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MR-Based Electrical Conductivity Imaging Using Second-Order Total Generalized Variation Regularization

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Abstract: Electrical properties provide essential information for cancer detection and specific absorption rate (SAR) estimation. Magnetic resonance electrical properties tomography (MREPT) is an approach to retrieve the distribution of electrical properties. The conventional method suffers from the locally homogeneous assumption and amplification of noise. In this study, a novel approach was introduced to improve the accuracy and the noise robustness of conductivity imaging. The proposed approach reformulated the central equation of the gradient-based method to avoid the calculation of the Laplacian operator. The equation was regularized using the second-order total generalized variation, which formulates an objective function. The optimization problem was solved by the alternating direction method of multipliers (ADMM) method. The proposed method was validated by the simulation data of the cylindrical phantom and Ella head model, and the performance was compared with existing methods. The results demonstrated that the proposed method reconstructed an accurate conductivity image and alleviated the noise effects. Furthermore, phantom and healthy volunteer experiments were implemented at a 3 Tesla (T) magnetic resonance imaging (MRI) scanner. The results suggested that the developed method can provide solutions for improved conductivity reconstruction and show potential for clinical application.

Keywords: electrical properties; electrical conductivity; magnetic resonance electrical properties tomography; total generalized variation (TGV); alternative direction method of multipliers

1. Introduction

The electrical properties (EPs) of biological tissues, which include electrical conductivity σ and permittivity ϵ , are fundamental properties that quantify the ability to transfer electrical current inside the medium and characterize the effect of electric polarization. EPs rely on the frequency of the applied electromagnetic field and are related to multiple tissue characteristics, which involve ion concentration, volume fraction, cellular membrane permeability, and pathological condition [1–3]. It has been reported that cancerous tissues show a significantly higher value of EPs than normal tissues according to the ex vivo experimental results; for example, the EP value of breast cancer is approximately >200% higher than normal tissue and that of bladder cancer is approximately >100% higher [4–6]. Thus, mapping EPs has the potential for cancer detection and diagnosis. Moreover, tissue EPs are critical for the application of transcranial magnetic stimulation and transcranial direct current stimulation, which provides potential therapeutic applications for a wide variety of disorders,

including Parkinson's disease, stroke, depression, and schizophrenia [7–9]. Furthermore, the estimation of the specific absorption rate (SAR), which is a crucial problem in high and ultra-high field magnetic resonance imaging (MRI) systems, requires accurate conductivity distribution [10,11]. This evidence suggests that imaging the distribution of EPs can provide essential information for both research and medical purposes.

Many efforts have been made to image *in vivo* EPs based on several distinct measuring techniques [12–14]. Among them, magnetic resonance electrical properties tomography (MREPT) is a non-invasive method to simultaneously map conductivity and permittivity using the MRI system [15,16]. MREPT exploits the function between EPs and electromagnetic field produced by the radiofrequency (RF) coil system, the B_1^+ field. The B_1^+ field can be measured by MR scanning. Therefore, MREPT reconstructs the distribution of tissue EPs from the B_1^+ measurement [17]. MREPT reconstruction algorithms can be divided into three categories, which are direct methods, inverse methods, and learning-based approaches.

The direct methods reconstruct EPs by applying Maxwell's equations to the measured RF field. The frequently used method of direct methods is the conventional method (referred to as CM); it depends on the assumption that the EPs distribution is locally homogeneous. This method has reconstructed EPs successfully [15], but it includes certain disadvantages. Firstly, the true EPs distribution in the human body, which is spatially heterogeneous, violates the above-mentioned assumption. Thus, the boundary artifacts are brought around the boundary between different tissues [18]. Several studies have attempted to address this problem by introducing the gradient information of EPs to the reconstruction method [19,20]. Another problem of the CM originates from obtaining phase information. MREPT reconstruction requires the magnitude and phase of B_1^+ . The magnitude information can be obtained using the B1 mapping methods [21–23], but phase information cannot be explicitly determined using existing technology. The transceive phase assumption (TPA) is used [24]. TPA approximates the B_1^+ phase as half of the transceive phase, namely the sum of the transmit and receive phase. Van der Liere et al. found that the TPA is valid in low field strength, low permittivity, and symmetric objects [25]. Lastly, the Laplacian operator is sensitive to noise and then introduces numerical errors. Lee et al. provided the theoretical relationship between the signal to noise ratio (SNR) of MREPT and the input B_1^+ data [26].

Apart from calculating the EPs distribution directly from the equation derived from Maxwell's equation, inverse methods leverage a forward model for calculating B1 maps and a fitting method for evaluating the EPs distribution [27–29]. These reconstruction approaches avoid the locally homogeneous assumption and alleviate the noise effect by avoiding the differentiation of measured data. For example, Serralles et al. proposed global Maxwell tomography on the basis of the volume integral equation formulations [30]. Balidemaj et al. introduced contrast source inversion EPT (CSI-EPT) [31]. However, these methods require extensive numerical efforts and have not been investigated in *in vivo* experiments.

The recent applications of machine learning algorithms in EPT show promising results [32,33]. These methods retrieve EPs from large datasets of transmit RF fields and their corresponding EPs via machine learning. Nils Hamp et al. investigated the challenges of deep learning-based methods and found that the networks trained on realistic simulation introduce artifacts when applied to *in vivo* data [34].

In contrast to acquiring both the conductivity and permittivity from MREPT algorithms, the conductivity reconstruction can be conducted solely by phase information based on the fact that the phase map primarily dominates the conductivity calculation [35]. The transceive phase map is used to reconstruct the conductivity. Thereby, it bypasses the TPA and decreases the scan time without B1 mapping scanning. Gurler et al. introduced an electrical conductivity imaging method, which includes the gradient information of conductivity, to improve the reconstruction accuracy. However, this method involves setting the boundary value and the diffusion parameter [36]. In our previous study, we proposed a double regularization method that contains total variation and wavelet terms [37]. This method suppresses spurious oscillation and enhances the accuracy of reconstruction.

However, the method needs the second spatial derivatives of the transceive phase, and staircase effects occur due to the total variation regularization.

In this study, we proposed a novel conductivity imaging method on the basis of the gradient-based conductivity imaging method. We reformulated the central equation through divergence properties, leading to the free measurements of the Laplacian operator. With the finite-difference method, the optimization problem was obtained, and a second-order total generalized variation (TGV) term was used to remove the staircase effect [38]. The problem was solved using the alternating direction method of multipliers (ADMM) method [39]. Numerical simulation and experimental were applied to validate the performance of the proposed method. The reconstruction results show that the proposed method accurately determines the distribution of conductivity and is robust in terms of noise contamination compared with the conventional and double regularization methods.

2. Theory

2.1. The Double Regularization Conductivity Imaging Method

The central equation used in the gradient-based electrical conductivity imaging method is as follows [36]:

$$\nabla \varphi^{tr} \cdot \nabla \rho + \nabla^2 \varphi^{tr} \cdot \rho - 2\omega\mu_0 = 0 \quad (1)$$

where $\rho = 1/\sigma$, μ_0 is the free space permeability, φ^{tr} is the transceive phase, and ω is the Larmor frequency. Several assumptions are applied to derive Equation (1), which assumes $\nabla|B_1^+| = 0$, $\nabla|B_1^-| = 0$, $\sigma^2 \gg (\omega\varepsilon)^2$ and neglects spatial derivatives of B_z . With the first-order central differential scheme, the discretized Equation (1) in an image matrix $M \times N \times L$ can be written as [37]:

$$\begin{aligned} & \left(\frac{\rho_{i,j+1,k} - \rho_{i,j-1,k}}{2\Delta x} \right) \cdot \frac{\partial \varphi^{tr}}{\partial x} + \left(\frac{\rho_{i+1,j,k} - \rho_{i-1,j,k}}{2\Delta y} \right) \cdot \frac{\partial \varphi^{tr}}{\partial y} + \left(\frac{\rho_{i,j,k+1} - \rho_{i,j,k-1}}{2\Delta z} \right) \cdot \frac{\partial \varphi^{tr}}{\partial z} \\ & + \rho_{i,j,k} \cdot \left(\frac{\partial^2 \varphi^{tr}}{\partial x^2} + \frac{\partial^2 \varphi^{tr}}{\partial y^2} + \frac{\partial^2 \varphi^{tr}}{\partial z^2} \right) = 2\omega\mu_0, \end{aligned} \quad (2)$$

where $i = 1, 2 \dots N$, $j = 1, 2 \dots M$, $k = 1, 2 \dots L$, Δx , Δy , Δz are the spatial resolution along the x , y , z directions, respectively. Equation (2) is applied to each point of the imaging region, and then an inverse problem is obtained:

$$A\rho = b, \quad (3)$$

where A is the sparse matrix with size $M \times N \times L \times M \times N \times L$, $b = 2\omega\mu_0$. According to Sun [37], Equation (3) is constructed into an optimization problem with additional double regularization terms of total variation (TV) and wavelet transform. This method is abbreviated as “DRM” in this study. Thus, the corresponding optimization problem is written as:

$$\rho = \operatorname{argmin} \frac{1}{2} \|A\rho - b\|_2^2 + \lambda_1 \|\rho\|_{tv} + \lambda_2 \|W\rho\|_1, \quad (4)$$

where W is a wavelet transform, $\|\rho\|_{tv} = \sum_{i,j} \sqrt{(\nabla_x \rho_{i,j})^2 + (\nabla_y \rho_{i,j})^2}$. λ_1 and λ_2 are the parameters of TV and wavelet transform, respectively. This problem is solved using the Split Bregman method [40]. However, ADMM was used in this study and is introduced in detail in a later section.

2.2. The Proposed Electrical Conductivity Imaging Method

Inspired by the modified finite difference scheme [41], we can use the divergence properties, which is $\nabla \cdot (ab) = (\nabla a) \cdot b + a(\nabla \cdot b)$; then, we can transform Equation (1) into:

$$\nabla \cdot (\rho \nabla \varphi^{tr}) = 2\omega\mu_0. \quad (5)$$

Equation (5) is free of the calculation of the Laplacian operator of the transceive phase. Given the central difference method, the discretized Equation (5) in an image region is:

$$\begin{aligned} & \frac{\rho_{i+1,j,k} \left(\frac{\partial \varphi^{tr}}{\partial y} \right)_{i+1,j,k} - \rho_{i-1,j,k} \left(\frac{\partial \varphi^{tr}}{\partial y} \right)_{i-1,j,k}}{2\Delta y} + \frac{\rho_{i,j+1,k} \left(\frac{\partial \varphi^{tr}}{\partial y} \right)_{i,j+1,k} - \rho_{i,j-1,k} \left(\frac{\partial \varphi^{tr}}{\partial y} \right)_{i,j-1,k}}{2\Delta x} \\ & + \frac{\rho_{i,j,k+1} \left(\frac{\partial \varphi^{tr}}{\partial y} \right)_{i,j,k+1} - \rho_{i,j,k-1} \left(\frac{\partial \varphi^{tr}}{\partial y} \right)_{i,j,k-1}}{2\Delta z} = 2\omega\mu_0. \end{aligned} \quad (6)$$

Equation (6) can be transformed into the same linear inverse problem as Equation (3) inside the imaging region. The formula $A\rho = b$ is used to represent the procedure result of the proposed method. Given that the diagonal of Matrix A is 0, the results cannot be obtained by the inverse matrix. Subsequently, the problem is expressed as an optimization problem, and second-order TGV regularization is adapted to stabilize the result and improve the accuracy of construction. The TGV regularization can preserve edges while suppressing the staircase effect and is proven as a favorable regularization for medical imaging problems [42–44]. As previously noted [43], the discrete $TGV_\alpha^2(\rho)$ can be written as the following equivalent form:

$$TGV_\alpha^2(\rho) = \min_v \alpha_1 \|\nabla \rho - v\|_1 + \alpha_2 \|\varepsilon(v)\|_1, \quad (7)$$

where $\nabla \rho = (D_1\rho, D_2\rho, D_3\rho)$, D_1, D_2, D_3 are the finite difference operators along the x -axis, y -axis, and z -axis, respectively; v represents an approximation of $\nabla \rho$ and is a matrix field with the same size of $\nabla \rho$; and $\varepsilon(v) = (1/2)(\nabla v + \nabla v^T)$ denotes symmetrized spatial derivatives.

The use of TGV as a regularization term leads to the following reconstruction model:

$$\rho = \operatorname{argmin}_{\rho, v} \frac{1}{2} \|A\rho - b\|_2^2 + \alpha_1 \|\nabla \rho - v\|_1 + \alpha_2 \|\varepsilon(v)\|_1, \quad (8)$$

where α_1 and α_2 are the regularization parameters.

The reconstruction problem is non-smooth and convex, and thus, it is difficult to solve through common methods such as the conjugate gradient (CG) method. The ADMM method is used to solve the optimization problem [39]. The key idea of ADMM is to derive an equivalent problem with separable sub-problems by introducing auxiliary variables. The ADMM method does not depend on the smoothness of the problem and converges quickly to a reasonable accuracy result.

2.3. Solutions to the Optimization Problem Using ADMM

First, two auxiliary variables $y = \nabla \rho - v$ and $z = \varepsilon(v)$ are introduced, and then Equation (8) is transformed into a constrained problem:

$$\begin{aligned} & \operatorname{argmin}_{\rho, p} \frac{1}{2} \|A\rho - b\|_2^2 + \alpha_1 \|\nabla \rho - v\|_1 + \alpha_2 \|\varepsilon(v)\|_1 \\ & \text{s.t. } y = \nabla \rho - v, z = \varepsilon(v) \end{aligned} \quad (9)$$

The corresponding augmented Lagrangian function of Equation (9) is:

$$\operatorname{argmin}_{\rho, y, z, v, \tilde{y}, \tilde{z}} \frac{1}{2} \|A\rho - b\|_2^2 + \alpha_1 \|y\|_1 + \alpha_2 \|z\|_1 + \frac{\beta_1}{2} \|\nabla \rho - v - y + \tilde{y}\|_2^2 + \frac{\beta_2}{2} \|\varepsilon(v) - z + \tilde{z}\|_2^2, \quad (10)$$

where β_1, β_2 are penalty parameters, and $\tilde{z}, \tilde{y}$ are Lagrange multipliers. Then, Equation (10) can be separated into sub-problems according to the variables, respectively. The sub-problems are as follows:

$$\rho^{n+1} = \operatorname{argmin}_{\rho} \frac{1}{2} \|A\rho - b\|_2^2 + \frac{\beta_1}{2} \|\nabla \rho - v^n - y^n + \tilde{y}^n\|_2^2, \quad (11)$$

$$y^{n+1} = \underset{y}{\operatorname{argmin}} \alpha_1 \|y\|_1 + \frac{\beta_1}{2} \|\nabla \rho^{n+1} - v^n - y + \tilde{y}^n\|_2^2, \quad (12)$$

$$z^{n+1} = \underset{z}{\operatorname{argmin}} \alpha_2 \|z\|_1 + \frac{\beta_2}{2} \|\varepsilon(v^n) - z + \tilde{z}^n\|_2^2, \quad (13)$$

$$v^{n+1} = \underset{v}{\operatorname{argmin}} \frac{\beta_1}{2} \|\nabla \rho^{n+1} - v - y^{n+1} + \tilde{y}^n\|_2^2 + \frac{\beta_2}{2} \|\varepsilon(v) - z^{n+1} + \tilde{z}^n\|_2^2. \quad (14)$$

Given that Equation (11) is differentiable, then the optimality condition for ρ^{k+1} is easily derived as follows:

$$(A'A + \beta_1 \nabla^T \nabla) \rho^{n+1} = A'b + \beta_1 \nabla^T (v^n + y^n - \tilde{y}^n). \quad (15)$$

Equation (15) can be calculated through the CG method or Gauss–Seidel method.

The y, z sub-problems are similar, and the solutions are given explicitly by a generalized shrinkage formula [45]. Specifically, the solution to the y sub-problem is:

$$y^{n+1} = \max \left\{ \|v^n - \nabla \rho^{n+1} - \tilde{y}^n\|_2 - \frac{\alpha_1}{\beta_1}, 0 \right\} \cdot \frac{v^n - \nabla \rho^{n+1} - \tilde{y}^n}{\|v^n - \nabla \rho^{n+1} - \tilde{y}^n\|_2}. \quad (16)$$

Likewise, we obtain the solution to the z sub-problem as:

$$z^{n+1} = \max \left\{ \|\tilde{z}^n + \varepsilon(v^n)\|_2 - \frac{\alpha_2}{\beta_2}, 0 \right\} \cdot \frac{\tilde{z}^n + \varepsilon(v^n)}{\|\tilde{z}^n + \varepsilon(v^n)\|_2}. \quad (17)$$

For the sub-problem v , we use the first-order necessary conditions for optimality as follows:

$$\begin{aligned} (\beta_1 + \beta_2 D_1^T D_1 + \frac{1}{2} \beta_2 D_2^T D_2 + \frac{1}{2} \beta_2 D_3^T D_3) v_1^{n+1} &= \frac{1}{2} \beta_2 (D_2^T D_1 v_2^n + D_3^T D_1 v_3^n) \\ &+ \beta_1 (D_1 \rho^{n+1} - y_1^{n+1} + \tilde{y}_1^n) + \beta_2 D_1^T (z_{1,1}^{n+1} - \tilde{z}_{1,1}^n) + \beta_2 D_2^T (z_{1,2}^{n+1} - \tilde{z}_{1,2}^n) + \beta_2 D_3^T (z_{1,3}^{n+1} - \tilde{z}_{1,3}^n), \end{aligned} \quad (18)$$

$$\begin{aligned} (\beta_1 + \beta_2 D_2^T D_2 + \frac{1}{2} \beta_2 D_2^T D_2 + \frac{1}{2} \beta_2 D_3^T D_3) v_2^{n+1} &= \frac{1}{2} \beta_2 (D_1^T D_2 v_1^{n+1} + D_3^T D_2 v_3^n) \\ &+ \beta_1 (D_2 \rho^{n+1} - y_2^{n+1} + \tilde{y}_2^n) + \beta_2 D_1^T (z_{1,2}^{n+1} - \tilde{z}_{1,2}^n) + \beta_2 D_2^T (z_{2,2}^{n+1} - \tilde{z}_{2,2}^n) + \beta_2 D_3^T (z_{2,3}^{n+1} - \tilde{z}_{2,3}^n), \end{aligned} \quad (19)$$

$$\begin{aligned} (\beta_1 + \beta_2 D_3^T D_3 + \frac{1}{2} \beta_2 D_1^T D_1 + \frac{1}{2} \beta_2 D_2^T D_2) v_3^{n+1} &= \frac{1}{2} \beta_2 (D_1^T D_3 v_1^{n+1} + D_2^T D_3 v_2^{n+1}) \\ &+ \beta_1 (D_3 \rho^{n+1} - y_3^{n+1} + \tilde{y}_3^n) + \beta_2 D_1^T (z_{1,3}^{n+1} - \tilde{z}_{1,3}^n) + \beta_2 D_2^T (z_{2,3}^{n+1} - \tilde{z}_{2,3}^n) + \beta_2 D_3^T (z_{3,3}^{n+1} - \tilde{z}_{3,3}^n). \end{aligned} \quad (20)$$

Equations (18)–(20) are solved by using the CG method or Gauss–Seidel method.

Correspondingly, the updated procedure of $\tilde{z}$ and $\tilde{y}$ is as follows:

$$\tilde{y}^{n+1} = \tilde{y}^n + \nabla \rho^{n+1} - v^{n+1} - y^{n+1}, \quad (21)$$

$$\tilde{z}^{n+1} = \tilde{z}^n + \varepsilon(v^{n+1}) - z^{n+1}. \quad (22)$$

Based on the above-described equations, the distribution of conductivity can be calculated by inverting the ρ point-wise.

3. Methods

3.1. Electromagnetic Simulations

Figure 1 shows the electromagnetic simulations conducted using a Finite-Difference Time-Domain (FDTD)-based software (SEMCAD X. 14.6, ZMT, Zurich, Switzerland). A high-pass shielded birdcage coil model was used for the numerical simulation. The length of the leg was 300 mm. The diameter of the RF shield and rings were 330 and 300 mm, respectively. By adjusting the capacitor in the rings, the quadrature coil was tuned at 128 MHz (3T) and was driven in a quadrature mode by two ports separated by 90°.

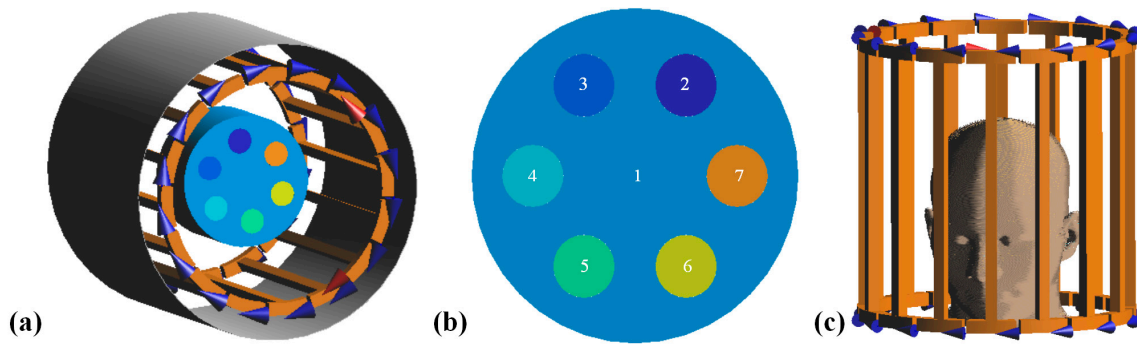


Figure 1. Simulation setup. (a) The birdcage coil loaded with a numerical phantom, (b) seven regions of phantom, (c) the birdcage coil loaded with the Ella model. The radiofrequency (RF) shield is not shown in (c).

The simulation model included a cylindrical phantom and Ella head model (Ella Model, the Virtual family [46]). The diameter and height of the cylindrical phantom were both 160 mm. Figure 1b illustrates that the phantom contained six same size cylinders with small diameters; different EP values were assigned to these cylinders. Figure 1c shows the Ella head model, and the conductivity value of the head tissues was appointed, according to Gabriel et al. [3]. The analysis of reconstruction results included three primary tissues of the head, namely gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF).

After the phase information of B_1^+ and B_1^- was obtained from the electromagnetic simulation, these data were added to acquire the transceive phase information. Given that the simulation grid was not uniform, the non-uniformly spaced grid was re-gridded into a regular grid by using a linear interpolation method to allow a comparison on the voxel level.

The proposed method was validated for noisy simulated data. The noise distribution in MR phase images is assumed as Gaussian noise. The standard deviation (SD) of Gaussian noise in phase images was $1/(\sqrt{2}\text{SNR})$, in which SNR is the signal-to-noise ratio in magnetic resonance (MR) magnitude images [47,48]. In the simulations, the different MR magnitude SNR values, such as 200, 100, and 50, were set to alter the SD of the Gaussian noise. Then, the noise was added to the transceive phase image to simulate the noisy phase image [36]. For the simulations, all methods were repeated for 100 implementations at each noise level to calculate the root mean square error (RMSE) over the reconstructed conductivity profile; the RMSE equation was:

$$RMSE = \sqrt{\frac{\sum_{i=1}^N (r_i - r_{it})^2}{N}} \quad (23)$$

where r_i is the reconstructed conductivity of pixel i and r_{it} is the target value.

3.2. Experimental Setup

A cylindrical phantom was used to verify the proposed approach. The structure of the cylindrical phantom contained inner and outer compartments that were separated by a tube. The materials of the phantom were distilled water, NaCl, agarose, and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. Agarose was used to solidify the phantom, whereas $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ was used to decrease the T1 values and then reduce the scanning time. The contrast of the phantom was prepared by adjusting the concentrations of saline. The mass ratio of distilled water, agarose, and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ was 100:1:0.1. The saline concentrations were 1.5% and 0.5% for the inner and outer compartments, respectively. Conductivity values were measured by a network analyzer (Agilent 4395A, Santa Clara, CA, USA) associated with an S-parameter test set (Agilent 87511A). The conductivity values for the inner and outer compartments were 2.01 and 0.97 S/m, respectively.

The in vivo experiment included a healthy 26-year-old male volunteer. The subject gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Southern Medical University (2018B030333001).

The phantom and in vivo experiments were carried out on a 3.0T MRI scanner (Philips Achieva, Best, The Netherlands) installed in NanFang Hospital. We used the standard body coil as transmitting and receiving and applied the spin-echo (SE) sequence to obtain the transceive phase information. The 2D SE sequence parameters in the phantom experiment were TR/TE = 1000/10 ms, with 5 averages in 20 min. The acquisitions were performed in a total of five slices with a resolution of $1.17 \times 1.17 \times 3 \text{ mm}^3$ and a field of view (FOV) of $150 \times 150 \text{ mm}^2$. For the in vivo experiment, the parameters of the 2D SE sequence were TR/TE = 1200/7 ms; 10 slices centered on the head center were scanned, with a resolution of $1.88 \times 1.88 \times 5 \text{ mm}^3$ and a FOV of $240 \times 240 \text{ mm}^2$. This scan took 3 min.

3.3. Image Reconstruction

The accuracy of reconstruction was enhanced using a Gaussian kernel to filter the noisy simulation data and experimental data, the kernel size of the filter was $7 \times 7 \times 3$ voxels, and the standard deviation was $1.2 \times 1.2 \times 1.2$ pixels. The proposed method was compared with the CM and the double regularization method (DRM). All calculations were conducted in MATLAB (The MathWorks, Natick, MA, USA).

For the DRM and proposed method, several parameters need to be set. The RMSE was used to estimate the performance of reconstruction for different parameters, and then the proper parameters were selected. Table 1 presents the actual regularization parameters.

Table 1. Parameters of the double regularization method (DRM) and the proposed method.

		DRM		Proposed Method			
		λ_1	λ_2	α_2	β_2	α_1	β_1
Simulation	Phantom	1	800	1	1	40	2
	Brain	2	500	1	1	10	1
Experiment	Phantom	1	800	1	1	40	2
	Human	5	500	1	1	10	1

4. Results

4.1. Phantom Simulation Results

The reconstructed conductivity images of the cylindrical phantom were compared with the corresponding target image, as shown in Figure 2. Under the noise-free condition, the conductivity distribution in the homogeneous region is accurate for all the methods in Figure 2a. The distinct difference between these methods depends on the boundary artifacts in the transition region between different contrast components. The boundary artifacts are obviously around the small cylindrical for the CM, with origins from the locally homogeneous assumption. In the DRM conductivity image, the artifacts are reduced due to the adoption of gradient information in the critical equation. However, several artifacts remain around the transition region because of the Laplacian operator. By contrast, the proposed method does not require the calculation of the Laplacian operator, yielding a more precise result than the DRM. Figure 2b depicts the conductivity profiles along the red line in Figure 2a. The proposed method represents a smoother result that is close to the target values. Figure 3 shows the mean and SD of the reconstructed conductivity in each region for different methods. In most areas, the proposed method leads to accurate values and lower SD values than other methods.

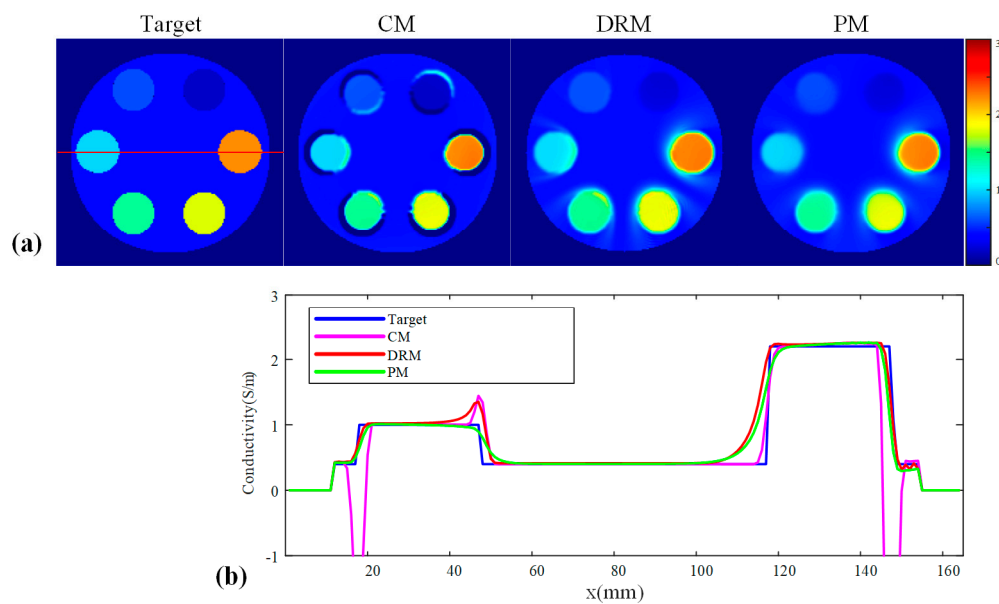


Figure 2. Comparison of reconstructed conductivity images using different methods under the noise-free condition. (a) The target image and reconstructed conductivity images using the conventional method (CM), double regularization method (DRM), and proposed method (PM). (b) The reconstructed conductivity profiles along the red line in the target image in (a).

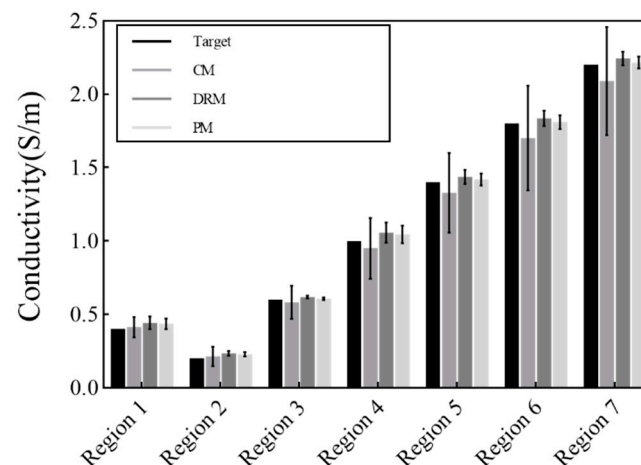


Figure 3. Bar graph of reconstructed conductivity value using conventional method (CM), double regularization method (DRM), and proposed method (PM). It corresponds to seven regions.

Figure 4 illustrates the conductivity images under different noise conditions by using three reconstruction methods. The CM conductivity results are severely affected by noise because the Laplacian operator is sensitive to noise. The use of a larger Laplacian kernel can alleviate this phenomenon, but it can also over smoothen the results. The DRM results demonstrate better suppression of the noise effect. In contrast to DRM, the proposed method shows superior conductivity images. The reconstructed results display a clear phantom structure, and the small inner regions retain a sharper edge than the other methods as the noise increase. Thus, the proposed method can alleviate noise effects.

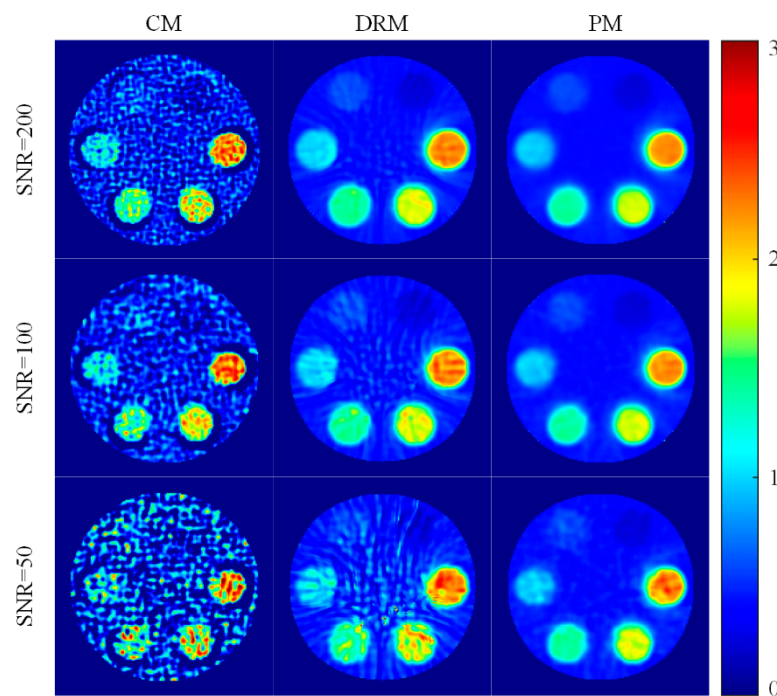


Figure 4. Reconstructed conductivity images under different noisy transceive phase data using the conventional method (CM), double regularization method (DRM), and the proposed method (PM).

The RMSE was used to assess the accuracy of three reconstruction methods with various noise levels. Figure 5 shows the results; the x -axis presents the SD of zero-mean Gaussian noise, in which the SD is $1/(\sqrt{2}SNR)$; the SNR is the signal to noise ratio in the MR magnitude image. Notably, the RMSE of the CM increases with noise and is much larger than that of other methods. For DRM and the proposed method, the change of RMSE in low noise stays small, and the DRM RMSE is larger than the proposed method. These two methods similarly show an increasing tendency of RMSE as the noise increases. The magnitude of the DRM is larger than that of the proposed method. The RMSE of the proposed method stays at a low level, even in severe noise corruption. Thus, the proposed method is robust for noisy phase data.

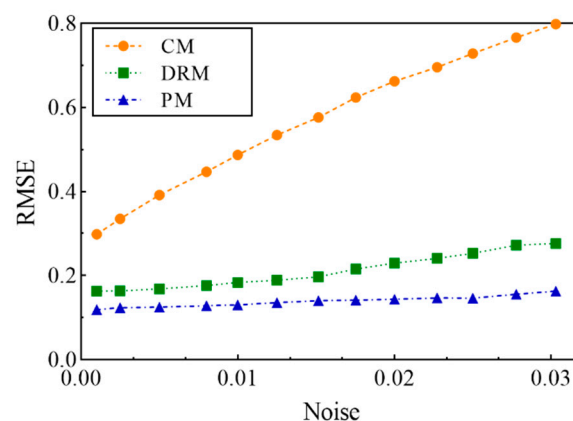


Figure 5. The root mean square error (RMSE) of reconstructed conductivity using the conventional method (CM), double regularization method (DRM), and the proposed method (PM).

4.2. Ella Head Simulation Results

Figure 6 depicts the reconstruction of the Ella head model simulation. Conductivity images are shown from different head positions under noise-free conditions. All the results display the basic

structure of the head, which includes WM and GM. Similar to the phantom simulation, the CM conductivity images yield artifacts in the boundary, especially around the CSF tissue. For the DRM, the reconstructed conductivity shows precise results compared with target images. However, the dispersal in the CSF boundary emerges evidently in positions 2 and 3. Compared with DRM, the proposed approach shows a more accurate structure, and the edge is sharper and precise.

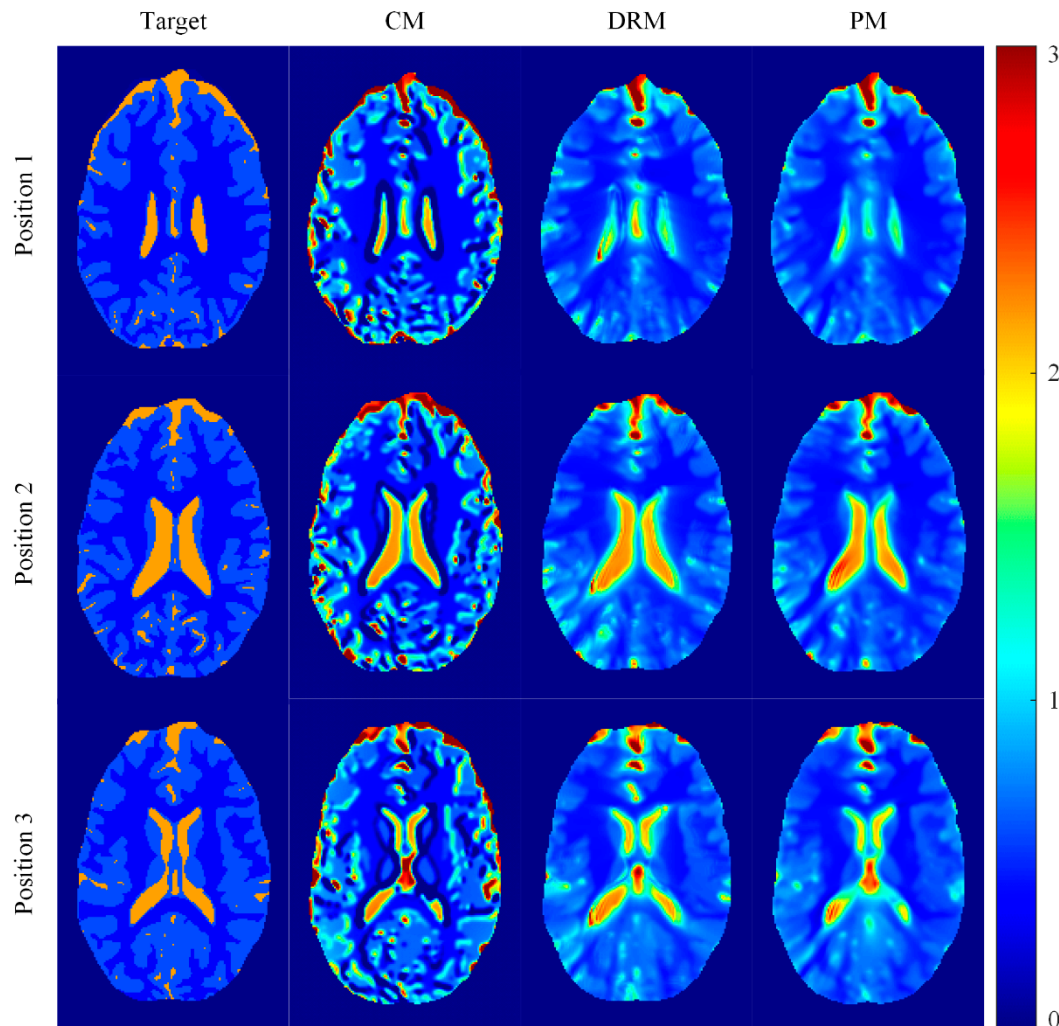


Figure 6. The reconstructed conductivity images of the Ella head model under noise-free conditions using the conventional method (CM), double regularization method (DRM), and proposed method (PM).

Figure 7 describes the head model results under various noise conditions, which are $\text{SNR} = 200$ and $\text{SNR} = 100$. The results of all methods get worse as the noise increase because the structure of the head is more complicated than the phantom. In addition, the larger Laplacian kernel and the first-order spatial derivative operator dismiss several small structures. The proposed method preserves more details than the results of DRM, such as the WM region in position 2. Figure 8 depicts the RMSE of the reconstructed conductivity images under noise conditions. The RMSE increases as the noise increases and the proposed method shows the lowest values, which display the advantage of the proposed method.

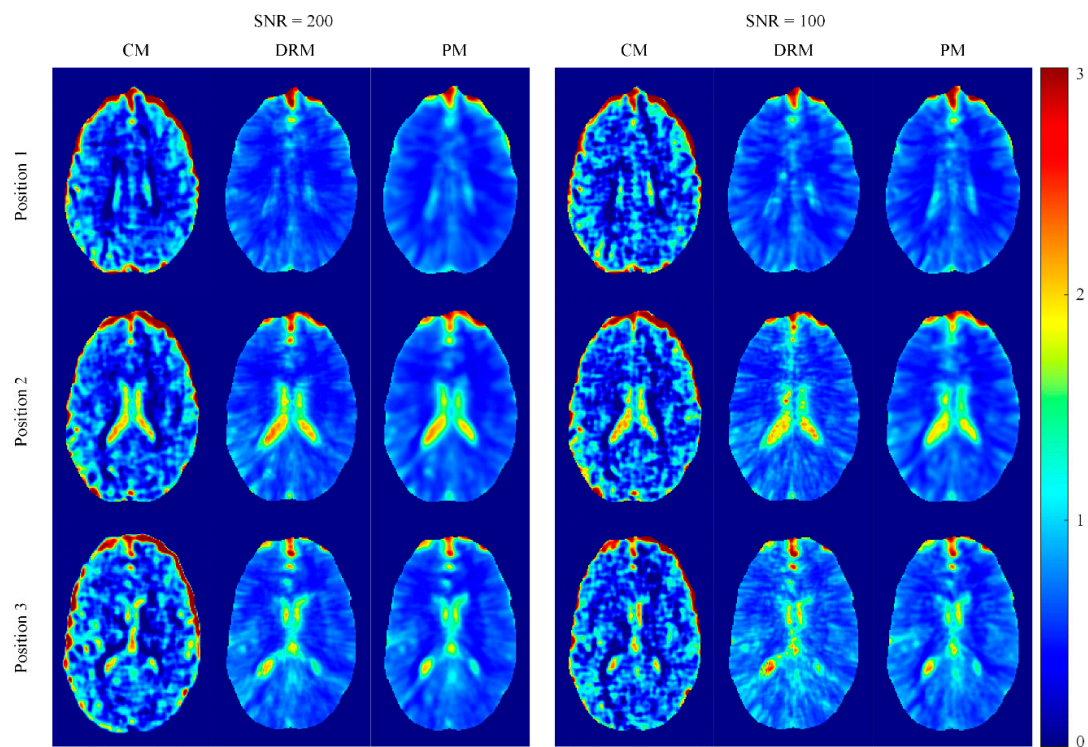


Figure 7. Reconstructed conductivity images of the Ella head model using the conventional method (CM), double regularization method (DRM) and proposed method (PM) under a signal to noise ratio (SNR) = 200 and SNR = 100.

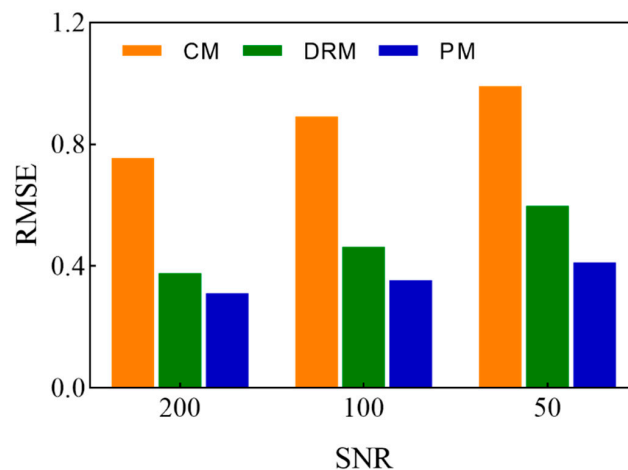


Figure 8. The RMSE of reconstructed conductivity images under noise conditions using the conventional method (CM), double regularization method (DRM), and proposed method (PM).

4.3. Experimental Results

Figure 9 describes the reconstructed conductivity image of the phantom experiment. Figure 9a,b represent the SE magnitude and phase images, respectively. The SNR of magnitude is 132. In the magnitude image, the region between the blue circles is region 1, while the red circle describes region 2. The black circle in the magnitude image is the material used to separate these two compartments. Figure 9b illustrates the conductivity using the CM, DRM, and proposed method. The conductivity of the proposed method exhibits more homogeneity in two regions than CM and DRM. Table 2 shows the calculated mean and SD of these two regions. The proposed method has more accurate mean values than CM and DRM, indicating its feasibility to reconstruct accurate conductivity.

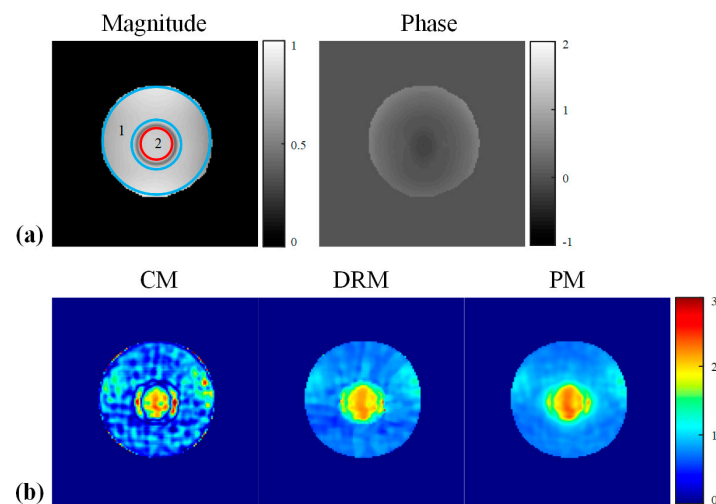


Figure 9. Phantom reconstruction result. (a) Magnitude and phase images of the phantom; the SNR of the magnitude image is 132. (b) The reconstructed conductivity images using the conventional method (CM), double regularization method (DRM), and the proposed method (PM).

Table 2. Reconstructed conductivity values of phantom experiment.

	Measured	Conventional Method	Double Regularizations Method	Proposed Method
Region 1	0.97	0.71 ± 0.31	0.84 ± 0.13	0.92 ± 0.08
Region 2	2.01	1.56 ± 0.59	1.92 ± 0.25	1.98 ± 0.19

Figure 10 shows the magnitude, phase, and reconstructed conductivity images of the in vivo experiment. The SNR of the magnitude image is 75. The proposed method shows a clearer structure than the results of the CM and DRM. The CSF region offers more errors, which are possibly caused by low-phase data.

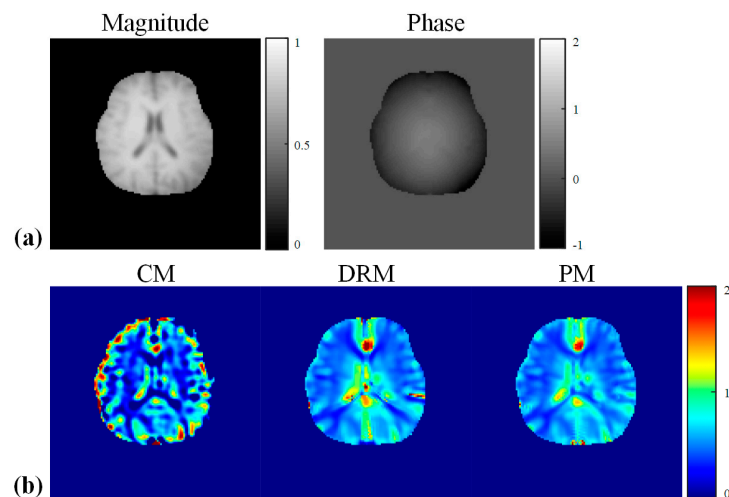


Figure 10. Magnitude, phase, and reconstructed conductivity images of head experiment. (a) Spin-echo (SE) magnitude and phase images; the SNR of the magnitude image is 75. (b) Conductivity images using the conventional method (CM), the double regularization method (DRM), and the proposed method (PM).

5. Discussion

In the present study, a novel approach was proposed for imaging the conductivity distribution from the MR transceive phase. On the basis of the gradient-based method, the proposed method

reformulates the central equation through divergence properties and then leverages the finite difference method to construct an inverse problem. The resultant optimization problem is regularized by TGV and solved by ADMM. The proposed method does not require the Laplacian operator of the transceive phase, which is the origin of the dominant errors of general approaches. A systematic investigation using numerical simulations and experiments at 3T illustrate that the proposed method can improve the reconstruction accuracy and is more robust to the noise than the CM and DRM.

The CM, which relies on the locally homogeneous assumption, is applicable for those objects with a simple structure but not for complicated objects such as the brain, as shown in Figure 5. The pre-segmentation of objects can partially mitigate these adverse effects before reconstruction. However, this method introduces extra work, and the assumption remains. Therefore, it cannot solve the problem fundamentally. By contrast, the proposed method uses conductivity gradient information and thus in principle is immune to the effects of the above-mentioned assumption. The Ella model simulation results indicate that the proposed approach is favorable for objects with complicated structures.

The CM and DRM require the calculation of the Laplacian operator, which is sensitive to noise. The results of the CM show the effect of noise, while those of the DRM show the impact of the Laplacian operator despite applying conductivity gradient information. A noise-robust Laplacian kernel was used to alleviate the effect of noise [49]. However, despite the noise suppression, this leads to over-smoothed reconstruction results. Another method reconstructs conductivity profiles by using the first-order differencing of the RF filed data [50]. However, the induced current density image must be determined to obtain the EPs. By contrast, the proposed method transforms the equation to remove the necessity of the Laplacian operator of the transceive phase and directly retrieve the conductivity. The simulation and experiments show that the proposed method decreases the impact of noise.

The proposed method depends on the central equation of the gradient-based method [36]. The following three assumptions are made. The first assumption is that the spatial derivatives of B_1^+ and B_1^- are negligible. This assumption is valid in the quadrature birdcage coil central region when the coil is used to transmit and receive. However, this assumption appears untrue at high field strengths ($>3T$). The RF shimming technique may provide a resolution to improve the homogeneity of the RF field. The second assumption is $\sigma^2 \gg (\omega\epsilon)^2$, which is sufficient for common tissues at field strengths $\leq 3T$. The reconstructed conductivity value shows overestimation compared to the real value when violating the assumption, such as region 2 of the phantom simulation. This assumption is close to the assumption used in the conventional approach, which is $\sigma \gg \omega\epsilon$ [25]. Third, the spatial derivatives of B_z are negligible compare to B_1^+ and B_1^- , which appear rational in the central region of the birdcage coil from the simulation. From the perspective of clinical application, the B_z information cannot be directly acquired.

The optimization problem of the proposed method includes a second-order TGV regularization term that can suppress the noise while omitting the staircase effect. ADMM was applied to address the problem and then obtain accurate conductivity images. Compared with DRM, the proposed method eliminates the staircase effect and shows better results in terms of noise suppression. The implementation of the proposed method requires four parameters, which are determined by using RMSE as a criterion. The optimal parameters for different regions vary. Thus, selecting spatially dependent parameters provides the potential to obtain a more accurate result than before, as observed in other applications [51]. During the calculation, there are a few iterations to acquire moderate conductivity results, indicating that the time cost is short. The phantom and brain reconstructions take approximately 2 s and 10 s, respectively, on a standard PC with an Intel i5 (2.9 GHz) and 16 Gb of RAM.

The proposed method reformulates the central equation to remove the Laplacian operator through divergence properties. In the discretization for the imaging region, different points are used to construct an inverse problem compared with DRM. Inspired by the recent research [52], we can also use the

divergence theorem to transform the equation into an integral formula that can suppress noise, further improving the reconstruction.

The distribution of conductivity is reconstructed using only transceive phase information. Thus, any sequences can be used to obtain the transceive phase, theoretically. However, other factors, such as the homogeneity of the main field strength, eddy currents, and the phase contribution from flow and motion contaminate the phase data [16]. In this study, SE was chosen to acquire the phase. In other studies, the steady-state free precession (SSFP) sequence shows advantages for scanning because of its short time [53]. During the present experiment, a volume coil was used for transmitting and receiving, which is a typical configuration in clinical application. The multi-channel coil as the receive coil improves the SNR of the MR image and saves time [54]. It would be exploring in future research. In addition, when the phase image is achieved, the magnitude image is also obtained. The magnitude image includes the structural information of the object, the incorporation of which should be explored to get better results.

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References

- Gabriel, C.; Gabriel, S.; Corthout, E. The dielectric properties of biological tissues: I. Literature survey. *Phys. Med. Biol.* **1996**, *41*, 2231–2249. [[CrossRef](#)] [[PubMed](#)]
- Gabriel, S.; Lau, R.W.; Gabriel, C. The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz. *Phys. Med. Biol.* **1996**, *41*, 2251–2269. [[CrossRef](#)] [[PubMed](#)]
- Gabriel, S.; Lau, R.W.; Gabriel, C. The dielectric properties of biological tissues: III. Parametric models for the dielectric spectrum of tissues. *Phys. Med. Biol.* **1996**, *41*, 2271–2293. [[CrossRef](#)] [[PubMed](#)]
- Surowiec, A.J.; Stuchly, S.S.; Barr, J.R.; Swarup, A. Dielectric properties of breast carcinoma and the surrounding tissues. *IEEE Trans. Biomed. Eng.* **1988**, *35*, 257–263. [[CrossRef](#)]
- Jossinet, J. The impedivity of freshly excised human breast tissue. *Physiol. Meas.* **1998**, *19*, 61–75. [[CrossRef](#)] [[PubMed](#)]
- Wilkinson, B.A.; Smallwood, R.H.; Keshtar, A.; Lee, J.A.; Hamdy, F.C. Electrical impedance spectroscopy and the diagnosis of bladder pathology: A pilot study. *J. Urol.* **2002**, *168*, 1563–1567. [[CrossRef](#)]
- Wagner, T.A.; Zahn, M.; Grodzinsky, A.J.; Pascual-Leone, A. Three-dimensional head model simulation of transcranial magnetic stimulation. *IEEE Trans. Biomed. Eng.* **2004**, *51*, 1586–1598. [[CrossRef](#)]
- Wagner, T.; Fregni, F.; Fecteau, S.; Grodzinsky, A.; Zahn, M.; Pascual-Leone, A. Transcranial direct current stimulation: A computer-based human model study. *Neuroimage* **2007**, *35*, 1113–1124. [[CrossRef](#)]
- Roy, A.; Baxter, B.; He, B. High-definition transcranial direct current stimulation induces both acute and persistent changes in broadband cortical synchronization: A simultaneous tDCS-EEG study. *IEEE Trans. Biomed. Eng.* **2014**, *61*, 1967–1978. [[CrossRef](#)]
- Zelinski, A.C.; Angelone, L.M.; Goyal, V.K.; Bonmassar, G.; Adalsteinsson, E.; Wald, L.L. Specific absorption rate studies of the parallel transmission of inner-volume excitations at 7T. *J. Magn. Reson. Imaging* **2008**, *28*, 1005–1018. [[CrossRef](#)] [[PubMed](#)]
- Katscher, U.; Findekle, C.; Voigt, T. B1-based specific energy absorption rate determination for nonquadrature radiofrequency excitation. *Magn. Reson. Med.* **2012**, *68*, 1911–1918. [[CrossRef](#)] [[PubMed](#)]
- Woo, E.J.; Seo, J.K. Magnetic resonance electrical impedance tomography (MREIT) for high-resolution conductivity imaging. *Physiol Meas* **2008**, *29*, R1–R26. [[CrossRef](#)] [[PubMed](#)]
- Xu, Y.; He, B. Magnetoacoustic tomography with magnetic induction (MAT-MI). *Phys. Med. Biol.* **2005**, *50*, 5175–5187. [[CrossRef](#)]

14. Metherall, P.; Barber, D.C.; Smallwood, R.H.; Brown, B.H. Three-dimensional electrical impedance tomography. *Nature* **1996**, *380*, 509–512. [[CrossRef](#)]
15. Haacke, E.M.; Petropoulos, L.S.; Nilges, E.W.; Wu, D.H. Extraction of conductivity and permittivity using magnetic resonance imaging. *Phys. Med. Biol.* **1991**, *36*, 723–734. [[CrossRef](#)]
16. Katscher, U.; Kim, D.-H.; Seo, J.K. Recent progress and future challenges in MR electric properties tomography. *Comput. Math. Methods Med.* **2013**, *2013*, 546562. [[CrossRef](#)]
17. Zhang, X.; Liu, J.; He, B. Magnetic-resonance-based electrical properties tomography: A review. *IEEE Rev. Biomed. Eng.* **2014**, *7*, 87–96. [[CrossRef](#)]
18. Seo, J.K.; Kim, M.-O.; Lee, J.; Choi, N.; Woo, E.J.; Kim, H.J.; Kwon, O.I.; Kim, D.-H. Error analysis of nonconstant admittivity for MR-based electric property imaging. *IEEE Trans. Med. Imaging* **2012**, *31*, 430–437. [[CrossRef](#)]
19. Liu, J.; Zhang, X.; Schmitter, S.; Moortel, P.-F.V.d.; He, B. Gradient-based electrical properties tomography (gEPT): A robust method for mapping electrical properties of biological tissues in vivo using magnetic resonance imaging. *Magn. Reson. Med.* **2015**, *74*, 634–646. [[CrossRef](#)]
20. Hafalir, F.S.; Oran, O.F.; Gurler, N.; Ider, Y.Z. Convection-reaction equation based magnetic resonance electrical properties tomography (cr-MREPT). *IEEE Trans. Med. Imaging* **2014**, *33*, 777–793. [[CrossRef](#)]
21. Insko, E.K.; Bolinger, L. Mapping of the Radiofrequency Field. *J. Magn. Reson.* **1993**, *103*, 82–85. [[CrossRef](#)]
22. Yarnykh, V.L. Actual Flip-Angle Imaging in the Pulsed Steady State: A Method for Rapid Three-Dimensional Mapping of the Transmitted Radiofrequency Field. *Magn. Reson. Med.* **2007**, *57*, 192–200. [[CrossRef](#)]
23. Sacolick, L.I.; Wiesinger, F.; Hancu, I.; Vogel, M.W. B1 mapping by Bloch-Siegert shift. *Magn. Reson. Med.* **2010**, *63*, 1315–1322. [[CrossRef](#)]
24. Wen, H. Noninvasive quantitative mapping of conductivity and dielectric distributions using RF wave propagation effects in high-field MRI. In Proceedings of the Medical imaging 2003 Conference, San Diego, CA, USA, 5 June 2003; pp. 471–477.
25. Lier, A.L.H.M.W.v.; Raaijmakers, A.; Voigt, T.; Lagendijk, J.J.W.; Luijten, P.R.; Katscher, U.; Berg, C.A.T.v.d. Electrical properties tomography in the human brain at 1.5, 3, and 7T: A comparison study. *Magn. Reson. Med.* **2014**, *71*, 354–363. [[CrossRef](#)]
26. Lee, S.-K.; Bulumulla, S.; Hancu, I. Theoretical Investigation of Random Noise-Limited Signal-to-Noise Ratio in MR-Based Electrical Properties Tomography. *IEEE Trans. Med. Imaging* **2015**, *34*, 2220–2232. [[CrossRef](#)]
27. Borsic, A.; Perreard, I.; Mahara, A.; Halter, R.J. An Inverse Problems Approach to MR-EPT Image Reconstruction. *IEEE Trans. Med. Imaging* **2016**, *35*, 244–256. [[CrossRef](#)]
28. Hong, R.; Li, S.; Zhang, J.; Zhang, Y.; Liu, N.; Yu, Z.; Liu, Q.H. 3-D MRI-Based Electrical Properties Tomography Using the Volume Integral Equation Method. *IEEE Trans. Microw. Theory Tech.* **2017**, *65*, 4802–4811. [[CrossRef](#)]
29. Remis, R.F.; Webb, A.; Mandija, S.; Leijssen, R.L.; Fuchs, P.S.; Stijnman, P.R.S.; Berg, C.A.T.v.d. Electrical properties tomography using contrast source inversion techniques. In Proceedings of the 2017 International Conference on Electromagnetics in Advanced Applications (ICEAA), Verona, Italy, 11–15 September 2017; pp. 1025–1028.
30. Serralles, J.E.C.; Giannakopoulos, I.I.; Zhang, B.; Ianniello, C.; Cloos, M.A.; Polimeridis, A.G.; White, J.K.; Sodickson, D.K.; Daniel, L.; Lattanzi, R. Noninvasive Estimation of Electrical Properties from Magnetic Resonance Measurements via Global Maxwell Tomography and Match Regularization. *IEEE Trans. Biomed. Eng.* **2020**, *67*, 3–15. [[CrossRef](#)]
31. Balidemaj, E.; Berg, C.A.T.v.d.; Trinks, J.; Lier, A.L.H.M.W.v.; Nederveen, A.J.; Stalpers, L.J.A.; Crezee, H.; Remis, R.F. CSI-EPT: A Contrast Source Inversion Approach for Improved MRI-Based Electric Properties Tomography. *IEEE Trans. Med. Imaging* **2015**, *34*, 1788–1796. [[CrossRef](#)]
32. Mandija, S.; Meliado, E.F.; Huttinga, N.R.F.; Luijten, P.R.; van den Berg, C.A.T. Opening a new window on MR-based Electrical Properties Tomography with deep learning. *Sci. Rep.* **2019**, *9*, 8895. [[CrossRef](#)]
33. Gavazzi, S.; van den Berg, C.A.T.; Savenije, M.H.F.; Kok, H.P.; de Boer, P.; Stalpers, L.J.A.; Lagendijk, J.J.W.; Crezee, H.; van Lier, A. Deep learning-based reconstruction of in vivo pelvis conductivity with a 3D patch-based convolutional neural network trained on simulated MR data. *Magn. Reson. Med.* **2020**. [[CrossRef](#)]
34. Hampe, N.; Katscher, U.; Van den Berg, C.A.T.; Tha, K.K.; Mandija, S. Investigating the challenges and generalizability of deep learning brain conductivity mapping. *Phys. Med. Biol.* **2020**. [[CrossRef](#)] [[PubMed](#)]

35. Voigt, T.; Katscher, U.; Doessel, O. Quantitative conductivity and permittivity imaging of the human brain using electric properties tomography. *Magn. Reson. Med.* **2011**, *66*, 456–466. [\[CrossRef\]](#)
36. Gurler, N.; Ider, Y.Z. Gradient-based electrical conductivity imaging using MR phase. *Magn. Reson. Med.* **2017**, *77*, 137–150. [\[CrossRef\]](#)
37. Sun, X.; Lu, L.; Qi, L.; Mei, Y.; Liu, X.; Chen, W. A robust electrical conductivity imaging method with total variation and wavelet regularization. *Magn. Reson. Imaging* **2020**, *69*, 28–39. [\[CrossRef\]](#)
38. Bredies, K.; Kunisch, K.; Pock, T. Total Generalized Variation. *SIAM J. Imaging Sci.* **2010**, *3*, 492–526. [\[CrossRef\]](#)
39. Boyd, S.; Parikh, N.; Chu, E.; Peleato, B.; Eckstein, J. Distributed Optimization and Statistical Learning via the Alternating Direction Method of Multipliers. *Found. Trends Mach. Learn.* **2011**, *3*. [\[CrossRef\]](#)
40. Goldstein, T.; Osher, S. The Split Bregman Method for L1-Regularized Problems. *SIAM J. Imaging Sci.* **2009**, *2*, 323–343. [\[CrossRef\]](#)
41. Liu, C.; Jin, J.; Guo, L.; Li, M.; Tesiram, Y.; Chen, H.; Liu, F.; Xin, X.; Crozier, S. MR-based electrical property tomography using a modified finite difference scheme. *Phys. Med. Biol.* **2018**, *63*, 145013. [\[CrossRef\]](#)
42. Knoll, F.; Bredies, K.; Pock, T.; Stollberger, R. Second order total generalized variation (TGV) for MRI. *Magn. Reson. Med.* **2011**, *65*, 480–491. [\[CrossRef\]](#) [\[PubMed\]](#)
43. Chen, J.; Wang, L.; Yan, B.; Zhang, H.; Cheng, G. Efficient and robust 3D CT image reconstruction based on total generalized variation regularization using the alternating direction method. *J. X-ray Sci. Technol.* **2015**, *23*, 683–699. [\[CrossRef\]](#)
44. Knoll, F.; Holler, M.; Koesters, T.; Bredies, K.; Sodickson, D.K. Simultaneous PET-MRI reconstruction with vectorial second order total generalized variation. In Proceedings of the 2015 IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), San Diego, CA, USA, 31 October–7 November 2015; pp. 1–4.
45. Michailovich, O.V. An iterative shrinkage approach to total-variation image restoration. *IEEE Trans. Image Process* **2011**, *20*, 1281–1299. [\[CrossRef\]](#)
46. Christ, A.; Kainz, W.; Hahn, E.G.; Honegger, K.; Zefferer, M.; Neufeld, E.; Rascher, W.; Janka, R.; Bautz, W.; Chen, J.; et al. The Virtual Family—Development of surface-based anatomical models of two adults and two children for dosimetric simulations. *Phys. Med. Biol.* **2010**, *55*, N23–N38. [\[CrossRef\]](#)
47. Scott, G.C.; Joy, M.L.G.; Armstrong, R.L.; Henkelman, R.M. Sensitivity of Magnetic-Resonance Current-Density Imaging. *J. Magn. Reson.* **1992**, *97*, 235–254. [\[CrossRef\]](#)
48. Gudbjartsson, H.; Patz, S. The Rician Distribution of Noisy MRI Data. *Magn. Reson. Med.* **1995**, *34*, 910–914. [\[CrossRef\]](#) [\[PubMed\]](#)
49. Lier, A.L.H.M.W.v.; Brunner, D.O.; Pruessmann, K.P.; Klomp, D.W.J.; Luijten, P.R.; Lagendijk, J.J.W.; Berg, C.A.T.v.d. B1+ phase mapping at 7 T and its application for in vivo electrical conductivity mapping. *Magn. Reson. Med.* **2012**, *67*, 552–561. [\[CrossRef\]](#)
50. Fuchs, P.S.; Mandija, S.; Stijnman, P.R.S.; Brink, W.M.; van den Berg, C.A.T.; Remis, R.F. First-Order Induced Current Density Imaging and Electrical Properties Tomography in MRI. *IEEE Trans. Comput. Imaging* **2018**, *4*, 624–631. [\[CrossRef\]](#)
51. Lv, Y. Weighted total generalized variation model for Poisson noise removal. *SN Appl. Sci.* **2019**, *1*. [\[CrossRef\]](#)
52. Liu, C.Y.; Guo, L.; Li, M.; Chen, H.; Jin, J.; Chen, W.; Liu, F.; Crozier, S. Divergence-based Magnetic Resonance Electrical Properties Tomography. *IEEE Trans. Biomed. Eng.* **2020**. [\[CrossRef\]](#)
53. Ozdemir, S.; Ider, Y.Z. bSSFP phase correction and its use in magnetic resonance electrical properties tomography. *Magn. Reson. Med.* **2019**, *81*, 934–946. [\[CrossRef\]](#)
54. Shin, J.; Kim, M.J.; Lee, J.; Nam, Y.; Kim, M.-O.; Choi, N.; Kim, S.; Kim, D.-H. Initial study on in vivo conductivity mapping of breast cancer using MRI. *J. Magn. Reson. Imaging* **2015**, *42*, 371–378. [\[CrossRef\]](#) [\[PubMed\]](#)

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