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MREIT experiments with 200 μ A injected currents: a feasibility study using two reconstruction algorithms, SMM and Harmonic B_z

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Abstract

Magnetic resonance electrical impedance tomography (MREIT) is a technique that produces images of conductivity in tissues and phantoms. In this technique electrical currents are applied to an object and the resulting magnetic flux density is measured using magnetic resonance imaging (MRI) and the conductivity distribution is reconstructed using these MRI data. Currently the technique is used in research environments, primarily studying phantoms and animals. In order to translate MREIT to clinical applications, strict safety standards need to be established, especially for safe current limits. However, there are currently no standards for safe current limits specific to MREIT. Until such standards are established, human MREIT applications need to conform to existing electrical safety standards in medical instrumentation, such as the IEC601. This protocol limits patient auxiliary currents to 100 μ A for low frequencies. However, published MREIT studies have utilized currents 10 to 400 times larger than this limit, bringing into question whether the clinical applications of MREIT are attainable under current standards. In this study, we investigated the feasibility of MREIT to accurately reconstruct the relative conductivity of a simple agarose phantom using 200 μ A total injected current and we tested the performance of two MREIT reconstruction algorithms. These reconstruction algorithms used are the iterative sensitivity matrix method (SMM) by Ider and Birgul in 1998 with Tikhonov regularization and the Harmonic B_z proposed by Oh *et al* in 2003. The reconstruction techniques were tested at both 200 μ A and 5mA injected currents to investigate their noise sensitivity at low and high current conditions. It should be noted that 200 μ A total injected current into a cylindrical phantom generates only 14.7 μ A current in imaging slice. Similarly, 5mA total injected current results in 367 μ A in imaging slice. Total acquisition time for 200 μ A and 5mA experiments were about one hour and 8.5 minutes respectively. The results demonstrate that conductivity imaging is possible at low currents using the suggested imaging parameters and reconstructing the images using iterative SMM with Tikhonov regularization, which appears to be more tolerant to noisy data than Harmonic B_z .

Keywords

Magnetic Resonance; Electrical Impedance Tomography; MREIT

1. Introduction

Magnetic resonance electrical impedance tomography (MREIT) is an emerging imaging modality in which the electrical conductivity of an object is reconstructed using magnetic resonance imaging (MRI) measurements of the magnetic flux density generated by applied electrical currents. Such conductivity imaging may have numerous clinical applications. For example, several studies have reported that the electrical impedance of malignant tumors is significantly lower than benign lesions and normal tissues (Surowiec *et al* 1988, Jossinet 1998, Haemmerich *et al* 2003). In support of these findings, the first reported *in vivo* application of MREIT found an increase in the conductivity of malignant tumors in rats (Muftuler *et al* 2006b). Conductivity imaging could thus potentially be utilized for cancer diagnosis in humans. Accurate knowledge of the conductivity distribution within the human body would also allow for better modeling of internal currents and fields. Such information would improve the accuracy of electrophysiological diagnostic methods and could be used to improve the design and application of other applied current devices, such as those used in cardiac defibrillation and tumor electrotherapy. Additionally, the tissue conductivity information is also becoming more important in MRI as the main magnetic fields reach ultra high field strengths (7T and higher). As the field strength increases, the wavelengths become comparable to the dimensions of the body; therefore, the electrical properties of tissues play an important role in B1 shimming and Specific Absorption Rate (SAR) calculations. Other than those mentioned above, various clinical and research applications of conductivity imaging have also been reported (Brown *et al* 1985, Morucci and Rigaud 1996).

Despite these potential clinical applications, there are only a few *in vivo* MREIT studies reported (Muftuler *et al* 2006b, Kim *et al* 2008, Kim *et al* 2009). Probably the most important obstacle to the clinical application of MREIT is the limitation on the amount of electrical current that can be safely injected to a patient. Unfortunately, there are no standards specifically developed for current injection at very low frequencies for medical imaging purposes. In this regard, the only standard developed for medical devices is the International Electrotechnical Commission IEC601 standard, which limits “patient auxiliary currents” to $100\mu\text{A}$ from 0.1Hz to 1kHz, $100*f\mu\text{A}$ from 1kHz to 100kHz (where f is the frequency in kHz) and 10mA above 100kHz (Lionheart *et al* 2001). Since the primary frequency component of the bipolar current pulses used in MREIT is on the order of 10Hz, a safe level for clinical use can be considered as $100\mu\text{A}$, until new standards are developed by the research community.

Although other standards have been established that allow higher currents limits for specific devices like nerve and muscle stimulators, those instruments are primarily designed for applications such as physiotherapy where risks and discomfort could be acceptable. Therefore, it is conceivable that those limits would be deemed unacceptable for imaging devices.

A survey of recent MREIT publications shows that injected current levels used in studies conducted to date are at least an order of magnitude or higher than the IEC601 standard (table 1). Since the size of the imaged object and the size of the electrodes have a direct impact on the signal to noise ratio (SNR) of MREIT, it is difficult to make a head-to-head performance comparison. However, it is still clear that none of the studies conducted to this date managed to reach the current levels that are considered safe for clinical *in vivo* human studies. It should also be noted that despite the high current magnitudes used in those studies, the scan times for *in vivo* studies were very long (1.7 hours for human and 3–7 hours for *in vivo* animal scans). Given that the lowest level of injected currents reported in those studies was about 1mA, it is essential that either new standards be established for

impedance imaging systems at low frequencies or the sensitivity of the systems has to be increased in order to operate within the IEC601 standard.

Recently, several investigators explored whether the IEC601 standards impose unnecessarily strict limits in impedance imaging experiments (Gilad *et al* 2007 and Kim *et al* 2009). Gilad *et al* (2007) suggested that this limit could possibly be increased up to 200 μ A for on-skin and 600 μ A for recessed electrodes for conductivity imaging of the head at low frequencies. They conducted simulations and experiments to demonstrate the feasibility. On the other hand, Kim *et al* (2009) reported successful human MREIT experiments at much higher currents (7mA –9mA) to image extremities.

Another way to operate within the standard is to increase the frequency of the applied current which allows an increase in the current limit. While there exist a few studies in which the frequency of the applied current was near 100Hz (e.g. Birgul *et al* 2006), the frequency would have to be increased to the kHz region to warrant higher current magnitudes. However, in MREIT the maximum frequency that can be achieved is also limited by several factors. One would need rapid repetition of very short RF pulses in synchrony with cycling currents to achieve higher frequencies. This may be difficult to implement due to hardware capabilities of the MRI system as well as increased SAR in subjects.

Previously, we have published various animal and phantom studies using currents around 1mA (Birgul *et al* 2006 and Muftuler *et al* 2006). However, until recently we have not explored the feasibility of MREIT at current amplitudes imposed by IEC601 or those proposed by Gilad *et al* (2007). In this study, we acquired MREIT data using 200 μ A total injected current, which was reported to be safe by Gilad *et al* (2007). We suggested that this could be achieved by minimizing sources of noise in the system, using data averaging and exploring reconstruction algorithms that are more robust at low SNR conditions. Although reducing the applied currents and then recovering SNR by means of averaging seems to be a trivial process, autocorrelated noise or systematic errors in the system would limit the amount of SNR improvement that could be achieved by signal averaging (Nalcioglu and Cho 1984).

We reconstructed the conductivity data using both sensitivity matrix method (SMM) (Ider and Birgul 1998, Birgul *et al* 2003) and Harmonic B_z algorithm (Seo *et al* 2003, Ider and Onart 2004) to explore the performance of the two algorithms on low SNR data. The experiment was repeated with 5mA total injected current in order to compare the performance of two reconstruction methods at high SNR conditions as well. We expected that the Harmonic B_z algorithm would be more sensitive to noise compared to SMM due to the derivative operation used in the algorithm. Our findings are in accord with the simulation results reported by Eyuboglu *et al* (2010), which showed that SMM reconstruction performed better at low SNR compared to other techniques.

2. Methods

Data were collected using a 4T whole body MRI system that has a Magnex magnet (Magnex Scientific Inc., UK) equipped with a whole body gradient coil set (Tesla Eng. UK), which provides up to 3G/cm gradient fields. The clear bore size of the magnet with gradient assembly is 650mm. A 13 channel room-temperature high-order shim system with MXA-13-4 shim power supply (Resonance Research, Billerica, MA) is available to minimize B₀ field inhomogeneities. This system is interfaced with a MRRS console (Magnetic Resonance Research Systems, Guildford, UK) that has broadband RF transmit and receive channels. A 16 leg, quadrature, high-pass birdcage coil with 10 cm diameter and 18 cm length was designed and built in-house for the MREIT experiments.

2.1. Phantom

The phantom was built using a hollow acrylic cylinder with an inner diameter of 6.5cm and a length of 6.8cm. This cylinder was filled with a gel containing 4mM CuSO₄, 1% (weight/volume) NaCl and 2% (weight/volume) agarose resulting in a conductivity of 1.77Sm⁻¹. Those concentrations were selected to mimic the T₁, T₂ and conductivity values of the human breast tissues (Mitchell 1986). This way, the MRI signals in our phantom experiments would be similar to those we would obtain from in vivo experiments. Inside this cylinder, two smaller cylindrical shells each 8.8mm in diameter and separated by 9.5mm horizontally and 15.5mm vertically were placed to simulate electrically insulating regions. Three copper strips, each 2mm wide, were placed equidistant to each other along the length of the inner wall and used as electrodes to inject current into the interior region. The phantom was placed coaxially inside the 4T MRI system such that its axis was parallel to the main static MRI field (z-direction). A schematic of the phantom is shown in figure 1.

2.2. Current injection and data acquisition

A pair of electrodes selected for current injection forms an “injection profile.” Since an infinite number of conductivity distributions can generate a given magnetic flux distribution, data from at least two different injection profiles are required to obtain a unique solution (Kwon *et al* 2002). For this study, we acquired MREIT data using only three electrodes and two injection profiles. Data was collected first using electrode pairs AB and then repeated with AC as shown in figure 1. Data acquisition with BC is redundant because the magnetic flux density distribution would be the linear combination of the fields generated using AB and AC. Even though orthogonal current injection pattern with four electrodes became somewhat standard in MREIT experiments, the three-electrode configuration was found to be sufficient to satisfy the uniqueness criteria. This reduced various sources of error that could arise from poor electrode contact and an excessive amount of metal electrodes and wires inside the RF coil. Moreover, the errors in modeling the exact location of electrodes for numerical modeling were also reduced with fewer electrodes. For each injection profile, a bipolar current pulse was applied to the phantom. Each phase encoding step was repeated twice with opposite polarities of electric current, hence changing the polarity of current-generated magnetic field distribution. When resulting phase terms were subtracted, those coming from the static field inhomogeneities and delays in MRI hardware were eliminated, leaving only the terms caused by the injected currents. Two separate sets of data were collected with two different current levels, 200μA and 5mA, respectively. The current density inside the phantom along the z-direction (axis of the cylinder) was assumed to be uniformly distributed, since there was no variation in geometry in the z-direction and the electrodes ran along the entire length of the phantom. Therefore, the total current flowing in the imaging slice can be found from the ratio of slice thickness to the total length of the phantom. Using this assumption, it can be calculated that the total current in the imaging slice would be 14.7μA and 367μA for the 200μA and 5mA cases, respectively. For the 200μA case, the total acquisition time was about one hour. For the 5mA case, a data acquisition time of 8.5 minutes was sufficient since fewer averages were needed.

The data was acquired using the pulse sequence proposed by Scott *et al* (1991), which is shown in figure 2. The images were acquired in the axial orientation and the scan parameters were: repetition time (T_R) = 500ms, echo time (T_E) = 50ms, slice thickness = 5mm, field of view (FOV) = 80×80mm, matrix = 64×64, bandwidth = 33.3kHz. The data were collected with the number of excitations (averages, NEX) equaling 28 and 4 for 200μA and 5mA experiments, respectively. A co-registered, high resolution spin-echo image was also acquired with the following scan parameters: T_R = 500ms, T_E = 50ms, slice thickness = 5mm, FOV = 80×80mm, matrix = 256×256, and NEX = 2.

In this pulse sequence, the z -component of the magnetic flux density distribution (B_z) generated from the injected current was encoded into the phase of the MR image as:

$$\phi(r) = \gamma T_c B_z(r) \quad (1)$$

where r is the position vector, $\phi(r)$ is the phase shift at point r , γ is the gyromagnetic ratio, T_c is the total duration of the injected current and $B_z(r)$ is the amplitude of the z -component of the injected current-generated magnetic flux density at position r . Data were collected twice, each with opposite polarities of the applied current waveform. The resulting phase maps were subtracted and then divided by two to cancel out contributions to the image phase from sources other than the injected current.

A current source was constructed and used to generate the injected currents (Baumann *et al* 1997) with OPA277 low noise operational amplifiers (Texas Instruments, Dallas, TX). OPA277 series precision operational amplifiers were used in the current source construction because of the improved noise performance, wider output voltage swing, ultra-low offset voltage, high common-mode rejection and high power supply rejection compared to traditional operational amplifiers. RF current leakage through the current injection wires was suppressed by adding an L-C trap circuit tuned to MR Larmor frequency and the wires were twisted around each other to minimize electromagnetic induction. Synchronization of the current source output with the pulse sequence was controlled by the scanner computer through a digital interface. Wires connecting the current source to the electrodes were aligned parallel to the main static MRI field, so that the magnetic flux density generated by currents passing through them contained no z -component and thus did not perturb the MRI signal.

2.3. Noise Calculations

28 complete data sets were acquired with a total scan time of one hour for the 200 μ A case. Each data set contained measurements from the two injection profiles and both current waveform polarities. On the other hand, only four data sets were collected for the 5mA case with a total scan time of 8.5 minutes. Groups of 1, 4, 9, 16 and 28 data sets were then averaged to generate B_z maps for 200 μ A data. For the 5mA data either a single data set was used or four data sets were averaged.

In order to quantify the SNR improvement by signal averaging, the noise in each group of B_z maps was calculated using the method proposed by Sadleir *et al* (2006). Based on their technique, the noise was calculated using equation 2:

$$std(B_z) = \frac{1}{\sqrt{2} \gamma T_c \Upsilon_M} \quad (2)$$

where $std(B_z)$ is the standard deviation of the B_z maps and Υ_M is the corresponding magnitude image SNR. The magnitude image SNR was calculated by taking the mean intensity of the phantom, multiplying it by 0.665 and dividing by the standard deviation of the background. The 0.665 factor accounts for the Rayleigh distribution of the background noise

2.4. Conductivity reconstruction

Various algorithms have been proposed to reconstruct the conductivity distribution using the B_z maps obtained from MRI. These include the SMM (Ider and Birgul 1998, Birgul *et al* 2003), Harmonic B_z algorithm (Seo *et al* 2003, Ider and Onart 2004), and projected J-substitution algorithm (Nam *et al* 2007). For this study, we tested both the SMM and

Harmonic B_z algorithm and compared the performances of the methods at both low and high SNR cases. Once B_z is obtained from the MRI phase maps, one can only reconstruct the relative conductivity distribution inside the object (i.e. the overall conductivity map might be scaled by an arbitrary value with respect to the actual conductivity distribution). Additional surface voltage measurements are required to determine the absolute conductivity values (Kwon *et al* 2002 and Birgul *et al* 2003). In both reconstruction algorithms, no additional noise reduction techniques were implemented in order to compare these reconstruction algorithms in an unbiased way.

2.4.1. Sensitivity Matrix Method—In this technique, the object domain was discretized into a mesh of 2048 first-order triangular elements, chosen for compatibility with the finite element method (FEM). An initial uniform conductivity distribution ($\sigma_{\text{initial}} = 1 \text{ S/m}$) was assumed and the problem was linearized around this initial condition:

$$\Delta B = B_{\text{final}} - B_{\text{initial}} = S(\sigma_{\text{final}} - \sigma_{\text{initial}}) = S\Delta\sigma \quad (3)$$

where B_{initial} is the B_z map calculated from the given σ_{initial} using the FEM and Biot-Savart law, B_{final} is the MRI-measured B_z maps, σ_{final} is the actual (unknown) conductivity distribution, and S is the sensitivity matrix with elements:

$$S_{i,j} = \left[\frac{\partial B_i}{\partial \sigma_j} \right]_{\sigma=\sigma_{\text{initial}}} \approx \left[\frac{\Delta B_i}{\Delta \sigma_j} \right]_{\sigma=\sigma_{\text{initial}}} \quad (4)$$

In general, S is an ill-conditioned matrix, therefore a simple least-squares approach may not converge to the actual conductivity distribution ($\sigma_{\text{final}} = \sigma_{\text{actual}}$). For that reason, equation (3) was solved using the conjugate gradient method with Tikhonov regularization, where σ_{final} was found by:

$$\min_{\sigma_{\text{final}}} \{ \|S\Delta\sigma - \Delta B\|^2 + \lambda \|\Delta\sigma\|^2 \} \quad (5)$$

Here λ is called the regularization parameter and was chosen adaptively by the algorithm (in the range of $[10^{-50}, 10^{-10}]$) such that the calculated B_z maps generated using the reconstructed σ_{final} were closest to the MRI-measured B_z maps. Equation (5) is solved iteratively by assigning the σ_{final} calculated from the previous iteration as the updated σ_{initial} , for the next iteration. Based on our experience, the solution usually converged in six iterations. For each iteration, S was recalculated using the updated σ_{initial} and a new σ_{final} was found.

2.4.2. Harmonic B_z method—Harmonic B_z algorithm is another MREIT reconstruction technique that is widely used in MREIT studies. Therefore, we also implemented this reconstruction technique to observe if it would provide better MREIT data at low currents. The algorithm was first proposed by Oh *et al* in (2003). In this technique, the following equation (6) is obtained from the z -component of the expression $\nabla^2 \mathbf{B} = -\mu_0 \nabla u \times \nabla \sigma$ for each position inside the object.

$$\frac{1}{\mu_0} \nabla^2 B_z^j = \left(\frac{\partial \sigma}{\partial x}, \frac{\partial \sigma}{\partial y} \right) \cdot \left(\frac{\partial u^j}{\partial y}, -\frac{\partial u^j}{\partial x} \right) \quad j=1, \dots, N \quad (6)$$

Here u^j is the voltage obtained from the solution of the classical boundary value problem (bvp) due to the I^j for $j = 1, \dots, N$ injection current. In vector matrix form equation (6) can be written as

$$\mathbf{U} = \mathbf{b} \quad (7)$$

where

$$\mathbf{U} = \begin{bmatrix} \frac{\partial u^1}{\partial y} & -\frac{\partial u^1}{\partial x} \\ \vdots & \vdots \\ \frac{\partial u^N}{\partial y} & -\frac{\partial u^N}{\partial x} \end{bmatrix} \quad \mathbf{s} = \begin{bmatrix} \frac{\partial \sigma}{\partial x} \\ \frac{\partial \sigma}{\partial y} \end{bmatrix} \quad \text{and} \quad \mathbf{b} = \frac{1}{\mu_0} \begin{bmatrix} \nabla^2 B_z^1 \\ \vdots \\ \nabla^2 B_z^N \end{bmatrix} \quad (8)$$

Computing (7) for each pixel or position, $\mathbf{s}$ distribution is obtained inside the object. The $\mathbf{U}$ and $\mathbf{b}$ matrices are allocated such that the accuracy of the $\mathbf{s}$ vector is improved especially at the boundaries of the phantom. It is clear that, this distribution is actually a two dimensional gradient field of unknown conductivity σ . In order to calculate σ from its gradients, a layer potential technique is employed. Details of this technique can be found in the paper published by Oh *et al* (2003).

Harmonic B_z algorithm involves several steps. First, the potential distributions are obtained for all current injection patterns by solving the *boundary value problem* for an initial conductivity distribution. Then conductivity gradient and therefore conductivity are calculated using (7). Finally, the layer potential technique is employed. These steps are repeated until a predefined stopping criterion is satisfied. This method that can also be used for the anisotropic case, which was successfully implemented and tested on various studies reported in Degirmenci's Ph.D thesis (Degirmenci 2010).

2.5. Correcting for the contribution of currents flowing outside the slice of interest

The height of the phantom used in this study was 68mm while the imaging slice thickness was 5mm. Since the current flows in the whole 3D volume, the measured magnetic field in the slice of interest would be the superposition of magnetic flux densities generated by currents inside the imaging slice as well as out of the imaging slice currents. The current inside the imaging slice can be computed as the surface integral of current density along an orthogonal surface within the slice of finite thickness. According to Biot-Savart law, generated magnetic flux density is due to close proximity currents. If a 2D reconstruction algorithm is used as in our case, the effect of out of slice currents has to be taken into account. A 3D reconstruction technique inherently overcomes the effects of outer slice currents. But the reconstruction using a 3D model will be computationally expensive and it might increase the reconstruction errors due to the increase in the number of unknowns. In some cases, the acquisition time might be longer to cover the 3D volume. These problems could be alleviated by using a 2D reconstruction technique in which off-slice information is incorporated into the forward problem as demonstrated by Hamamura (2005).

3. Results

MRI data were collected as described in the previous section and the B_z maps were calculated. The noise in the B_z maps were calculated for different numbers of data averaging and presented in the next section to demonstrate the noise characteristics in the

data. Then, the conductivity images reconstructed using SMM and Harmonic B_z are presented.

3.1. B_z standard deviation

The noise in the B_z maps is given in table 2, which was calculated for the 200 μA and 5mA cases using the method described in section 2.3. The noise was estimated under the assumption that the data contains only random, uncorrelated noise.

It can also be seen from the table that the noise calculations were similar for 200 μA and 5mA cases. This is expected since the noise measurements are not influenced by the magnitude of the injected current.

3.2. Results of SMM Reconstruction

The relative conductivity images reconstructed by the SMM algorithm and corresponding MRI magnitude image are shown in figure 3. The full data set with 28 averages was used for the resulting conductivity maps shown here. The two electrically insulated inner cylinders can be clearly resolved in the reconstructed data. The average relative conductivities in background and insulator regions were measured to be 1.02 and 0.198, respectively for the 200 μA case. The same measurements for the 5mA case yielded average relative conductivities of 1.06 and 0.077 in the background and insulator regions, respectively. The conductivity profiles across the two inner cylinders were plotted in figure 4 to illustrate the edge resolution for edges E1, E2, E3 and E4. The profiles were taken across the dashed line shown in figure 3(a) through the edges labeled E1 to E4 in figure 3. Along the edges E1 and E3, the reconstructed conductivity decreases from 90% to 10% of its maximum value in 1.78mm and 2.02mm on average for 200 μA and 5mA cases, respectively. Along the edges E2 and E4, the reconstructed conductivity increases from 10% to 90% in 2.36mm on average for 200 μA case and 2.02mm for 5mA case. It should be noted that the profiles depicted in figure 4 were all normalized to [0, 1] range in order to compare edge-spread functions for each case.

3.3. Results of Harmonic B_z Algorithm

The relative conductivity images (reconstructed using Harmonic B_z algorithm) for the 200 μA case were too noisy and no structure could be resolved; therefore, they were not shown here. In figure 5, the conductivity map for the 5mA case was illustrated. A significant amount of image artifacts can still be seen for the 5mA case, compared to the reconstruction with SMM shown in figure 3(c). As noted previously, we did not implement any noise reduction techniques for the two reconstruction methods to achieve a fair comparison. In this conductivity map, the average relative conductivities in background and insulator regions were calculated to be 1.02 and 0.924, respectively.

The cross-sectional profiles across the two inner cylinders were plotted in figure 6 for Harmonic B_z algorithm to illustrate the edge resolution for the same edges E1, E2, E3 and E4 as shown in figure 3(a). It can be seen from the results that the reconstructed conductivity decreases from 90% to 10% of its maximum value in 4.01mm on average for edges E1 and E3. For edges E2 and E4, the reconstructed conductivity increases from 10% to 90% in 7.56mm. The profiles are shown only for the 5mA case because of the excessive noise in conductivity images reconstructed using the 200 μA data.

4. Discussion

It is well documented that the accuracy of the conductivity reconstruction in MREIT depends on the SNR of the B_z maps. Larger injected current levels increase SNR and result

in more accurate conductivity images. However, existing safety standards limit the current amplitude for human studies thereby limiting the amount of SNR improvement that can be achieved. On the other hand, existing standards do not directly address application of electric currents for the purpose of conductivity imaging. Several authors have argued that the present IEC601 standards are too strict and that a higher safe current level should be adopted for imaging (Gilad, 2007; Kim *et al* 2009). Although their approaches may be acceptable for research studies, its subjective nature makes it harder to establish a clinical standard that is safe and comfortable for patients. Furthermore, the absence of pain does not necessarily exclude the possibility that injected currents cause short or long term injury to the subjects. While further research may eventually justify higher safe current levels, presently approved standards should still be followed for clinical applications until such revisions are officially adopted or a new standard is formed for impedance imaging with injected currents. We as the authors strongly aspire to have a specific standard for EIT and MREIT devices with higher current limits, which leads to better SNR. A debate regarding the revision of safety standards is beyond the scope of this study; our objective was simply to explore the feasibility of MREIT using the presently established standard currents within a reasonable scan time.

In our previously published studies cited in table 1 (Muftuler *et al* 2009 and Birgul *et al* 2006), we had conducted phantom studies using 1mA injected currents and a disc-shaped phantom with 10mm height. That configuration lead to significantly higher SNR because the geometry confined the current mostly into the imaging slice (total current in the imaging slice is 500 μ A), hence increasing the measured magnetic fields. In the presented study, we lowered the current amplitude five-fold while we utilized a cylindrical phantom that was 68mm high and the current in imaging slice was 14.7 μ A. For this particular case the in-slice current can be found by taking the slice thickness, phantom height ratio and multiplying by total current, since there is no variation along the z direction. Thus we explored the feasibility of MREIT in much lower SNR conditions, which would mimic an in vivo study more closely, such as breast or lower limb imaging.

It should be noted that the contrast was high in the phantom that we used in order to study the edge-spread function. As the contrast decreases and approaches the noise floor it would be harder to distinguish structures with different conductivity values.

4.1. MREIT reconstruction methods and SNR

Our results provide evidence that MREIT at low current amplitudes might be possible with SMM. In a previous study published by Nam *et al* (2007), a noise level of 0.196nT was reported in which they applied 1mA currents. They used the transversal J-substitution reconstruction algorithm to reconstruct the conductivity distribution of a phantom. But their reconstruction was adversely affected by the low SNR B_z maps. In addition, they reported that they were unable to generate an accurate reconstruction using the Harmonic B_z reconstruction algorithm, which is in accord with our findings. Nam *et al* and several others suggested that a minimum of 5mA was needed to successfully utilize this reconstruction method. Given that this is 50 times higher than the presently established standard, it remains a challenge to translate MREIT experiments into clinical studies.

Although, Lee *et al* (2005) proposed noise reduction techniques to improve the quality of B_z and Harmonic B_z reconstruction, similar algorithms could also be developed for SMM to further improve the fidelity of conductivity images. But this would make it harder to do a head-to-head performance comparison; therefore, we decided to compare the two methods without introducing any unknown bias by such additional techniques.

In our study the noise standard deviation was 0.153nT with 200 μ A injected current. When these are compared to the findings reported by Nam *et al*, a 5-fold decrease in the amplitude of the B_z maps and a 1.28 decrease in noise were obtained, with an overall 3.9 fold decrease in the SNR. It is possible that the SMM could be more robust in processing lower SNR data compared to other MREIT reconstruction algorithms since it does not require taking derivatives of the noisy B_z data. This can be clearly seen by comparing the reconstruction results shown in figures 3(c) and 5, where SMM and Harmonic B_z algorithm were applied to the same data. At 5mA, SMM produced a good quality conductivity image while there were significant artifacts in the image produced by the Harmonic B_z algorithm. A comparative analysis of noise sensitivity for various MREIT reconstruction techniques should be investigated further to gain a better insight. Utilizing the method that is least sensitive to noise in B_z data would be essential for human studies where restrictions on the maximum current levels result in relatively noisy B_z maps.

One drawback of SMM is the lower spatial resolution in the resulting conductivity images. While the Harmonic B_z and projected J-substitution reconstruction algorithms can produce detailed conductivity images at the same spatial resolution as the MR images, the SMM resolution is limited by the size of the FEM elements. Furthermore, the size and exact shape of the FEM elements are not identical, resulting in a non-uniform resolution. In this study, we used 2048 elements, with the longest edge of an element around 2.03mm. Higher resolution can be achieved by using smaller elements. However, this increases the total number of elements needed to model the object being imaged, which imposes increased demand on computational resources. This demand on computational power increases substantially if one uses 3D FEM models. In order to simplify the reconstruction, we are currently using 2D FEM models to solve the forward problem. This 2D FEM solution requires a correction to account for the contributions from currents flowing outside the imaging slice. The contributions of these off-center slices are incorporated into the sensitivity matrix using approximations as explained in the methods. This introduces errors if the geometry changes significantly along the longitudinal (z) direction. This may not be a problem in parts of arms or legs where z-variations are small. However, for a more generalized correction, we are currently studying various approaches to estimate a correction filter that will account for the contributions from currents flowing outside the slice of interest for more complex geometries. We anticipate that continuing advances in computing power will enable high resolution 3D SMM reconstructions to be feasible in the near future, eliminating the need for such approximations for 2D reconstruction.

4.2. Improving SNR for low current MREIT

A trivial approach to increase SNR would be to run the experiments in ultra-high field MRI systems. This study and the studies listed in table 1 were all performed in either at 3T or 4T field strengths. Utilizing MRI systems with 7T or higher field strengths will further increase the image SNR. Another straightforward approach would be to increase the voxel size in acquired MREIT images. But this will result in a loss of spatial details.

Further reduction of the noise can be achieved through signal averaging to improve the image SNR, as was done in this study. However, the presence of autocorrelated noise will ultimately limit the effectiveness of such averaging (Nalcioglu and Cho 1984). The noise in the B_z maps given in table 2 was calculated for the 200 μ A and 5mA cases using the method described in section 2.3. It is interesting to note that the standard deviation of the B_z maps did not decrease by the expected amount as the number of averages was increased. This probably indicates that the B_z maps were contaminated by some amount of systematic noise in addition to the random noise in the system. While a certain amount of signal averaging would still help, time constraints in *in vivo* human applications will limit the amount of

signal averaging that can be performed. To improve the total SNR *per unit time*, fast imaging pulse sequences could be utilized as an alternative (Hamamura and Muftuler 2008).

It may be possible to improve the accuracy of the reconstructed conductivity images by using several other approaches that increase the SNR of the B_Z maps. In equation (2) the noise in B_Z is inversely proportional to both T_C and the image SNR. Increasing T_E allows for a longer T_C , but decreases the image SNR due to transverse relaxation (T_2 decay). Scott *et al* (1992b) calculated that one reaches an optimum balance between these factors when the T_E is set close to the T_2 value of the object. For the standard imaging sequence proposed by Scott *et al* the current is applied for the whole duration of the pulse sequence except during slice selection and readout to avoid contaminating the MRI data. Similarly, Park *et al* (2007) developed the ICNE pulse sequence to increase T_C further, in which the current injection period was extended throughout the whole readout period in the standard MREIT pulse sequence. Use of phased array coils could also improve the image SNR. Such a configuration was optimized for MREIT by Muftuler *et al* for SENSE acceleration to achieve both an improvement in the SNR and a shorter data acquisition time. To the best of our knowledge, most MREIT studies were performed using a single transmit/receive volume coils for MR imaging.

The image SNR can also be improved by reducing the receiver bandwidth. However, this improvement will be accompanied by greater geometric distortions resulting from any nonuniformity in the B_0 field and larger chemical shift artifacts resulting from the presence of fat tissues. Reduction of the MRI resolution will also increase the image SNR, but this results in reduced data in the B_Z maps for the conductivity reconstruction. For the Harmonic B_Z and projected J-substitution reconstruction algorithms, this corresponds to an equivalent loss in the resolution of the conductivity images. For the SMM, the relationship between MRI resolution and accuracy of the conductivity reconstruction is more complex and should be investigated further.

Higher SNR in the B_Z maps may also be achieved by utilizing higher frequency currents, where the safety standards allow for larger electrical current levels. Instead of a bipolar pulse, 100Hz currents have been used in an MREIT experiment to measure dynamic conductivity changes in a phantom (Hamamura *et al* 2006). However, one has to use 1kHz or above to obtain larger allowable current magnitudes. Currently proposed measurement techniques are mostly limited to frequencies below 2kHz (Ider and Muftuler 1997; Mikac *et al* 2001) with the exception of RF current density imaging (RF-CDI) at the Larmor frequency (Scott *et al* 1992a). However, RF-CDI requires rotation of the object in the scanner to obtain orthogonal components of the magnetic fields. As an alternative to injecting currents, (alternating) currents may also be generated by induction through the use of external coils (Ozparklak and Ider 2005). While this method of induced current MREIT avoids the use of surface electrodes, the technique still lacks a way to measure frequencies above 2 kHz where the advantages of higher safety limits can be exploited.

5. Conclusion

Using a phantom with a simple geometry, we demonstrated that it is feasible to perform MREIT experiments with total injected currents in the 100 μ A – 200 μ A range by using SMM. These current levels are currently considered safe and comfortable for *in vivo* human applications.

The results also demonstrated that the Harmonic B_Z algorithm could be more sensitive to noise compared to SMM. Although several denoising techniques might have improved the quality of both reconstruction algorithms, they would have introduced an unknown factor into the comparison. Since the two reconstruction techniques use completely different

algorithms, it would have been harder to assess if the performance of the denoising algorithm used in a particular reconstruction or the reconstruction itself had superior performance. Even though this study required a large number of averages and one hour scan time, it is possible to bring the scan time down considerably by improvements described in the previous section. It is especially critical to identify the sources of coherent noise and eliminate them from the data. Although these coherent noise components are small in magnitude and negligible for larger injected currents, they become a source of artifacts at low currents.

We believe that the results of these preliminary studies presented here provide evidence that clinical applications of MREIT might be feasible. Further improvements outlined above could facilitate shorter scan times so that in vivo human MREIT studies could be conducted within a reasonable amount of time.

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Figure 1.

(a) Side view and (b) axial view of the phantom. Each cylindrical shell was filled with an agarose gel, which was mixed with NaCl and CuSO₄ to mimic electromagnetic properties of human tissues. The plastic shells of smaller cylinders act as insulators to produce high conductivity contrast. Electrodes are shown with orange stripes running along the inside of the outer cylinder.

Figure 2.

MREIT pulse sequence diagram. RF channel shows RF excitation and refocusing pulses and the data acquisition window. G_x , G_y , G_z are the gradient channels. The I channel shows applied current. Solid and dashed lines in I channel show two consecutive data acquisitions with opposite polarities of the injected current.

Figure 3. (a) MR magnitude image and (b) reconstructed conductivity distribution with SMM using 200μA injected current, (c) reconstructed conductivity distribution with SMM using 5mA of injected current. Dotted lines in (a) were used to generate the profiles in figure 4 and 6. E1 through E4 show the associated edges.

Figure 4.

Cross-sectional profiles taken from the relative conductivity images reconstructed by the SMM method. The profiles were taken across the dotted lines shown in figure 3(a). The profiles for the edges E1 and E3 are illustrated in (a) and for the edges E2 and E4 in (b). The magnitudes are normalized to [0 1] range for comparison.

Figure 5. Conductivity image reconstructed using Harmonic B_z and 5mA injected current data. Significant artifacts can be seen in the reconstructed conductivity image. The result for the 200 μ A case is not presented, since no structure could be identified in the image.

Figure 6.

Cross-sectional profiles taken from the relative conductivity images reconstructed by the Harmonic B_z method. The profiles were taken across the dotted lines shown in figure 3(a). The profiles for the edges E1 and E3 are illustrated in (a) and for the edges E2 and E4 in (b). The magnitudes are normalized to [0 1] range for comparison.

Table 1

Summary of recent MREIT studies listed from low to high applied currents.

Study	Injected Current	Imaging Time	Object Imaged (Obj. diameter, Electr. length)	std(B_z)
Muftuler <i>et al</i> (2009)	1mA	47 sec	phantom (R=44mm, h_E =10mm)	0.9nT
Birgul <i>et al</i> (2006)	1mA	8 min	phantom(R=70mm, h_E =10mm)	NA
Hamamura and Muftuler (2008)	4mA	40 sec	phantom(R=70mm, h_E =10mm)	NA
Nam <i>et al</i> (2007)	1–5mA	34 min	phantom(R=120mm, h_E =20mm)	NA
Kim <i>et al</i> (2008)	5mA	6.8 hrs	<i>in vivo</i> canine brain (R=90mm, h_E =50mm)	NA
Kwon <i>et al</i> (2007)	5–20mA	55–14 min	phantom (R=120mm, h_E =20mm)	0.54–1.02nT
Kim <i>et al</i> (2009)	7–9mA	1.7 hrs	<i>in vivo</i> human leg (R=80mm, h_E =80mm)	NA
Kim <i>et al</i> (2010)	10mA	3 hrs	<i>in vivo</i> canine pelvis (R=110mm, h_E =NA)	NA
Nam <i>et al</i> (2008)	10mA	27 min	phantom (R=120mm, h_E =NA)	NA
Lee <i>et al</i> (2007)	20mA	27 min	phantom (R=135mm, h_E =NA)	0.89–1.38nT
Park <i>et al</i> (2007)	20mA	27 min	phantom (R=140mm, h_E =20mm)	0.92–1.2nT
Jeon <i>et al</i> (2009)	25–35mA	2 hrs	postmortem canine abdomen (R=135mm, h_E =80mm)	NA
Kim <i>et al</i> (2008)	40mA	1.7 hrs	postmortem canine brain (R=45mm, h_E =50mm)	NA
Kim <i>et al</i> (2007)	40mA	1.7 hrs	postmortem canine brain (R=90mm, h_E =50mm)	1.5–1.7nT

The object diameter (R), electrode lengths along the orthogonal direction to the imaging axis (h_E) and the standard deviation of the measured B_z were listed for comparison. If an organ was imaged, approximate dimensions of the organ were given. (NA: not available)

Table 2

Noise calculated in the B_Z maps for different number of data averaging. The values are given in nT.

	200 μ A (total NEX=28)	5mA (total NEX=4)
	std(B_Z)	std(B_Z)
1 average	0.612	0.591
4 averages	0.307	0.290
9 averages	0.230	-
16 averages	0.163	-
28 averages	0.153	-