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Tissue Electrical Property Mapping from Zero Echo-Time Magnetic Resonance Imaging

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Abstract

The capability of magnetic resonance imaging (MRI) to produce spatially resolved estimation of tissue electrical properties (EPs) *in vivo* has been a subject of much recent interest. In this work we introduce a method to map tissue EPs from low-flip-angle, zero-echo-time (ZTE) imaging. It is based on a new theoretical formalism that allows calculation of EPs from the product of transmit and receive radio-frequency (RF) field maps. Compared to conventional methods requiring separation of the transmit RF field (B_1^+) from acquired MR images, the proposed method has such advantages as: (i) reduced theoretical error, (ii) higher acquisition speed, and (iii) flexibility in choice of different transmit and receive RF coils. The method is demonstrated in electrical conductivity and relative permittivity mapping in a salt water phantom, as well as *in-vivo* measurement of brain conductivity in healthy volunteers. The phantom results show the validity and scan-time efficiency of the proposed method applied to a piece-wise homogeneous object. Quality of *in-vivo* EP results was limited by reconstruction errors near tissue boundaries, which highlights need for image segmentation in EP mapping in a heterogeneous medium. Our results show the feasibility of rapid EP mapping from MRI without B_1^+ mapping.

Index Terms

magnetic resonance imaging; electrical properties; MREPT; ZTE

I. INTRODUCTION

In-Vivo imaging of tissue permittivity and electrical conductivity can prove useful for a number of applications. For example, specific absorption rate (SAR) modeling relies on the availability of spatially resolved maps of tissue electrical properties (EPs) as input [1]. Accurate classification of tumor tissue as benign or malignant can also benefit from the additional information provided by EP mapping; while some disagreement exists in literature [2], prompting for further, properly controlled experimental verification, it is generally agreed upon that cancers tend to exhibit higher conductivity and permittivity than normal tissues [3–5].

MRI was recognized more than two decades ago as having the capability of producing conductivity and permittivity maps [6]. However, progress in implementing tissue EP mapping in the clinic has been slow. In most common implementations, two acquisitions are required for EP reconstruction: the first one maps the magnitude of the transmit radio-frequency (RF) field (B_1^+), using one of the many B_1^+ mapping techniques [7–9]; the second one maps the transceive RF phase, which is then used to approximate the phase of B_1^+ [10]. The complex B_1^+ maps, thus obtained with a phase approximation, are subsequently processed using the integral or differential forms of Maxwell's equations to retrieve permittivity and conductivity maps [11–13]. This general approach has been known as MR-based electrical property tomography (MREPT). Unfortunately, B_1^+ mapping is typically a relatively slow process, seldom used clinically for diagnostic purposes. Its acquisition adds burden to the total scan time for a patient and B_1^+ maps usually have lower SNR compared to standard, clinical gradient echo (GRE) or spin echo (SE) images. Since processing in Maxwell's equations involves computation of the derivatives of B_1^+ , an operation very sensitive to noise, low SNR in the input B_1^+ can severely degrade the quality of the EP maps. Reconstruction of EPs out of more SNR-efficient acquisitions would therefore be beneficial, enabling one to determine tissue EPs faster, and with higher accuracy.

Recently, fast conductivity mapping methods have been demonstrated that are based on a single acquisition of a steady-state free precession (SSFP)[14] or an ultra-short echo time (UTE)[15] scan. These methods do not require B_1^+ magnitude mapping as they employ a "phase-only" approximation [16] of the conventional, complex B_1^+ -based method. These fast methods, however, intrinsically do not allow reconstruction of permittivity.

Furthermore, the speed afforded by the phase-only approximation comes at a cost of additional systematic error in conductivity estimation (at the level of 10%) [17, 18]. Marques et al. have reported a novel, single-acquisition mapping of EPs using relative sensitivity maps of multiple receive coils [19]. This method enabled both permittivity and conductivity mapping without B_1^+ , and was compatible with a wide range of imaging sequences. However, its dependence on the 3rd order derivative of the coil sensitivity data made it more sensitive to input image noise.

In this work, we show that by rearranging Maxwell's equations, conductivity and permittivity mapping is possible from a single, low flip-angle GRE acquisition. In particular, we propose to use a zero-echo-time (ZTE) sequence, due to its immunity to eddy current and static magnetic field (B_0) inhomogeneity-induced phase changes, as well as its speed and

SNR efficiency. By utilizing both the magnitude and phase information of the acquired images, our method achieves an acquisition speed higher than in the UTE method [15] while allowing both conductivity and permittivity reconstruction. In our approach, numerical processing of the image data can share the same routines developed for the conventional method [17], and therefore does not add more numerical complexity or processing time.

After theoretical derivation of the method, we show results obtained with the new formalism in phantom experiments. EPs reconstructed from human *in-vivo* brain images using the new formalism are also presented. The advantages and disadvantages of the method are discussed in the Discussion section.

II. THEORY

A. Background and motivation for a new formalism

In a medium of constant electrical conductivity (σ) and relative permittivity (ϵ_r), each of the circularly polarized components of the RF magnetic field satisfies the wave equation:

$$\nabla^2 B_1^+ + k^2 B_1^+ = 0 \quad (1)$$

$$\nabla^2 B_1^- + k^2 B_1^- = 0 \quad (2)$$

with the complex wave vector given by

$$k^2 = \mu \epsilon_r \epsilon_0 \omega^2 - i \mu \sigma \omega. \quad (3)$$

Here B_1^+ (B_1^-) is the complex amplitude of the transmit (receive) RF magnetic field inside the medium, μ is the magnetic permeability, $\epsilon_0 = 8.854 \times 10^{-12}$ F/m is the permittivity of vacuum, and $\omega = 2\pi f = \gamma B_0$ is the RF frequency; γ is proton's gyromagnetic ratio. In biological tissue, μ can be replaced by the permeability in vacuum, $\mu = \mu_0 = 4\pi \times 10^{-7}$ H/m.

A challenge in applying Eqs. (1–3) to MREPT is that in MRI, the absolute phase of either B_1^+ or B_1^- is not directly accessible. A much used approximation is to replace the B_1^+ phase by one half of the transceive phase [12],

$$\angle B_1^+ \approx \frac{1}{2}(\angle B_1^+ + \angle B_1^+ + \angle B_1^-). \quad (4)$$

Eqs. (1,3,4) lead to the conventional MREPT equations,

$$\epsilon_r \approx -\frac{1}{\mu \epsilon_0 \omega^2} \operatorname{Re} \left(\frac{\nabla^2 |B_1^+| e^{i(\angle B_1^+ + \angle B_1^-)/2}}{|B_1^+| e^{i(\angle B_1^+ + \angle B_1^-)/2}} \right) \quad (5)$$

$$\sigma \approx \frac{1}{\mu\omega} \text{Im} \left(\frac{\nabla^2 |B_1^+| e^{i(\angle B_1^+ + \angle B_1^-)/2}}{|B_1^+| e^{i(\angle B_1^+ + \angle B_1^-)/2}} \right). \quad (6)$$

Note that in this as well as in the new approach below, the z component of the RF magnetic field, B_{1z} , is not needed.

Eq. (4) transmit-receive coil *in vacuum* when the imaged object possesses certain symmetry [20]. In general, interaction of the tissue with the RF field renders B_1^+ and B_1^- different from each other, with the difference growing at higher frequencies [21, 22]. Since tissue-RF interaction is precisely what makes MREPT possible, this difference is unavoidable. In Appendix 1, we show that in EP reconstruction based on B_1^+ magnitude and Eq. (4), the error in EPs resulting from the B_1^+ , B_1^- difference is a first order effect with respect to the difference. In human MRI at 3 T and higher, such error can be significant. Thus, an important motivation of the present work is to demonstrate a theoretical formula which involves approximation that is less sensitive to the difference between B_1^+ and B_1^- .

B. Derivation

By multiplying Eq. (1) with B_1^- and Eq. (2) with B_1^+ , and adding them together, we obtain the following:

$$\nabla^2(B_1^+ B_1^-) + 2k^2 B_1^+ B_1^- - 2\nabla B_1^+ \cdot \nabla B_1^- = 0. \quad (7)$$

Replacing $B_1^+ B_1^-$ with $(\sqrt{B_1^+ B_1^-})^2$, we can show that (see Appendix 2 for details)

$$\frac{\nabla^2 \sqrt{B_1^+ B_1^-}}{\sqrt{B_1^+ B_1^-}} + k^2 + k_{error}^2 = 0 \quad (8)$$

in which

$$k_{error}^2 \equiv \frac{1}{4} \nabla \ln \frac{B_1^-}{B_1^+} \cdot \nabla \ln \frac{B_1^-}{B_1^+}. \quad (9)$$

Here the square root of a complex quantity $B_1^+ B_1^-$ can be defined unambiguously by defining the phase of $\sqrt{B_1^+ B_1^-}$ as 1/2 times the phase of $B_1^+ B_1^-$; as long as the latter is properly phase-unwrapped to avoid phase jump in the region of interest (ROI), so is $\sqrt{B_1^+ B_1^-}$ free from phase jump.

Ignoring k_{error}^2 and substituting Eq. (3) for k^2 in Eq. (8) lead to Eqs. (10–11). These define the proposed theoretical method of image-based EP mapping.

$$\varepsilon_r \approx -\frac{1}{\mu\varepsilon_0\omega^2} \text{Re} \left(\frac{\nabla^2 \sqrt{B_1^+ B_1^-}}{\sqrt{B_1^+ B_1^-}} \right) \quad (10)$$

$$\sigma \approx \frac{1}{\mu\omega} \text{Im} \left(\frac{\nabla^2 \sqrt{B_1^+ B_1^-}}{\sqrt{B_1^+ B_1^-}} \right). \quad (11)$$

C. Error estimation and analytical examples

In the limit where $B_1^+ = B_1^-$ (up to a constant factor, which we assume to be 1 without loss of generality), the error term k_{error}^2 is zero. When the ratio B_1^-/B_1^+ is spatially varying but is close to unity, k_{error}^2 can be estimated as

$$k_{\text{error}}^2 \approx \frac{1}{4} \nabla \left(\frac{B_1^- - B_1^+}{B_1^+} \right) \cdot \nabla \left(\frac{B_1^- - B_1^+}{B_1^+} \right). \quad (12)$$

Here we used the leading order Taylor expansion $\ln(1+z) \approx z$ for small z . Appendix 2 further breaks down k_{error}^2 into the real and imaginary parts and expresses each of them in terms of the magnitude and phase differences of B_1^+ and B_1^- (Eqs. (A19, A20)). The analysis shows that the error in the EPs is a second order effect. This is in contrast to the first order effect in the conventional method (Appendix 1). This provides a support for an argument that, when B_1^+ , B_1^- are close to each other, our method can be advantageous over the conventional one in terms of the theoretical accuracy of EP mapping.

We have previously demonstrated theoretical advantage of the new method through an RF simulation study [23]. Here we illustrate the benefit of the new method using known analytical solutions of the RF field inside an elliptical cylinder. Figure 1 shows the EPs of a homogeneous, elliptical cross-section cylinder reconstructed from analytical RF field solutions [24]. The cylinder, infinitely long, is axially located inside a circularly polarized RF transmit-receive coil (at 128 MHz) and has the following parameters: major axis = 20 cm, minor axis = 15 cm, $\varepsilon_r = 80$, $\sigma = 0.8$ S/m. The B_1^+ and B_1^- fields differ from each other by up to 37%, which did not make significant errors in ε_r and σ reconstructed by our method. On the other hand, in the ε_r and σ maps obtained by the conventional method, errors are very noticeable in regions with different B_1^+ and B_1^- . Similar errors in an object with broken cylindrical symmetry was reported in [18].

Next, we examine the magnitude of k_{error}^2 in comparison with the corresponding quantity in the conventional method for a range of model EPs. Figure 2(a,b) shows the magnitude and phase difference, respectively, between analytically calculated B_1^+ and B_1^- for different combinations of the model EPs of the cylinder, ranging from $\varepsilon_r = 10$ to 90, and $\sigma = 0.1$ to 0.9 S/m. Figure 2(c) shows the map of the relative error magnitude $|k_{\text{error}}^2/k^2|$, whereas Fig. 2(d) shows the corresponding quantity for the conventional method. Both methods show

small errors when the B_1^+ , B_1^- difference is small. As the latter grows, however, the error in the new method grows much more slowly than the conventional method. For example, for the geometry considered the new method is nearly error-free at $\sigma > 0.5$ S/m or $\varepsilon_r < 50$.

D. Phase-only method

When the magnitude of $\sqrt{B_1^+ B_1^-}$ varies more slowly in space than its phase, Eq. (11) can be further approximated as

$$\sigma \approx \frac{1}{\mu\omega} \nabla^2 \phi \quad (13)$$

where ϕ is the phase of $\sqrt{B_1^+ B_1^-}$. Here we used the fact that, after ignoring the magnitude variation, the imaginary part of the fraction $(\nabla^2 e^{i\phi})/e^{i\phi}$ equals $\nabla^2 \phi$. This represents a previously known, phase-only conductivity mapping method [15, 16, 25] derived in a different way.

E. Image-based tissue electrical property mapping

A practical advantage of Eqs. (10,11) is that the magnitude and phase of the product $B_1^+ B_1^-$ are more readily available from standard MR images than individual complex quantities B_1^+ and B_1^- . For example the complex image from a low-flip-angle spoiled GRE scan can be expressed as

$$I = I_0 B_1^+ B_1^- \quad (14)$$

Here I_0 is the "true" MR image determined by the proton density and other tissue contrasts. Separating out the RF term $B_1^+ B_1^-$ from the as-acquired image I has been a subject of intense research [26] for the purpose of image shading removal in high-field MRI. Whereas some of those methods could be adopted for our purpose, here we pay attention to the fact that MREPT typically targets localized reconstruction of piece-wise constant electrical properties. That is, because Eqs. (1,2) are only valid in regions of constant electrical properties, EP mapping methods derived from these equations are considered valid only in regions of constant EPs, such as regions of a single tissue type. If we therefore restrict ourselves to ROIs each of which containing a single tissue type, it is permissible to assume that I_0 is nearly constant in each region. We can then substitute Eq. (14) for $B_1^+ B_1^-$ in Eqs. (10,11), where I_0 factors out of the Laplacian operator and cancels out in the fraction. This results in a desired, image-based EP mapping method without B_1^+ mapping. We reiterate that the assumption of constant I_0 implies that the method best holds for individual segments in a tissue-segmented image, as was considered, for example, in [27, 28].

In practice, a GRE image can contain B_0 inhomogeneity-induced, spatially varying phase even inside a single tissue ROI, complicating isolation of the $B_1^+ B_1^-$ phase. While a separate SE scan can help this, in this work we propose using a low-flip-angle ZTE image for

simultaneous acquisition of the magnitude and phase of $B_1^+ B_1^-$. A ZTE sequence has negligible time for B_0 induced phase change, and in our implementation its limited gradient switching also minimizes eddy current concerns. In what follows, we calculated EPs by replacing $B_1^+ B_1^-$ of Eqs. (10,11) by a complex ZTE image I_{FGH} .

F. Use of a receiver array

Suppose that a low-flip-angle ZTE image was obtained with an N-channel receiver array. The complex combined image is proportional to

$$I_{\text{ZTE}} \propto B_1^+ \cdot (c_1 B_1^{-(1)} + c_2 B_1^{-(2)} + \dots + c_N B_1^{-(N)}) \quad (15)$$

where $c_1, c_2, \dots, c_N$ are the complex weights. If we denote the quantity in parenthesis in Eq. (15) as $B_1^{-(\text{tot})}$, such quantity satisfies the wave equation Eq. (2), as does each individual receiver field map. Therefore, the derivation leading to Eqs. (10,11) is valid as we replace B_1^- by $B_1^{-(\text{tot})}$ in Eqs. (7–11), and $B_1^+ B_1^{-(\text{tot})}$ can be replaced by I_{ZTE} , provided, as before, the true (unshaded) image varies slowly in an ROI. Here, the error in EP calculation (Eq. (12)) is determined by the fractional difference between the transmit B_1^+ field (usually from a body coil) and the combined receiver field $B_1^{-(\text{tot})}$. This suggests that the complex weights should be adjusted to better match the two RF field maps. When one of the RF field maps (typically B_1^+) is approximately homogeneous over an ROI, matching the two field maps roughly corresponds to homogenizing the magnitude of the image I_{ZTE} itself. Such optimization can be done separately for each ROI in which EP mapping is desired. Since homogenizing $|I_{\text{ZTE}}|$ aims at matching $B_1^{-(\text{tot})}$ with B_1^+ , rather than with B_1^- , it will be only effective in improving EP mapping results when B_1^+ itself is substantially homogeneous. We note that complex coil combination to improve the accuracy of MREPT, assuming homogeneity of body-coil B_1^+ , was demonstrated in [25] in the context of phase-only conductivity mapping.

III. EXPERIMENTAL METHODS

A. Image acquisition

All images were acquired with a Discovery 3.0 T MR750 scanner (GE Healthcare, Waukesha, WI) with a standard GE head birdcage coil and a GE 8-channel phased array coil.

ZTE imaging—ZTE imaging was implemented in a way similar to the RUFIS method [29]. This pulse sequence consists of a nonselective hard pulse excitation followed by three-dimensional (3D) center-out radial sampling. Image encoding starts immediately, leading to a nominal echo time $\text{TE} = 0$; consequently, the acquired images have little sensitivity to chemical shift and B_0 inhomogeneities. Note that the three sources of off-resonance phase accumulation in UTE imaging [30], i.e., finite excitation pulse width, ramp sampling, and readout interval, are minimized or eliminated through use of a short hard pulse, lack of ramp

sampling (Fig. (3)), and high-bandwidth readout. The effective off-resonance dephasing time estimated from the theories of ref. [30] was on the order of 20 μ s.

The pulse sequence was grouped into segments, each containing a number of spokes; a diagram of one of the segments is shown in Fig. (3). For typical B_1^+ amplitudes of clinical whole-body MR scanners ($\sim 15 \mu$ T), flip angles of only a few degrees are possible with the hard pulse, satisfying the low-flip-angle requirement. The 3D radial spokes were uniformly distributed in all directions and sequentially ordered along a spiral path [31]. This limits the gradient switching between repetitions to incremental directional updates only, resulting in reduced eddy currents. In our case the amplitude of the encoding gradient was 4.9 mT/m, with each update involving gradient switching of amplitude of only 0.13 mT/m.

The following parameters were used for both the phantom and *in-vivo* ZTE scans: Number of spokes = 128^2 , TE/TR = 0/1 ms, bandwidth = ± 31 kHz, flip angle = 3° , FOV = 28~30 cm, resolution = $128 \mu \times 128 \mu \times 128$, slice thickness = 2.2~2.3 mm. Each 3D scan lasted for 27 seconds.

Phantom scan—Three cylinders with diameters 7.7 cm, 7.7 cm, 9.4 cm were filled with water with varying salt concentrations. The cylinders were placed with their axes parallel to the main magnetic field. ZTE imaging on the phantom was done with both a head transmit/receive (T/R) coil and an 8 channel brain array. To verify the measured electrical properties, the same phantom was also scanned for conventional MREPT using B_1^+ map and SE phase [32]. The conventional scan data were acquired with the head T/R coil on 15 slices with slice thickness = 2 mm, FOV = 30 cm, in-plane resolution = 128×128 , and SAR-limited scan time of 11 min (B_1^+ map) and 3 min 44 sec (SE). Finally, the conductivity of liquids in all cylinders at 128 MHz was measured with an impedance analyzer (E4991A) coupled to a dielectric probe (E85070) (Agilent Technologies, CA, USA).

In-vivo scan—All *in-vivo* ZTE scans were carried out with the head T/R coil. Informed consent was obtained from the two volunteers enrolled for the study according to the Institutional Review Board of the lead author's institution.

B. Data processing and EP reconstruction

EPs on a particular slice were calculated from the Laplacian of a 3D complex map of $\sqrt{I_{ZTE}}$ centered around the slice of interest. For the 8 channel ZTE data, the individual coil's complex images were combined with complex weights determined by:

$$\{c_n\} = \underset{\{c_n\}}{\operatorname{argmin}} 1 / \min(\|c_1 I_1 + c_2 I_2 + \dots + c_8 I_8\|^2), \quad (16)$$

where $|c_1| = \dots = |c_8| = 1$. Here $I_1, \dots, I_8$ are individual complex ZTE images. One set of weights c_n was determined for each segment (cylinder) of the phantom. The optimization procedure found relative phases of different channels that maximized the minimum intensity of the combined image. Such max-min optimization was previously used in transmit RF shimming [33]. Phase-only optimization was adopted here because it was found to produce more smoothly-varying image phase than full complex optimization.

The Laplacian was numerically calculated by quadratic fitting in the three Cartesian directions [27]; depending on the proximity to the image mask boundary, typically 4–6 pixels on each side of the pixel of interest were used for fitting in one direction. To quantify the accuracy and precision of the method, the mean and pixel standard deviation of the EPs of each cylinder were calculated on an axial slice.

In-vivo brain EPs were reconstructed pixel by pixel without tissue segmentation. No post-processing filtering was applied to the EP maps. In the display of the conductivity results below, pixels with diverging conductivities near the skull (coming from reconstruction across tissue boundaries) were excluded by truncating the conductivity map with a mask obtained by 2D region growing from the center of the brain. For this a Matlab (Mathworks, Natick, MA, USA) code was written which let a user to graphically select a seed pixel in the raw conductivity map, from which a region was grown by adding neighboring pixels that satisfied a homogeneity criterion.

IV. RESULTS

Figure 4(a) shows the measured $|B_1^+|$ map and one half of the spin echo phase (φ_{SE}) map of the phantom on an axial slice, as well as the EP maps calculated from Eqs. (5,6). Figure 4(b,c) shows the magnitude and phase of the square root of I_{ZTE} and the EP maps obtained by the new method. Comparison of Fig. 4(a–c) shows that the new method, with both the head T/R coil (Fig. 4b) and the array coil (Fig. 4c), produced EPs that are in good agreement with the conventionally obtained map as well as the true map (Fig. 4e). For the 8 channel ZTE data, the individual coils' magnitude images and coil combination phases φ_c are shown in Fig. 4(d). The φ_c plot emphasizes the fact that the combination coefficients were determined for each cylinder separately.

Table 1 shows the mean and the pixel standard deviation of the EPs in each cylinder. The statistics on the phantom EPs obtained by the ZTE method are comparable to those obtained conventionally using B_1^+ and φ_{SE} . Given a significant scan time advantage of the ZTE method compare to B_1^+ map-based methods, our results suggest that the proposed method can be useful for fast estimation of both permittivity and conductivity in piece-wise homogeneous objects.

Figure 4(a,b) shows high degree of similarity between the (normalized) magnitude of $\sqrt{I_{ZTE}}$ and the $|B_1^+|$ map of the phantom. This is expected since for axially located cylindrical objects in a T/R birdcage coil, $|B_1^+| = |B_1^-|$ and $|I_{ZTE}|$ is proportional to their product (Eq. (14)).

Figure 5(a,b) shows orthogonal 3-plane *in-vivo* ZTE images and conductivity maps for two volunteers. The conductivity maps in the brain are shown overlaid on the amplitude images of the head. The average conductivity in the brain for the masked pixels (obtained by numerical averaging of all color pixel values in the three planes shown) was 0.55 S/m and 0.56 S/m for volunteers 1 and 2, respectively. The quality of the conductivity maps compares favorably with previously reported results obtained with an ultra-short TE

sequence [15]. Whereas no attempt was made to segment the brain into different tissue types, the observed average conductivity is compatible with the brain tissue conductivity values in literature: white matter (0.34 S/m), grey matter (0.59 S/m), and cerebrospinal fluid (2.14 S/m) [34, 35].

Significant noise and artifacts in *in-vivo* EP maps can come from reconstruction errors near tissue boundaries [36]. Whereas this is the case for any method based on Eqs. (1,2), an image-based method can be particularly sensitive to boundary effects, since in addition to EP discontinuities, image contrast at tissue boundaries can cause large errors in Laplacian calculation. *In-vivo* permittivity maps of Fig. 6(a,b) demonstrate this difficulty. Many pixels with unphysical permittivity values (negative or greater than 100) appear near tissue boundaries in the corresponding $|I_{ZTE}|$ images.

Thanks to the phase dominance in conductivity reconstruction [16], *in-vivo* conductivity maps were less affected by the $|I_{ZTE}|$ boundary effect. In order to check this, we recalculated conductivity maps with the I_{ZTE} phase only, emulating the method of [15]. Figure 5(c,d) shows the comparison between conductivity maps obtained from I_{ZTE} phase only vs complex I_{ZTE} . Qualitatively, including I_{ZTE} amplitude did not appear to increase the noise beyond what was already present in phase-only reconstruction (arrows). On the other hand, the difference map shows, consistently for the two volunteers, that phase-only reconstruction estimates conductivity about 10% higher than full I_{ZTE} reconstruction. This observation is interestingly similar to the previously reported amount of *overestimation* of conductivity when only phase is used for conductivity reconstruction [17]. This suggests that full I_{ZTE} reconstruction is likely more accurate than phase-only reconstruction of conductivity; i.e., including $|I_{ZTE}|$ in our method has merit.

V. DISCUSSION

A. Comparison with B_1^+ mapping-based methods

Quantitative comparison between different EP mapping methods must take into account different theoretical assumptions, image acquisition methods, and reconstruction algorithms. A recent review [17] provided a brief comparison between some of the existing, B_1^+ map-based MREPT methods. Whereas a comprehensive comparative analysis is outside the scope of this work, here we provide a qualitative explanation of the differences between the new, ZTE-based method and the B_1^+ map-based ones.

Scan time—The scan time advantage of the new method comes mainly from the elimination of the B_1^+ mapping step. Phase acquisition in both the conventional and the new methods can be quick; for example, a UTE [15] and a steady-state precession [37] sequence have been used for rapid conductivity mapping using phase acquisition alone. However, in order to map permittivity, or to improve the accuracy in conductivity, conventional methods require an additional B_1^+ mapping scan. The speed and accuracy of different B_1^+ mapping methods have been compared in a recent review [38]. It showed that the Bloch-Siegert phase shift method [8] provided good accuracy (a few % error) over a large flip angle range which is desirable for MREPT. In the same study, a representative scan time for *in-vivo* B_1^+ mapping at 3T with matrix size $128 \times 50 \times 48$ was 4 min 48 seconds, limited by SAR. We

estimate therefore that a 3D B_1^+ mapping scan with resolution comparable to our $128 \times 128 \times 128$ ZTE scan would be at least 10 minutes. This compares with 27 seconds used for the ZTE scan. Note that SAR limitation in B_1^+ mapping worsens at higher magnetic fields due to increased induced electric fields at higher RF frequencies. Overall, we estimate that the proposed method has scan time advantage of at least an order of magnitude compared to the conventional methods for a complete 3D EP mapping.

Accuracy—Main sources of errors in most common MREPT methods include: (i) systematic errors due to applying Eqs. (1,2) to EP-heterogeneous medium, (ii) systematic errors associated with replacing exact equations with approximate ones expressed in measurable quantities (such as replacing B_1^+ phase with one half of the transceiver phase), and (iii) random noise, especially amplified by derivative operation. Our method does not necessarily address the first and the third sources better than the existing methods, but rather improves EP accuracy by reducing the second type of error (when, of course, the other sources are not the limiting factors), through utilizing approximations (Eqs. (10, 11)) that are less sensitive to experimental conditions. Specifically, methods relying on transceiver phase approximation lose accuracy quickly as the object becomes asymmetric and the B_1^+ , B_1^- difference grows. The proposed method, on the other hand, is less sensitive to B_1^+ , B_1^- difference as was demonstrated here and previously [23] through numerical models.

Artifacts—Since our method operates directly on ZTE images, any image intensity artifact will more directly affect the EP results than in conventional methods. For example, radial k-space under-sampling is known to produce streaking artifacts [39]. In our case the number of radial spokes (128^2) was a factor of π smaller than what is required for Nyquist sampling. Although this did not cause significant artifacts in the images themselves, a low level artifact can be amplified to a high level through Laplacian operation. Similarly, Gibbs ringing from k-space truncation, commonly present near sharp edges of a phantom, can be more problematic in the Laplacian of the image. Our ZTE protocol is relatively insensitive to off-resonance and motion-related artifacts due to a high readout bandwidth and lack of ramp sampling. However, the protocol is more demanding of precise timing of RF and gradient pulses. In this work we have not investigated imperfections in the pulse sequence realization which can contribute to the observed EP noise.

In comparison, B_1^+ map-based methods can be sensitive to B_1^+ map inaccuracies caused by conditions such as relaxation time variation and resonance offset [38, 40]. Also, artifacts in images used to calculate B_1^+ can translate into EP artifacts, although such link is expected to be weak for phase-based B_1^+ mapping.

B. Comparison with phase-only conductivity mapping

B_1^+ phase-based conductivity mapping [16] shares two advantages with our method. First it allows fast, B_1^+ amplitude-free conductivity reconstruction [14, 15]. Second, separate transmit and receive coils can be used, including a receiver array [25, 40]. However, the phase-only method is different from our complex ZTE image-based method in the following ways. First, it is not applicable to permittivity, even in a homogeneous medium. Second, for conductivity, the phase-only method is known to introduce additional errors compared to

when B_1^+ amplitude is included in reconstruction. In ref. [17] such error was estimated to be about 10%, whereas our earlier analytical model [23] showed that the error can be much bigger near the edge of a high conductivity medium. What we demonstrated in this work is that, by utilizing the magnitude as well as the phase of transceive B_1 (measurable through I_{ZTE}), one can have a fast and RF-coil-flexible EP mapping method that includes permittivity, and estimates conductivity more accurately.

C. Prospect for in-vivo permittivity mapping

A challenge of the proposed method is that permittivity reconstruction is more severely affected by image intensity artifacts and tissue contrast, as compared to B_1^+ map-based methods. We have shown that including $|I_{ZTE}|$ in brain conductivity mapping did not increase the noise compared to phase-only reconstruction. For permittivity, however, we found that *in-vivo* permittivity maps calculated from I_{ZTE} were of poorer quality than typical published permittivity maps in brain based on B_1^+ maps. This is likely because permittivity is more affected by I_{ZTE} magnitude than its phase, and I_{ZTE} magnitude has more pronounced image discontinuity at tissue boundaries than I_{ZTE} phase or B_1^+ . In order for the proposed method to reliably produce permittivity values *in vivo* tissue of interest (e.g. tumor) should be segmented out first [27, 28] so that EP reconstruction is done within a segment of homogeneous tissue properties as much as possible. Further validation of the ZTE method for *in-vivo* permittivity mapping remains as a future work. Its success will likely depend on the quality and reliability of tissue segmentation, as well as the number of pixels within each segment.

VI. CONCLUSION

In conclusion, we have demonstrated a fast EP mapping method based on ZTE imaging. Compared to the conventional method, the proposed method is more tolerant to differences in spatial distributions of B_1^+ and B_1^- that arise from tissue-RF interaction. It also allows EP reconstruction from images acquired with receiver arrays. Its present limitation lies in greater boundary artifacts due to image intensity discontinuity at tissue contrast boundaries. For *in-vivo* applications, therefore, tissue segmentation to minimize the boundary effects is key to taking full advantage of the new method. Application of the method to EP mapping in anatomies where receiver arrays are typically used for imaging, such as breast, is one of the future research directions.

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APPENDIX 1: ERROR TERM IN CONVENTIONAL METHOD

The following shows how the error involved in the approximation Eq. (4) propagates into EP calculation.

The quantity which approximates the true complex B_1^+ in the conventional method is

$$|B_1^+| \exp\left(i \frac{\angle B_1^+ + \angle B_1^-}{2}\right) = |B_1^+| \exp(i \angle B_1^+) \exp\left(i \frac{\angle B_1^- - \angle B_1^+}{2}\right) = B_1^+ \exp(i \delta_p / 2) \quad (A1)$$

where

$$\delta_p \equiv \angle B_1^- - \angle B_1^+. \quad (A2)$$

The Laplacian of the right-hand side of Eq. (A1) is

$$\nabla^2(B_1^+ e^{i \delta_p / 2}) = e^{i \delta_p / 2} \{ \nabla^2 B_1^+ + B_1^+ (i \nabla^2 \delta_p / 2 - \nabla \delta_p \cdot \nabla \delta_p / 4) + i \nabla B_1^+ \cdot \nabla \delta_p \}. \quad (A3)$$

If we divide this equation by $B_1^+ e^{i \delta_p / 2}$, and use the fact that $(\nabla^2 B_1^+) / B_1^+ = -k^2$, we obtain

$$\frac{\nabla^2(B_1^+ e^{i \delta_p / 2})}{B_1^+ e^{i \delta_p / 2}} + k^2 + k_{error, conv}^2 = 0 \quad (A4)$$

where

$$k_{error, conv}^2 \equiv \frac{1}{4} \nabla \delta_p \cdot \nabla \delta_p - \frac{i}{2} \nabla^2 \delta_p - i \frac{\nabla B_1^+}{B_1^+} \cdot \nabla \delta_p. \quad (A5)$$

Substituting $B_1^+ = |B_1^+| e^{i \angle B_1^+}$ in the above equation, we can separate the real and imaginary parts of the error term as

$$Re(k_{error, conv}^2) = \frac{1}{4} \nabla \delta_p \cdot \nabla \delta_p + \nabla \angle B_1^+ \cdot \nabla \delta_p, \quad (A6)$$

$$Im(k_{error, conv}^2) = -\frac{1}{2} \nabla^2 \delta_p - \frac{\nabla |B_1^+|}{|B_1^+|} \cdot \nabla \delta_p. \quad (A7)$$

Dividing Eqs. (A6, A7) by $\mu \epsilon_0 \omega^2$ and $-\mu \omega$, respectively, gives the errors in ϵ_r and σ involved in the conventional method. We note that both Eqs. (A6, A7) contain a term (second term on the right-hand side) that is a product of $\nabla \delta_p$ and a quantity that is not necessarily as small as $\nabla \delta_p$. As δ_p departs from zero, therefore, we can say that the electrical property errors in the conventional method grow as a first order effect with respect to δ_p . Note that while "first order effect" refers to an order-of-magnitude estimate for $k_{error, conv}^2$, it does not necessarily mean that the actual spatial variation of errors in k^2 is proportional to δ_p , since Eqs. (A6, A7) depend on derivatives of δ_p as well as B_1^+ .

APPENDIX 2: DERIVATION OF EQS. (8,9) AND SMALLNESS OF k_{error}

Let us define $a \equiv \sqrt{B_1^+ B_1^-}$ and $b \equiv \sqrt{B_1^- B_1^+}$. Then Eq. (7) can be rewritten as

$$\nabla^2 a^2 + 2k^2 a^2 - 2\nabla \left(\frac{a}{b} \right) \cdot \nabla(ab) = 0. \quad (A8)$$

Using the identity $\nabla^2 a^2 = 2a\nabla^2 a + 2\nabla a \cdot \nabla a$, we can rewrite this as

$$2a\nabla^2 a + 2\nabla a \cdot \nabla a + 2k^2 a^2 - 2\nabla \left(\frac{a}{b} \right) \cdot \nabla(ab) = 0. \quad (A9)$$

Dividing Eq. (A9) by $2a^2$, we get

$$\frac{\nabla^2 a}{a} + k^2 + k_{error}^2 = 0 \quad (A10)$$

in which

$$\begin{aligned} k_{error}^2 &\equiv \frac{1}{a^2} \left(\nabla a \cdot \nabla a - \nabla \left(\frac{a}{b} \right) \cdot \nabla(ab) \right) \\ &= \frac{1}{a^2} \left(\nabla a \cdot \nabla a - \left(\frac{\nabla a}{b} - \frac{a}{b^2} \nabla b \right) \cdot (a \nabla b + b \nabla a) \right) \\ &= \frac{1}{b^2} \nabla b \cdot \nabla b \\ &= \frac{1}{4} \nabla \ln b^2 \cdot \nabla \ln b^2. \end{aligned} \quad (A11)$$

Finally, substituting the definitions of a and b in Eqs. (A10, A11) gives Eqs. (8,9), respectively.

Now we estimate the size of the real and imaginary parts of k_{error}^2 , to be compared with Eqs. (A6, A7). Recall that we are interested in k_{error}^2 when B_1^+ and B_1^- are close to each other. The closeness can be formally defined in terms of the magnitude of the complex fractional difference δ_B ,

$$\delta_B \equiv \left| \frac{B_1^- - B_1^+}{B_1^+} \right| \ll 1. \quad (A12)$$

Under this condition, we consider two additional small quantities; the fractional magnitude difference δ_m ,

$$\delta_m \equiv \frac{|B_1^-| - |B_1^+|}{|B_1^+|}. \quad (A13)$$

and the phase difference δ_p of Eq. (A2).

Figure (A1) graphically demonstrates the inequalities:

$$|\delta_m| \leq \delta_B \quad (\text{A14})$$

$$|\delta_p| \leq \arcsin \delta_B \approx \delta_B. \quad (\text{A15})$$

Fig. A1. Relationship among magnitude, phase, and complex differences between B_1^+ and B_1^- . In the complex plane, B_1^- lies on a circle centered at B_1^+ with radius $|B_1^- - B_1^+|$. Among all possibilities, $|B_1^-|$ is the most different from $|B_1^+|$ when B_1^- is at an intersection between the circle and a line passing B_1^+ and the origin (O). The maximum magnitude difference is $|B_1^- - B_1^+|$. This proves Eq. (A14). The maximum phase difference occurs when the line OB_1^- is tangential to the circle. The phase difference $\delta_{p,max}$ in this case satisfies $\sin \delta_{p,max} = \delta_B$, proving Eq. (A15).

The last approximation follows from $\delta_B \ll 1$. Eqs. (A14, A15) say that δ_m, δ_p are always both at most as small as δ_B . This allows us to use δ_m, δ_p as well as δ_B as a small parameter in the error analysis.

We now express the real and imaginary parts of $(B_1^- - B_1^+)/B_1^+$ in terms of δ_m and δ_p .

$$\text{Re} \left(\frac{B_1^- - B_1^+}{B_1^+} \right) = \frac{|B_1^-|}{|B_1^+|} \cos \delta_p - 1 = (1 + \delta_m) \left(1 - \frac{1}{2} \delta_p^2 + \frac{1}{4!} \delta_p^4 - \dots \right) - 1 = \delta_m - \frac{1}{2} \delta_p^2 - \frac{1}{2} \delta_m \delta_p^2 + \dots = \delta_m + O(\delta_B^2). \quad (\text{A16})$$

Here $O(\delta_B^2)$ means that the rest of the terms are at most on the order of δ_B^2 . In the second line of Eq. (A16) we used the Taylor expansion of the cosine function.

Similarly, using the Taylor expansion of $\sin x$ we get

$$\text{Im} \left(\frac{B_1^- - B_1^+}{B_1^+} \right) = \frac{|B_1^-|}{|B_1^+|} \sin \delta_p = (1 + \delta_m) \left(\delta_p - \frac{1}{3!} \delta_p^3 + \dots \right) = \delta_p + O(\delta_B^2). \quad (\text{A17})$$

Eqs. (A16, A17) show that, to the leading order, the real and imaginary parts of $(B_1^- - B_1^+)/B_1^+$ equal δ_m and δ_p , respectively.

Using these relations, Eq. (12) can be expressed as

$$k_{\text{error}}^2 \approx \frac{1}{4} \nabla(\delta_m + i\delta_p) \cdot \nabla(\delta_m + i\delta_p) \quad (\text{A18})$$

from which we get

$$\text{Re}(k_{\text{error}}^2) \approx -\frac{1}{4} \nabla \delta_p \cdot \nabla \delta_p + \frac{1}{4} \nabla \delta_m \cdot \nabla \delta_m, \quad (\text{A19})$$

$$\text{Im}(k_{\text{error}}^2) \approx \frac{1}{2} \nabla \delta_m \cdot \nabla \delta_p. \quad (\text{A20})$$

All terms on the right-hand side contain a product of a pair of small quantities. In this sense, the theoretical error in k^2 involved in our method is a second order effect with respect to the B_1^+, B_1^- difference.

Comparing Eq. (A19) with Eq. (A6), we find that $\text{Re}(k_{\text{error,conv}}^2)$ will be larger than $\text{Re}(k_{\text{error}}^2)$ in magnitude if $\nabla \angle B_1^+ \cdot \nabla \delta_p$ is much larger than $\nabla \delta_m \cdot \nabla \delta_m/4$ in magnitude. Although this may not be true in all cases, it is still expected to hold in a majority of cases given the smallness of δ_p, δ_m . Similarly, comparing Eq. (A20) with Eq. (A7), we find that although $|\text{Im}(k_{\text{error,conv}}^2)| > |\text{Im}(k_{\text{error}}^2)|$ may not be always true (depending on the specifics of B_1^+, B_1^-), it may hold in most cases due to the second order nature of Eq. (A20). Lack of rigorous proofs calls for experimental tests for practical validation. Numerical examples in the text provide a support for the qualitative arguments made here.

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Fig. 1.

EPs of a homogeneous elliptical cylinder reconstructed from analytical RF solutions. (a) Magnitudes of B_1^+ and B_1^- in a circularly polarized transmit-receive coil. (b) Magnitude of the fractional difference. (c) True EPs. (d,e) Reconstructed EPs from Eqs. (10-11) (d), and Eqs. (5-6) (e).

Fig. 2.

Magnitude (a) and phase (b) difference between analytically calculated B_1^+ and B_1^- in an elliptical cylinder (at 128 MHz), and theoretical error in k_2 in the proposed (c) and the conventional (d) method. Color scales are identical for all images. Each ellipse represents an axial cross section of an infinitely long elliptical cylinder (inset).

Fig. 3.
Pulse sequence for zero TE imaging. Four "spokes" in a 3D radial k -space scan are shown.

Fig. 4.

Phantom data. (a) $|B_1^+|$ map (normalized) and one-half of the SE phase on an axial slice, and

EPs calculated from them using Eqs. (5,6). (b) Magnitude and phase of $\sqrt{|I_{ZTE}|}$, and EPs calculated with the new method. Head T/R birdcage coil was used. (c) Same as (b) but with body coil transmission and an 8-channel array reception, after coil combination. (d) 8-channel $|I_{ZTE}|$ magnitudes and coil combination phases optimized per segment. (e) True EPs.

Fig. 5.

(a–b) Three-plane *in-vivo* brain ZTE images (amplitude, left column; phase, middle column) and conductivity maps (right column) overlaid on the amplitude image. Average conductivity values were 0.55 S/m (volunteer 1) and 0.56 S/m (volunteer 2). (c–d) Comparison of conductivity maps reconstructed from I_{ZTE} phase only vs complex I_{ZTE} . Black arrows indicate noise that is stronger in phase-only reconstruction.

(a) Volunteer 1

(b) Volunteer 2

Fig. 6. Normalized I_{ZTE} image amplitudes on a zoomed color scale (left) and reconstructed permittivity maps (right) on an axial slice of head. Black arrows indicate tissue boundaries around which unrealistic permittivity values were obtained (white arrows).

Table 1

Measured (mean $\pm$ standard deviation) and true EPs in each cylinder (segment) of the phantom. True values are taken from the literature (permittivity) and dielectric probe measurement (conductivity).

Method		Segment	ϵ_r	σ [S/m]
ZTE	head T/R	1	83.7 ± 15.7	0.11 ± 0.09
		2	88.6 ± 15.1	0.44 ± 0.11
		3	82.0 ± 14.9	0.90 ± 0.10
	8 ch array	1	89.1 ± 16.0	0.08 ± 0.08
		2	90.3 ± 12.6	0.45 ± 0.11
		3	84.6 ± 12.7	0.94 ± 0.09
B_1^+ and SE with head T/R		1	79.1 ± 12.1	0.10 ± 0.09
		2	80.9 ± 18.3	0.43 ± 0.11
		3	78.3 ± 11.1	0.95 ± 0.11
True values		1	80	0.08
		2	80	0.46
		3	80	0.92