathbf{r}\right) & \text{in } \Omega \\ -\sigma \nabla u \cdot \mathbf{n} = 0 & \text{on } \partial\Omega \end{cases} \tag{1}$$

where $\sigma(\mathbf{r})$ is the conductivity at $\mathbf{r}$ inside the head denoted by Ω with its boundary $\partial\Omega$, u is the voltage, f is the neural current source and $\mathbf{n}$ is the outward unit normal vector on $\partial\Omega$. Denoting the internal current density at $\mathbf{r}'$ in Ω as $\mathbf{J}\left(\mathbf{r}'\right)$, we have a magnetic flux density $\mathbf{B}\left(\mathbf{r}\right)$ at $\mathbf{r}$ inside and also outside the head as

$$\mathbf{B}\left(\mathbf{r}\right) = \frac{\mu_0}{4\pi} \int_{\Omega} \frac{\mathbf{J}\left(\mathbf{r}'\right) \times \left(\mathbf{r} - \mathbf{r}'\right)}{\left|\mathbf{r} - \mathbf{r}'\right|^3} d\mathbf{r}' \tag{2}$$

where μ_0 is the magnetic permeability of the free space and also most biological tissues.

We note that the neural current source term $f(\mathbf{r})$ in (1) is directly and instantaneously related with the neural activity. The conductivity $\sigma(\mathbf{r})$ at $\mathbf{r}$ inside the head is determined by molecular composition, cellular structure, amounts of intra- and extra-cellular fluids, concentration and mobility of ions in those fluids, temperature and other factors [3,4]. As summarized in [5], it is also well known that neural activities alter the conductivity directly and instantaneously.

Functional brain imaging must seek for $f(\mathbf{r})$ and/or $\sigma(\mathbf{r})$ in (1) to directly and instantaneously monitor neural activities in the brain. Measurable quantities in (1) and (2) using noninvasive methods include voltage u on the surface $\partial\Omega$ (that is, EEG), magnetic flux density $\mathbf{B}$ outside Ω (that is, MEG) and inside Ω (that is, MR magnitude or phase imaging). Measurements of $\mathbf{B}$, or its z-component B_z, in (2) using an MRI scanner are very difficult since the endogenous B_z signal is

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much smaller than a typical noise level of a currently available MRI scanner. Therefore, most existing direct source imaging methods rely on EEG or MEG measurements.

In this paper, we focus on visualizing the conductivity $\sigma(\mathbf{r})$ at $\mathbf{r}$ inside the brain by using two impedance imaging methods of EIT and MREIT with intention of monitoring neural activities. This idea was proposed by D. Holder in his early paper [6] and has been a long-standing research goal [5]. After examining requirements and feasibility of each technique as a functional brain imaging method, we will consider the feasibility of a multi-modal approach including EIT, EEG, MREIT and MRI.

II. EIT as a Funtional Brain Imaging Modality

In EIT, we attach multiple electrodes on the boundary $\partial\Omega$ of a three-dimensional imaging object Ω, which is the human head in our case [7]. When we inject current through all or several chosen electrodes, the externally injected current induces a voltage u in Ω satisfying

$$\begin{cases} \nabla\cdot\big(\sigma(\mathbf{r})\nabla u(\mathbf{r})\big) = 0 & \text{in } \Omega \\ -\sigma\nabla u\cdot\mathbf{n} = j & \text{on } \partial\Omega \end{cases} \tag{3}$$

where j is a magnitude of the current density on $\partial\Omega$ subject to the injected current. Note that j is non-zero only on the boundary regions underneath current-injection electrodes. We emphasize that the voltage u in (3) is the exogenous one induced by the externally injected current whereas the endogenous voltage u in (1) is originated from internal neural current sources. Since there is no coherence between the externally injected current and internal neural current sources, we set the right hand side of the first equation in (3) to be zero in EIT, where only the exogenous voltage u is of concern to reconstruct images of the bulk conductivity σ.

One may use an EIT system to measure induced boundary voltages on all or several chosen electrodes. Cross-sectional images of the conductivity σ in Ω can be reconstructed from its relation with the measured boundary current-voltage data sets subject to multiple injection currents. In functional brain imaging of EIT, it suffices to produce images of conductivity changes with time. The time-difference imaging in EIT takes the boundary voltage data at time t_0 as a reference and utilizes voltage differences between a set of newly acquired boundary voltage data at time t and the reference data set. This data subtraction process is advantageous since it can cancel out modeling errors and measurement artifacts common to both data sets.

As explained and demonstrated in numerous literatures [7], almost all EIT methods including time-difference imaging techniques suffer from the ill-posedness of the corresponding inverse problems resulting in conductivity images with a poor spatial resolution. Using 32 electrodes, one may expect a pixel size of 10 mm for an imaging object with 200 mm diameter. We may try to enhance the spatial resolution by increasing the number of electrodes but this usually makes the problem more ill-posed. Furthermore, voltages between neighboring electrode pairs get smaller as they get closer resulting in reduce SNRs in measured boundary voltage data.

The most important factor to determine the feasibility of the time-difference EIT method as a functional brain imaging modality is the sensitivity of the boundary voltage with respect to a local conductivity change inside the brain induced by neural activities. Numerous previous studies indicate that the change in boundary voltage data measured on the head subject to such a conductivity change inside the brain is below an achievable measurement resolution in most EIT systems [5,8,9].

Without technical breakthroughs in EIT to significantly enhance its measurement sensitivity, we may not be able to monitor brain neural activities using a currently available noninvasive time-difference EIT imaging method. We suggest EIT to estimate conductivity values of different tissues in the head as a passive material property. It would be worthwhile to incorporate this information in (1) to improve the performance of an EEG source imaging method.

III. MREIT as a Functional Brain Imaging Modality

MREIT has been suggested to overcome the ill-posedness of the conductivity image reconstruction problem in EIT [10,11]. It also relies on an externally injected current to induce the voltage u in (3). As expressed in (2), the internal current density $\mathbf{J}$ subject to the externally injected current produces a magnetic flux density distribution inside as well as outside the head Ω. Unlike the endogenous magnetic flux density subject to the internal neural current source f in (1), the induced exogenous magnetic flux density can be significantly larger since it is directly proportional to the amplitude of the externally injected current.

The most distinct feature of MREIT is to measure the z-component B_z of the induced exogenous magnetic flux density $\mathbf{B}$ inside the imaging object by using an MRI scanner with its main field in the z-direction. The exogenous B_z signal induced by the externally injected current produces phase changes in MR images above the noise level of the MRI scanner as long as the injection current amplitude is high enough. The current-injection MRI technique [12] enables us to extract the B_z data in a form of a cross-sectional image for a subsequent conductivity image reconstruction.

The conductivity image reconstruction in MREIT is based on the interrelation between the conductivity σ and the z-components B_z of the induced magnetic flux density. We note that the internal current density $\mathbf{J}$ is

$$\mathbf{J}(\mathbf{r}) = -\sigma(\mathbf{r})\nabla u(\mathbf{r}) = \nabla\times\mathbf{B}(\mathbf{r})/\mu_0 .$$

Taking the curl operation on both sides, we get

$$\nabla\times\nabla\times\mathbf{B}(\mathbf{r})/\mu_0 = -\nabla\sigma(\mathbf{r})\times\nabla u(\mathbf{r}) .$$

Since $\nabla\times\nabla\times\mathbf{B} = -\nabla^2\mathbf{B} - \nabla\nabla\cdot\mathbf{B} = -\nabla^2\mathbf{B}$, we have

$$\nabla^2\mathbf{B}(\mathbf{r})/\mu_0 = -\nabla u(\mathbf{r})\times\nabla\sigma(\mathbf{r}) . \tag{4}$$

From the z-component of (5), we finally get

$$\nabla^2 B_z(\mathbf{r}) = \mu_0\left(\frac{\partial u(\mathbf{r})}{\partial y}\frac{\partial\sigma(\mathbf{r})}{\partial x} - \frac{\partial u(\mathbf{r})}{\partial x}\frac{\partial\sigma(\mathbf{r})}{\partial y}\right). \tag{5}$$

The relation in (5) indicates that B_z is a complicated nonlinear function of the conductivity σ since the voltage u is a nonlinear function of σ as shown in (3).

Reviewing recent progress in MREIT including theory, algorithm, experimental techniques for phantoms, animals and human subjects [10,11], we may conclude that MREIT can produce cross-sectional conductivity images with a spatial resolution of the adopted MRI scanner as long as the externally injected current generates B_z signals with enough SNR. Using a common clinical scanner, this requires an imaging current of a few mA. For example, *in vivo* animal and human MREIT imaging experiments demonstrated conductivity image reconstructions with a spatial resolution of one to a few mm by using injection currents of 3 to 5 mA.

The feasibility of MREIT as a functional brain imaging modality depends on the sensitivity of an MRI scanner in capturing the induced magnetic flux density B_z from its phase images [13-16]. We may assume that the current density threshold to stimulate a nerve fiber with 20 μm diameter could be 1 A/m^2 at frequencies below 1 kHz. If the current density underneath a current-injection electrode is below 1 A/m^2, we may limit the internal current density inside the head below 1 A/m^2 on the average. In this case, we can inject 2.5 mA without stimulating such a nerve when the current-injection electrode has a contact area of 50×50 mm^2. Here, we assume that we use a current-injection electrode which was designed to produce a uniform current density underneath it [17].

Using a high-performance clinical 3 T MRI scanner, the current MREIT technique may produce cross-sectional conductivity images of the human head with a spatial resolution of about 1 mm by using imaging currents of 2.5 mA amplitude. Since the externally injected current widely spreads inside the head, we anticipate that the internal current density will be much lower than 1 A/m^2 though we cannot guarantee that it is below 1 A/m^2 everywhere inside the brain. Further reduction of the current amplitude will be possible by optimizing the details of the MREIT data collection process. The imaging time to achieve a 1-mm spatial resolution is, however, in the range of tens of minutes without further technical improvement in MREIT.

Unlike EIT, MREIT has a potential to be a functional brain imaging modality. We suggest numerical simulation studies of a realistic three-dimensional head model to compute internal current density distributions. We may find an optimal electrode configuration to inject 2.5 mA current, which will produce much less than 1 A/m^2 current density everywhere inside the skull. At the same time, we need to reduce the noise level in MR phase images by using highly sensitive multiple RF coils. We should devise new MREIT pulse sequences to enhance changes in MR phase images for given current amplitudes. Post-processing methods including denosing and statistical image processing will be helpful together with better conductivity image reconstruction algorithms. In functional brain imaging, we should also note that we do not need to provide absolute conductivity values of brain tissues. MREIT does not need to provide structural information since it is available from conventional MR images. These mean that we may simplify the inverse problem in functional MREIT as an anomaly detection problem rather than an image reconstruction problem.

Together with advances in experimental techniques, these signal processing methods will be able to enhance the temporal resolution of functional MREIT as well. We speculate that the temporal resolution of several frames per minute will be achievable by incorporating fast imaging methods such as EPI and bSSFP into MREIT scans. It is, however, too premature to predict if we can improve the temporal resolution as fast as 1 frame per second or faster.

IV. Multi-modal Approach

Currently, neither EIT nor MREIT is readily applicable to functional brain imaging applications. While we plan to sophisticate our MREIT techniques, we may also consider a multi-modal approach combining (1), (2) and (3) as

$$\begin{cases} \nabla \cdot \big(\sigma(\mathbf{r})\nabla u(\mathbf{r})\big) = f(\mathbf{r}) & \text{in } \Omega \\ -\sigma \nabla u \cdot \mathbf{n} = j & \text{on } \partial\Omega \end{cases} \tag{7}$$

and

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi}\int_\Omega \frac{\mathbf{J}(\mathbf{r}')\times(\mathbf{r}-\mathbf{r}')}{|\mathbf{r}-\mathbf{r}|^3} d\mathbf{r}' \quad \text{in } \Omega. \tag{8}$$

Note that we restricted observing the magnetic flux density within the head Ω in (8) to exclude MEG to reduce the amount of technical complexity. In (7), the voltage u includes both endogenous and exogenous components subject to the internal neural current source f and the externally injected current j, respectively.

We may measure EEG and EIT voltage signals separately on the head. Performing the EEG and EIT measurements inside the bore of an MRI scanner, we may acquire images of B_z, which is a z-component of (8) including both endogenous and exogenous components subject to the internal neural current source f and the externally injected current j, respectively. We, however, presumably exclude using the endogenous magnetic flux density primarily due to its very small signal strength.

In this type of multi-modal system, we can estimate bulk conductivity values or ratios of head tissues using MREIT to be used in EEG source imaging, as already suggested by Gao *et al.* [18,19]. We may cross-validate neural source images using EEG with functional MREIT images of conductivity changes originated from neural activities. We may also implement a multi-step algorithm where EIT and MREIT conductivity images are fed to EEG source imaging steps, then EEG source images are fed to functional MREIT image reconstructions and then functional MREIT images are fed to EIT and MREIT static conductivity image reconstructions.

This multi-model approach is based on the bioelectromagnetic phenomena as much as possible and also MRI signal generation process. Incorporating an MRI scanner, there will be abundant contrast information available beyond the structural information. The multi-modal system will require integration of high-performance electronics of EEG and EIT with a clinical MRI scanner.

V. Discussion and Conclusion

Electrophysiological phenomena and bioelectromagnetism in (1)-(3) indicate that a direct and instantaneous functional brain imaging of neural activities is possible by visualizing either a neural current source distribution or a conductivity distribution or both. In doing so, measurable quantities by using noninvasive methods are voltages on the head and magnetic flux densities inside or outside the head. We may consider measurements of endogenous and exogenous voltages on the head for EEG source imaging and EIT conductivity imaging, respectively. Excluding MEG, we may consider measurements of exogenous magnetic flux densities only inside the head for MREIT conductivity imaging.

Can we use conductivity images from EIT and MREIT for functional brain imaging? Can we incorporate conductivity images from EIT and MREIT in EEG source imaging? Can we integrate EIT, EEG, MREIT and MRI as a multi-modal functional brain imaging method?

Though it is unlikely that EIT will be useful as a neuro-imaging modality, we speculate that MREIT will possibly find its application in functional brain imaging. Incorporation of EIT and MREIT conductivity images into an EEG source imaging method is definitely feasible but requires very careful implementations of both hardware and software. It is highly desirable and promising to develop a multi-modal functional brain imaging method by integrating EIT, EEG, MREIT and MRI.

Considering numerous advantages of including an MRI scanner as a basic building block of a functional brain imaging system, we argue that it will be desirable to construct a multi-modal imaging system based on a clinical MRI scanner. This requires interdisciplinary expertise in MR physics, MRI data collection methods, bioelectromagnetism of EEG and EIT, electronics for MRI-compatible EEG and EIT instrumentation, mathematical theories and algorithms of nonlinear inverse problems.

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