

# **3D IMPLEMENTATION OF BIAS-CORRECTED PHASE-BASED CR-MREPT**

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3D Implementation of Bias-Corrected Phase-Based cr-MREPT

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We certify that we have read this dissertation and that in our opinion it is fully adequate, in scope and in quality, as a dissertation for the degree of Doctor of Philosophy.

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# ABSTRACT

## 3D IMPLEMENTATION OF BIAS-CORRECTED PHASE-BASED CR-MREPT

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Ph.D. in Electrical and Electronics Engineering

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Electrical property imaging has been a point of interest for decades as it has promising applications such as anatomical imaging, tumor detection, stroke detection and classification, early diagnosis of Alzheimer disease and dementia, RF safety and SAR calculations, and therapy planning and monitoring. Among different electrical property imaging methods, MREPT has the advantage of using a standard MRI device so that its non-invasive, does not use external coils or electrodes, and does not rely on ionizing radiation.

Many MREPT methods are proposed, but most of them suffer from similar limitations such as internal boundary artifacts, transceive phase approximation, concave bias, and long imaging times caused by high SNR requirements. These problems significantly limit the clinical feasibility of MREPT. cr-MREPT, especially in phase-based form, overcomes internal boundary artifacts without using the transceive phase approximation but still suffers from concave bias and high SNR requirements. Moreover, even though implementation in 3D is straightforward, phase-based cr-MREPT is not previously employed in 3D since hardware requirements and reconstruction times make the method impractical for clinical applications.

In this thesis, we aim to develop an MREPT method that overcomes all the mentioned limitations and is feasible to use in clinical applications. To achieve this, a novel bias correction method is proposed to overcome the concave bias. The proposed method is evaluated on the basis of simulation and experimental phantoms, and the conductivity distributions are successfully reconstructed in each case. Later on, the bias corrected phase-based cr-MREPT method is implemented in 3D and a new, practical reconstruction method is proposed to improve feasibility of the method applying on conductivity reconstructions of large objects. The method divides the object into smaller volumes so that the reconstruction of each volume is more manageable and can be parallelized to accelerate the solution process. Small region sizes are determined by performing sensitivity analysis on

phase-based cr-MREPT, and the performance of the proposed method is proven on various noiseless and noise-added simulation data. Last but not least, a cr-MREPT library is developed to improve the availability of 2D/3D bias corrected cr-MREPT for researchers, increase collaboration between different groups and provide better comparative evaluation of different methods.



*Keywords:* magnetic resonance electrical properties tomography (MREPT), 3D convection reaction equation based MREPT (cr-MREPT), phase based EPT, electrical property imaging, conductivity imaging, bias correction..

## ÖZET

# İÇBÜKEY EĞİM DÜZELTMELİ FAZA DAYALI KR-MREÖT'NİN 3B UYGULAMASI

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Dokuların elektriksel özelliklerinin görüntülenmesi; anatomik görüntülemenin yanında tümör tespiti, inme tespiti ve sınıflandırması, Alzheimer ve bunama gibi hastalıkların erken tespiti, radyo frekans soğurma ve lokal özgül soğurma oranının (ÖSO) hesaplanması, tedavi planlama ve takibi gibi alanlarda kullanılmaktadır ve bu sebeple popüler bir araştırma konusu haline gelmiştir. Farklı elektriksel özellik görüntüleme yöntemleri arasında, manyetik rezonans elektriksel özellik tomografisinin (MREÖT) yaygın MR cihazları ile kullanılabilmesi ve ek bir donanım gerektirmemesi, invaziv olmaması ve iyonize edici radyasyon kullanmaması gibi avantajları bulunmaktadır.

Son yıllarda birçok farklı MREÖT yöntemi önerilmiş olsa da, bu yöntemler genel olarak benzer problemlerden muzdariptir. Bu problemler sınır artefaktı, toplam faz varsayımı (TFV), içbükey eğim, yüksek sinyal/gürültü oranı gereklilikleri kaynaklı uzun görüntüleme süreleri şeklinde sıralanabilir. kr-MREÖT yöntemi, faza dayalı versiyonu kullanıldığında sınır artefaktı ve TFV kaynaklı sorunlardan etkilenmemekte, ancak içbükey eğim ve uzun görüntüleme süreleri gibi problemler devam etmektedir. Bunlara ek olarak, yöntemin 3 boyutlu uygulaması donanımsal açıdan yüksek gereksinimlere sahiptir ve geriçatım süreleri pratik olmayacak kadar uzundur. Bu da yöntemi klinik uygulamalar için elverişsiz hale getirmektedir.

Bu çalışmada, bahsedilen sorunlardan etkilenmeyen, hızlı ve klinik uygulamalara uygun bir kr-MREÖT yöntemi geliştirilmesi hedeflenmiştir. Bu amaçla, içbükey eğim problemini düzeltecek özgün bir yöntem geliştirilmiştir. Önerilen yöntem simülasyon ve deney sonuçlarıyla doğrulanmış ve elektriksel iletkenlik dağılımları her durumda başarıyla elde edilebilmiştir. Sonrasında, içbükey eğim düzeltmeli faza dayalı kr-MREÖT yöntemi 3B olarak uygulanmış ve büyük nesnelerin iletkenlik geriçatım uygulanabilirliğini artırmak için yeni ve pratik bir geriçatım yöntemi önerilmiştir. Yöntem, nesneyi daha küçük 3B bölgelere bölerek

her bir bölge için iletkenlik geriçatımını pratik olara daha uygulanabilir hale getirir ve toplam çözüm süresini kısaltmak amacıyla küçük bölgelerde yapılan geriçatımlar eş zamanlı olarak yapılabilir. Faza dayalı kr-MREÖT üzerinde hassasiyet analizi yapılarak küçük bölge boyutları belirlenmiş ve önerilen yöntemin performansı çeşitli gürültüsüz ve gürültü eklenmiş simülasyon verileri üzerinde kanıtlanmıştır. Son olarak, araştırmacılar arasında içbükey eğim düzeltmeli faza dayalı kr-MREÖT yönteminin kullanılabilirliğini artırmak, farklı gruplar arasındaki iş birliğini artırmak ve farklı yöntemlerin karşılaştırmasının daha kolay yapılabilmesini sağlamak amacıyla bir kr-MREÖT kütüphanesi geliştirilmiştir.

*Anahtar sözcükler:* manyetik rezonans elektriksel özellik tomografisi (MREÖT), konveksiyon reaksiyon denkleminde dayalı MREÖT (kr-MREÖT), faza dayalı EÖT, elektriksel özellik görüntüleme, iletkenlik görüntüleme, içbükey eğim düzeltme.

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# List of Abbreviations

|          |                                                                    |
|----------|--------------------------------------------------------------------|
| AFI      | Actual Flip Angle Imaging                                          |
| bSSFP    | Balanced Steady-State Free Precession                              |
| CPU      | Central Processing Unit                                            |
| cr-MREPT | Convection-Reaction Magnetic Resonance Electrical Property Imaging |
| CSI-EPT  | Contrast Source Inversion Electrical Properties Tomography         |
| DREAM    | Dual Refocusing Echo Acquisition Mode                              |
| EIT      | Electrical Impedance Tomography                                    |
| EM       | Electro-magnetic                                                   |
| EP       | Electrical Properties                                              |
| EPT      | Electrical Properties Tomography                                   |
| gEPT     | Gradient-Based Electrical Properties Tomography                    |
| GPU      | Graphics Processing Unit                                           |
| HPC      | High-Performance Computing                                         |
| LCF      | Low Convection Field                                               |
| MR       | Magnetic Resonance                                                 |
| MREIT    | Magnetic Resonance Electrical Impedance Tomography                 |
| MREPT    | Magnetic Resonance Electrical Property Imaging                     |
| MRI      | Magnetic Resonance Imaging                                         |
| MSE      | Mean Squared Error                                                 |
| PDE      | Partial Differential Equation                                      |
| RF       | Radio Frequency                                                    |
| ROI      | Region-of-Interest                                                 |
| SAR      | Specific Absorption Ratio                                          |
| SNR      | Signal-to-Noise Ratio                                              |
| TPA      | Transceive Phase Approximation                                     |
| QBC      | Quadrature Birdcage Coil                                           |
| UMRAM    | Ulusal Manyetik Rezonans Araştırma Merkezi                         |

# Chapter 1

## Introduction

Magnetic Resonance Imaging (MRI) is one of the most widely used medical imaging methods as it is non-invasive, it offers high spatial resolution and soft tissue contrast without using ionizing radiation. Since its introduction, MRI has significantly improved our understanding of the structure and function of the human brain.

Similarly to other imaging methods, magnetic resonance imaging requires a mechanism to create contrast between tissues in order to be useful for medical purposes. Employing different pulse sequences during imaging, different properties of tissues can be utilized as the contrast creating mechanism in MRI. Electrical properties, namely conductivity ( $\sigma$ ) and permittivity ( $\epsilon$ ), can be used as one of these properties.

In this thesis, some of the problems related to magnetic resonance electrical properties tomography (MREPT) are discussed, and possible solutions to these problems are proposed. This Chapter gives an introduction to the topic and the research presented in this thesis.

## 1.1 Electrical Properties and Electrical Property Imaging

Electrical properties (EPs) of tissues, i.e., conductivity ( $\sigma$ ) and permittivity ( $\epsilon$ ), have been topics of interest for decades for researchers, as they provide significant information about tissues and their interaction with electromagnetic fields. Hence, imaging of these properties and obtaining accurate conductivity and permittivity distributions of tissues are critical for many applications. As electrical conductivities of healthy tissues and various pathological tissues vary significantly, MREPT can be used for tumor detection [2–12], stroke detection and classification [13–17], early diagnosis of Alzheimer disease and dementia [18–21], epilepsy [22–24]. EPs are also useful for determining how tissues behave under electromagnetic fields, hence can be used to quantify MR safety and calculate the specific absorption ratio (SAR) [25, 26], hypothermia treatment [8, 27], radio frequency ablation [28–30], and planning and monitoring of radiotherapy [31].

The electrical properties of tissues at different frequencies have been a topic of interest for many decades. As a result, several methods have been proposed for different frequencies. At low frequencies, 1 kHz to 1 MHz, electrical impedance tomography (EIT) [32–36] and magnetic induction tomography (MIT) [37–39] are used. Both of these methods are based on surface electrodes or coils inducing current in the tissue, mostly working on regions close to the body surface. However, the sensitivity of these equipments is low in the inner regions of the body. This results in impedance maps that have low spatial resolution, especially in the inner regions of the body. Magnetic resonance electrical impedance tomography (MREIT) is proposed to overcome this problem [40–46]. Thanks to the MR machine, the sensitivity of the measurements is equal throughout the object in MREIT. However, the method still relies on surface electrodes to induce current in tissues. Employing such electrodes is tricky in MR machines due to the constant magnetic field, in addition to any discomfort caused to the patient to be imaged. Later, magnetic resonance electrical properties imaging (MREPT) was proposed [47–49] to obtain electrical properties at Larmor frequency. Unlike

EIT methods where a current is induced in tissues, main source of contrast in MREPT is the perturbation of RF magnetic fields ( $B_1$  is the transceive magnetic field, where  $B_1^+$  is the transmit and  $B_1^-$  is the receive fields) by the electrical properties of the imaged object. Since no current is induced by electrical or magnetic induction, standard MRI equipment is sufficient to obtain EPs of the tissue without any surface electrodes or additional coils. EP maps can be obtained using  $B_1$  maps, which can be obtained employing common MRI hardware and well-known pulse sequences [50, 51].

The earlier MREPT based on the Helmholtz equation [47] assumes uniform EPs within tissues, i.e. the gradients of EPs are zero. This is a significant assumption that results in artifacts along and near the tissue boundaries [52], which are called internal boundary artifacts. In order to overcome this problem, convection-reaction equation based magnetic resonance electrical properties tomography (cr-MREPT) is proposed [53]. The cr-MREPT method is capable of reconstructing conductivity distributions without artifacts around internal boundaries. The method acts like a low-pass filter, preventing large changes of conductivity values but also causing some blunting.

Both methods mentioned up to now, Helmholtz MREPT and cr-MREPT, are in complex form. These are also known as full-form methods and require knowledge of both the magnitude and phase of  $B_1$  fields. The phase of  $B_1$  can be obtained much faster compared to its magnitude [54]. In order to shorten imaging times and simplify the reconstruction process, phase-based MREPT algorithms are developed [50, 51, 55]. Phase-based methods only require the phase of  $B_1$ , and have simpler main equations that are easy to implement. Moreover, phase-based methods do not require the so-called transceive phase approximation (TPA). The trade off of using phase-based methods instead of full-form solutions is that phase-based methods are able to reconstruct only the conductivity of the object, where full-form methods give both conductivity and permittivity.

## 1.2 Objective and Scope of the Thesis

As discussed in Sect.1.1, EP imaging, especially obtaining tissue conductivities, is beneficial for both anatomical imaging and detection of various diseases, as well as SAR calculations and RF safety. Since it is a non-invasive method without any electrodes or coils to induce current in patients and offer uniform sensitivities through the object, MREPT is the most promising of EP imaging methods.

Nevertheless, MREPT is a relatively new imaging technique that is still developing and has some significant problems that require attention. The full-form MREPT methods require both phase and magnitude of  $B_1$ , which are measured separately and require significant imaging time in the MRI machine. Phase-based MREPT has some advantages over full-form methods, such as requiring only the phase of  $B_1$ , thus reducing the imaging times. However, the derivations of the phase-based methods assume that  $|B_1^+|$  is almost uniform ( $\nabla|B_1^+| = 0$ ) throughout the region of interest [50, 51, 55]. This assumption holds at lower frequencies where the wavelength of the RF excitation pulse is large compared to the imaged object. On the other hand, in 3T MRI devices the Larmor frequency is around  $127.74MHz$ , which corresponds to wavelengths comparable to the object to be imaged. This causes a central brightness in the  $|B_1^+|$  distribution. Due to the assumption that  $\nabla|B_1^+| = 0$ , a low frequency concave bias is observed in the reconstructed conductivity maps [56]. Couple of heuristic methods are proposed to overcome the concave bias. These methods use an approximated sinc function [57] or a fitted low order polynomial [56] for bias correction. Both of these methods are post-processing methods for conductivity distributions, and [57] is only applied to phase-based Helmholtz MREPT.

As will be discussed in detail in Chapter 2, both Helmholtz and cr-MREPT methods are 3-dimensional problems, and conductivity reconstruction depends on fields in all three directions. However, most of the previous studies in cr-MREPT, especially phase-based cr-MREPT, ignore the Z-dependence of the equations and calculate the conductivity in a single slice in the XY-plane. This approximation holds for z-independent phantom experiments but clearly causes errors in more

realistic cases, such as human experiments. Another option would be to implement cr-MREPT in 3 slices in z-direction in order to calculate the z-derivative terms and improve the reconstruction accuracy for the central slice. However, this method gives results for only a single slice of interest and cannot obtain the conductivity distribution for the whole volume at once. Several studies employ cr-MREPT in 3D [56, 58, 59], but focus on a full-form solution and inclusion of 3D solutions is somewhat limited. The most significant reason for focusing on 2D solutions of cr-MREPT is that large regions-of-interest (ROIs) in 3D results with a very large number of nodes to solve for, causing heavy hardware requirements and significantly long computational times.

Last but not least, as a relatively new and developing imaging technique, the number of people working MREPT, especially cr-MREPT is quite limited. In order to fully reach its potential, it is critical that the method reach more researchers to employ cr-MREPT in their studies. However, implementation of cr-MREPT can be tricky. All MREPT methods include partial differential equations and derivatives of the unknowns have to be calculated. These calculations and solving partial differential equations can get complicated and can take a lot of time and effort, discouraging new researchers.

In this thesis, the main purpose is to develop solutions to some of the main problems of phase-based cr-MREPT. Hence, results of the thesis are divided into 3 main topics;

- A bias correction method for both Helmholtz and cr-MREPT in their phase-based forms is proposed. The proposed method does not require any additional data other than the phase of  $B_1$ . It is also not an empirical post processing method, unlike the previously proposed bias correction methods. The derivation of the method is presented in the later chapters, as well as applications on both simulation and experimental phantom data. Detailed evaluation of the bias correction for both Helmholtz and cr-MREPT is also given.
- A solution method for phase-based cr-MREPT in 3D tetrahedral mesh is

developed. The smallest region size where the conductivity values can be successfully reconstructed is found by calculating the sensitivity maps of the reconstructions with respect to the phase of  $B_1^+$ . The ROI is then divided into small regions with the determined size and the conductivity distributions are obtained individually for each region. By parallelization of individual solutions, the total solution time is significantly decreased.

- An MREPT library is developed for phase-based methods with the option to correct the concave bias. Many examples of both simulation and experimental data are included. The library is intended to be as user friendly as possible with added comments at each line explaining the details of the operations. This work is aimed to be useful for any MREPT enthusiast that desires to employ phase-based cr-MREPT in their studies.

## 1.3 Organization of the Thesis

This thesis consists of 6 chapters. Chapter 1 gives an introduction to the thesis, while Chapter 2 presents theoretical background information about various MREPT methods and discusses their advantages, problems, and limitations. In Chapter 3, a bias correction method is proposed for phase-based MREPT methods. The derivation of the main equation of the method is given with rigorous discussions about various assumptions made during the derivation steps. The results, both numerical and visual, of the proposed method are given for various simulation and experimental phantoms. Chapter 4 focuses on 3D implementation of cr-MREPT and acceleration of the solution. Sensitivity maps of the reconstructed conductivity values with respect to the phase of  $B_1^+$  are calculated and presented. The details of how to properly determine the size of the small regions are discussed. Reconstructed conductivity results for various phantoms are shown. Chapter 5 discusses the details of the developed cr-MREPT library. Similarly to the previous sections, reconstruction results for various phantoms are shown. Finally, in Chapter 6, the work presented in this thesis is summarized and future direction of the topic is discussed.

# Chapter 2

## Theory

MREPT utilizes the perturbation of magnetic fields in tissues to calculate electrical properties, conductivity  $\sigma$  and permittivity  $\epsilon$  of tissues. This chapter gives the theoretical background information necessary to understand the physics behind the commonly used MREPT methods. Derivations of the central equations of the methods are presented, and problems and limitations of the methods are discussed.

### 2.1 Helmholtz MREPT

#### 2.1.1 Full-Form and Phase-Based Approaches

In order to obtain the relationship between EPs of the tissues and magnetic field, we start from Ampere's Law and substitute the electric field with the magnetic field using Faraday's law:

$$-\nabla^2 \mathbf{B} = \left( \frac{\nabla \gamma}{\gamma} \right) \times (\nabla \times \mathbf{B}) - i\omega\mu_0\gamma\mathbf{B} \quad (2.1)$$

Here;  $\mathbf{B} = (B_x, B_y, B_z)$  is the magnetic flux density in 3D,  $\gamma = \sigma + i\omega\epsilon$  is the complex electrical properties,  $\omega$  is the Larmor frequency, and  $\mu_0$  is the magnetic permeability of free space. Throughout the thesis,  $\omega = 127.74\text{MHz}$  (corresponding to a 3T MRI system) and  $\mu = \mu_0$ , the permeability of the free space is used. The complete derivation can be found in Katscher et al [48].

The equation simplifies significantly if we assume that EPs are constant through the object, i.e.  $\nabla\gamma = 0$ :

$$\nabla^2\mathbf{B} = i\omega\mu_0\gamma\mathbf{B} \quad (2.2)$$

Rearranging Eq. 2.2 and writing in terms of quantities that can be measured in the MRI system, we obtain the central equation of the full-form Helmholtz MREPT:

$$\gamma = \frac{\nabla^2 B_1^\pm}{i\omega\mu_0 B_1^\pm} \quad (2.3)$$

Physically,  $B_1^\pm$  given in Eq. 2.3 corresponds to transmit ( $B_1^+$ ) and receive ( $B_1^-$ ) sensitivity of the RF coil used during the measurements. In terms of spatial components of  $\mathbf{B}$ , these can be written as  $B_1^+ = \frac{B_x + iB_y}{2}$  and  $B_1^- = \frac{B_x - iB_y}{2}$ .  $B_1^+$  and  $B_1^-$  correspond to the left- and right-hand rotating component of the magnetic field  $\mathbf{B}$ .

To further simplify Eq. 2.3, real and imaginary components of  $B_1^+$  and  $\gamma$  can be separated using  $B_1^+ = |B_1^+|e^{i\phi^+}$  and  $\gamma = \sigma + i\omega\epsilon$ :

$$\sigma + i\omega\epsilon = \frac{\nabla^2 |B_1^\pm| e^{i\phi^\pm}}{i\omega\mu_0 |B_1^\pm| e^{i\phi^\pm}} \quad (2.4)$$

Using the identity  $\nabla^2(ab) = a\nabla^2b + 2\nabla a\nabla b + b\nabla^2a$ , and rearranging terms, we get:

$$\sigma + i\omega\epsilon = \frac{\nabla^2|B_1^\pm| - |B_1^\pm|(\nabla\phi^\pm \cdot \nabla\phi^\pm) + i(2\nabla|B_1^\pm| \cdot \nabla\phi^\pm + |B_1^\pm|\nabla^2\phi^\pm)}{i\omega\mu_0|B_1^\pm|} \quad (2.5)$$

Eq. 2.5 can be separated into real and imaginary components;

$$\sigma = \frac{1}{\omega\mu_0} \left( \frac{2\nabla|B_1^\pm| \cdot \nabla\phi^\pm}{|B_1^\pm|} + \nabla^2\phi^\pm \right) \quad (2.6)$$

$$\epsilon = \frac{1}{\omega\mu_0^2|B_1^\pm|} (|B_1^\pm|(\nabla\phi^\pm \cdot \nabla\phi^\pm) - \nabla^2|B_1^\pm|) \quad (2.7)$$

Making the assumption that  $\nabla|B_1^\pm|$  is negligible and  $\nabla^2\phi^\pm \gg \frac{2\nabla|B_1^\pm| \cdot \nabla\phi^\pm}{|B_1^\pm|}$ , we cancel the  $|B_1^\pm|$  term and get the central equation for the phase-based Helmholtz MREPT:

$$\sigma = \frac{\nabla^2\phi^\pm}{\omega\mu_0} \quad (2.8)$$

Eq. 2.8 includes the term  $\phi^\pm$ , where  $\phi^+$  and  $\phi^-$  correspond to the transmit and receive phase, respectively. However, only the sum of these, i.e. the transceive phase, can be measured in MRI experiments. It is therefore more convenient to rearrange Eq. 2.8 as:

$$\sigma = \frac{\nabla^2\phi^{tr}}{2\omega\mu_0} \quad (2.9)$$

where  $\phi^{tr} = \phi^+ + \phi^-$  is the transceive phase and the measurements of the MRI experiments can be used directly to obtain the conductivity distributions.

## 2.1.2 Problems and Limitations

The full-form (Eq. 2.3) and phase-based (Eq. 2.9) Helmholtz MREPT methods are quite simple but powerful methods that allow for the determination of

conductivity distributions of tissues with common MRI hardware and pulse sequences. Especially phase-based Helmholtz MREPT is very commonly used in clinical studies because it is simple, easy to implement, and requires only phase data. However, both methods suffer from some well-known and investigated problems, as some significant assumptions were made during the derivations. These problems can be summarized in 4 main points:

### 2.1.2.1 Internal Boundary Artifacts

Helmholtz MREPT, both in full-form and in phase-based forms, assumes that EPs are constant throughout the object during reconstruction. Obviously, this is not the case and the assumption does not hold where the conductivity values change because different tissues have different conductivity and permittivity values. Hence, significant artifacts are observed along internal boundaries [52, 60]. Fig. 2.1 gives the true conductivity values, and conductivity values obtained using full-form (Eq. 2.3) and phase-based (Eq. 2.9) Helmholtz MREPT methods for a cylindrical simulation phantom with 4 conductivity anomalies. The details of the phantom will be discussed in later sections. It can be seen that, even for a relatively simple phantom, internal boundary artifacts are very visible and affect the obtained conductivity distributions greatly. When a more complicated object with more internal boundaries is imaged, such as a human brain, the artifacts become even more dominant.

### 2.1.2.2 Transceive Phase Approximation (TPA)

As mentioned above, only the transceive phase  $\phi^{tr} = \phi^+ + \phi^-$  can be measured in MRI. However, Eq. 2.3, the central equation of the Helmholtz MREPT in full-form, relies on  $\phi^+$  to calculate the EP values. To solve this problem, transceive phase approximation (TPA) is made; it is assumed that  $\phi^+ \approx \phi^-$ . Then  $\phi^+$  can be calculated simply by taking half of the measured phase  $\phi^{tr}$ , as  $\phi^{tr} = \phi^+ + \phi^- \approx 2\phi^+$  by TPA.

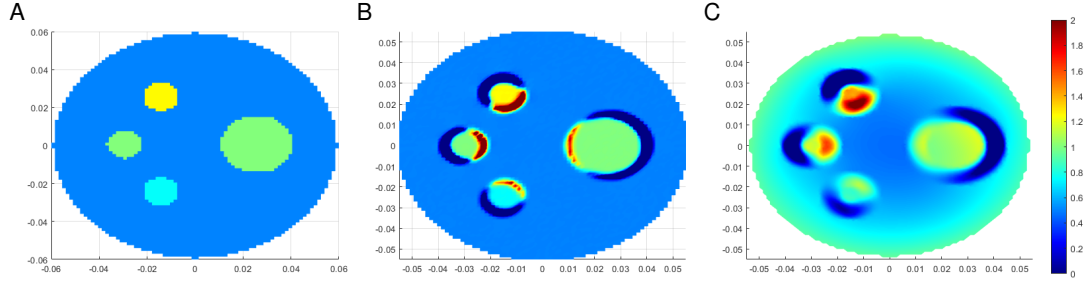


Figure 2.1: True conductivity values and conductivity reconstruction results for full-form and phase-based Helmholtz MREPT, for a simulation phantom with 4 conductivity anomalies. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) True conductivity values of the phantom. (B) Full-form Helmholtz MREPT reconstruction. (C) Phase-based Helmholtz MREPT reconstruction.

Physically, this means that the transmit and receive sensitivities of the RF coils are equal. This can be the case where a birdcage coil is used for transmitting and receiving signals, but fails in other cases where different coils are employed. It has been found that the approximation does not always hold for non-spherical objects, such as the human brain [61].

TPA is used in full-form MREPT, but, as given in Eq. 2.9, phase-based Helmholtz MREPT has the term  $\phi^{tr}$  in its central equation and does not require the application of TPA.

### 2.1.2.3 Concave Bias

Phase-based MREPT is advantageous compared to full-form MREPT since it does not require TPA but assumes a constant  $|B_1^+|$  through the object. This will be discussed in detail in later chapters, but the assumption does not hold at high magnetic field MRI systems because the wavelength of the applied RF field being comparable to the object sizes, causing central brightness. As a result, the reconstructed conductivity maps have a concave bias, and the ROI edges have elevated conductivity values. Fig. 2.2 shows an example of this, as the reconstructed conductivity values are  $0.65s/m$  (30%) for a homogeneous phantom with constant conductivity,  $0.5s/m$ .

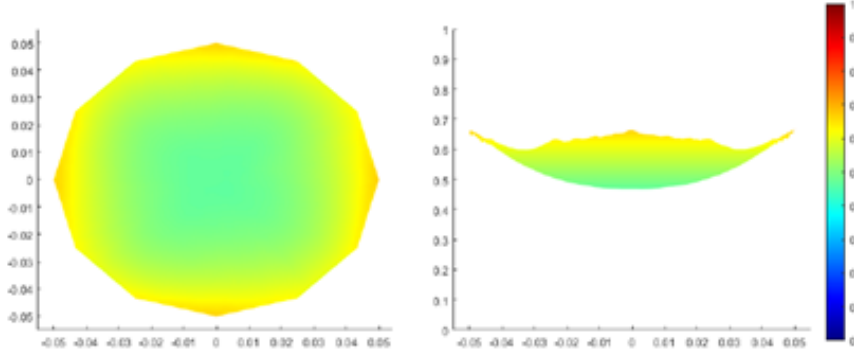


Figure 2.2: Phase-based cr-MREPT reconstruction for cylindrical phantom with uniform conductivity of  $0.5s/m$ . Concave bias is visible around the edges of the Region-of-Interest (ROI). Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases.

#### 2.1.2.4 High SNR Requirements

MREPT methods, both full-form and phase-based, have Laplacian operators in their central equations. Due to this, solutions are quite sensitive to the noise of MRI experiments. The noise sensitivity of EP imaging methods is well investigated [40, 62], but the general solution to the problem is to apply a low pass filter to eliminate noise or increase the repetition factor when imaging for  $B_1$  maps. Low pass filtering obviously lowers the detail level in conductivity maps in addition to eliminating noise, hence not desirable. Imaging with a high number of repetition factor and averaging improves SNR but is also problematic, since it also increases the total imaging time. Complex  $B_1$  maps are typically obtained by obtaining the magnitude and phase of the  $B_1$  field separately. Phase data can be obtained relatively fast, but obtaining  $|B_1^+|$  maps with high SNR can take significant time [54].

## 2.2 cr-MREPT

Internal boundary artifacts are a significant problem with Helmholtz MREPT. To overcome this, convection-reaction equation based magnetic resonance electrical

properties tomography (cr-MREPT) is proposed and its phase based form is developed [1,53], which can handle internal boundaries without causing artifacts.

### 2.2.1 Full-Form and Phase-Based Approaches

To solve the internal boundary problem, Hafalir et. al [53] re-derived the MREPT equation starting from Eq. 2.1, but without assuming  $\nabla\gamma = 0$ . The complete derivation of the method is not given here, but the final form of the central equation of full-form cr-MREPT is obtained as:

$$\beta^+ \cdot \nabla u - \nabla^2 B_1^+ u = i\omega\mu_0 B_1^+ \quad (2.10)$$

Here,  $\gamma = \sigma + i\omega\epsilon$  and  $\beta^+$  are defined as:

$$\beta^+ = \begin{bmatrix} \beta_x^+ \\ \beta_y^+ \\ \beta_z^+ \end{bmatrix} = \begin{bmatrix} \frac{\partial B_1^+}{\partial x} - i\frac{\partial B_1^+}{\partial y} + \frac{1}{2}\frac{\partial B_1^+}{\partial z} \\ i\frac{\partial B_1^+}{\partial x} + \frac{\partial B_1^+}{\partial y} + i\frac{1}{2}\frac{\partial B_1^+}{\partial z} \\ -\frac{1}{2}\frac{\partial B_z}{\partial x} - i\frac{1}{2}\frac{\partial B_z}{\partial y} + \frac{\partial B_1^+}{\partial z} \end{bmatrix} \quad (2.11)$$

Eq. 2.10 is in the same form as the convection-diffusion-reaction equation [63] when the diffusion term is 0. An artificial diffusion term  $-c\nabla^2 u$  can be added for additional regularization of the system, where  $c$  is a constant to be determined. Selecting  $c$  is a trade off between regularization and resolution of obtained conductivity distributions as the term acts as a low pass filter. The final form of the equation then becomes:

$$-c\nabla^2 u + \beta^+ \cdot \nabla u - \nabla^2 B_1^+ u = i\omega\mu_0 B_1^+ \quad (2.12)$$

Eq. 2.12 is able to handle EP reconstruction at internal boundaries but still employs TPA and suffers from any problems it causes. Moreover, it requires

both the magnitude and the phase of  $B_1$  and is sensitive to noise. Hence, either long imaging times are used for improving SNR or stronger low pass filtering (or high diffusion coefficient) is applied to suppress noise in the expense of image quality and blunting. The Phase-based form of cr-MREPT is later developed to eliminate the need for  $|B_1^+|$  [15], which uses the following central equation to obtain conductivity distributions:

$$-c\nabla^2\rho + \nabla\phi \cdot \nabla\rho + \nabla^2\phi\rho = 2\omega\mu_0 \quad (2.13)$$

In Eq. 2.13, we only have  $\rho = 1/\sigma$  as the unknown to solve for, similar to the phase-based Helmholtz MREPT as we only have phase of the field  $B_1$ . There is also the diffusion term  $-c\nabla^2\rho$  for regularization.

## 2.2.2 Problems and Limitations

cr-MREPT is developed to overcome internal boundary artifacts and is able to do so successfully. Fig. 2.3 shows the reconstructed conductivity distributions using full-form and phase based cr-MREPT. Compared to Fig. 2.1, it is clear that boundary artifacts are eliminated and the obtained conductivity distribution is very similar to the actual conductivity values.

Although the internal boundary artifacts are eliminated with cr-MREPT, other problems that are discussed in Sect. 2.1.2 still exist in the reconstruction results. Full-form cr-MREPT suffers from TPA and long imaging times due to high SNR requirements, and phase-based cr-MREPT suffers from a concave bias similar to phase-based Helmholtz MREPT. In addition to these, a new artifact due to the formulation of MREPT occurs, called Low Convection Field Artifact (LCF). Moreover, a slight blunting effect is observed in the conductivity distributions.

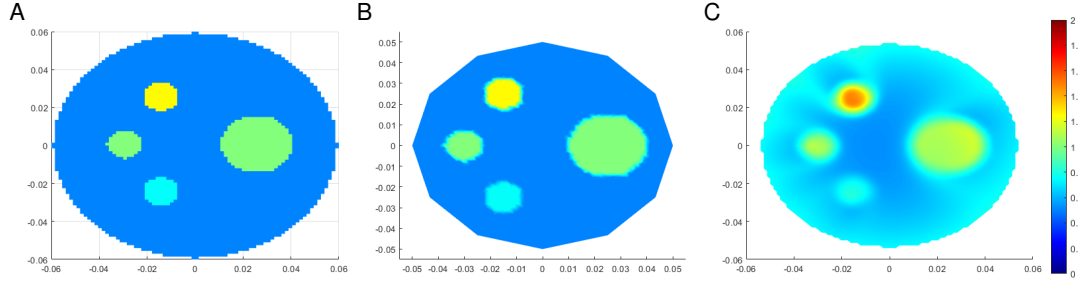


Figure 2.3: True conductivity values and conductivity reconstruction results for full-form and phase-based cr-MREPT, for a simulation phantom with 4 conductivity anomalies. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) True conductivity values of the phantom. (B) Full-form Helmholtz MREPT reconstruction. (C) Phase-based Helmholtz MREPT reconstruction.

### 2.2.2.1 Low Convection Field (LCF) Artifact

The convection field term in Eq. 2.12  $\beta^+$  may get close to zero, mostly around the center of the object, and this allows the  $\cdot \nabla \gamma$  term to become large. Because of this, very large local artifacts around the regions where convection field is small occur. This artifact is named Low Convection Field (LCF), or "spot-like" artifact. An example of the artifact is shown in Fig. 2.4, where the LCF artifact is left uncorrected. The LCF artifacts are thoroughly investigated and many methods to overcome them are proposed [59, 64–67]. One of these solutions is to use a proper value for diffusion coefficient, which is used throughout this thesis.

### 2.2.2.2 Blunting

The gradient terms of EPs and the artificial diffusion term in Eqs 2.12 and 2.13 help to regularize the PDEs and obtain a stable solution. However, they also have slight blunting effects around the internal boundaries, as they act like low pass filters. The significance of the blunting effect can be decreased by employing a smaller diffusion coefficient, but this causes problems for low SNR data. Hence, a trade off must be made to select the correct value of diffusion coefficient [68].

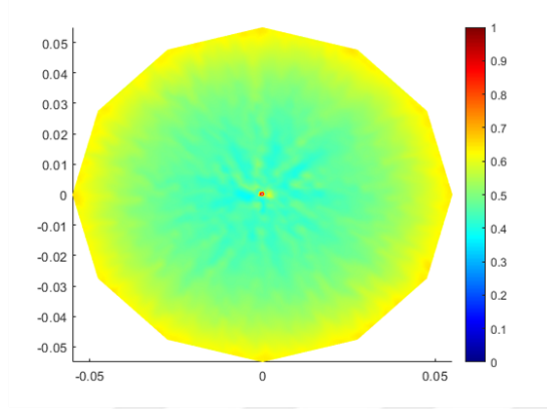


Figure 2.4: Reconstruction results for phase-based cr-MREPT for a uniform phantom. LCF artifact can be seen in the center of the phantom. Conductivity unit is  $s/m$ , distance unit is  $m$ .

## 2.3 Other MREPT Methods

Although Helmholtz and cr-MREPT, especially in phase-based form, are the most commonly used MREPT methods, there are other methods developed by different groups, working on similar principles. Local Maxwell Tomography was proposed to overcome the transceive phase approximation [69], but suffers from the slow-varying EP assumption. Global Maxwell tomography is proposed later and solves a series of volume integrals to calculate conductivity distributions [70]. To achieve high SNR measurements faster, methods depending on  $B_1^-$  are proposed [71–73]. Balidemaj et al. suggested a technique based on a 2D integral equation called contrast source inversion electrical properties tomography (CSI-EPT) [74]. Gradient-based EPT (gEPT) is another method that uses integral equations to improve the quality of reconstruction around internal boundaries [75, 76]. Various iterative methods for the estimation of EPs are also proposed [77–79]. In addition to these models based on physics, many methods employing artificial intelligence and deep learning are also developed [80–87].

## Chapter 3

# Bias Correction for Phase-Based MREPT

Full-form Magnetic Resonance Electrical Properties Tomography (MREPT) requires both phase and magnitude of  $B_1^+$ . Between these, the phase of  $B_1^+$  can be obtained faster and with a higher SNR compared to the magnitude of  $B_1^+$ . To utilize this, several phase-based methods have been developed for conductivity imaging. However, methods that rely only on the phase of  $B_1^+$  suffer from a concave bias due to the assumption that  $\nabla|B_1^+|$  is negligible in the ROI. In this section, we re-derive the central equation of phase-based cr-MREPT without assuming that  $\nabla|B_1^+|$  is negligible and thus propose a bias correction method directly integrated into the equation system. The proposed correction method gives conductivity maps that are similar in quality to full-form solution and does not require full resolution  $\nabla|B_1^+|$ , therefore providing a significant acceleration in imaging times. Moreover, alternative methods are proposed to fully obtain  $|B_1^+|$  and the extension of these methods to full-form MREPT is discussed.

### 3.1 Motivation

Phase-based MREPT methods, both Helmholtz and cr-MREPT, use the assumption that  $|B_1^+|$  is constant throughout the imaged object. However, this is not the case for 3T systems, since at the Larmor frequency of  $\sim 127MHz$ , the wavelength of RF pulses becomes comparable to the imaged object. Due to this, a phenomenon called “central brightness” is observed;  $|B_1^+|$  becomes higher at the central region of the image compared to the sides. An example of this is shown in Fig. 3.1, where a quadrature birdcage coil, tuned at Larmor frequency, is simulated to excite a uniform cylindrical phantom.

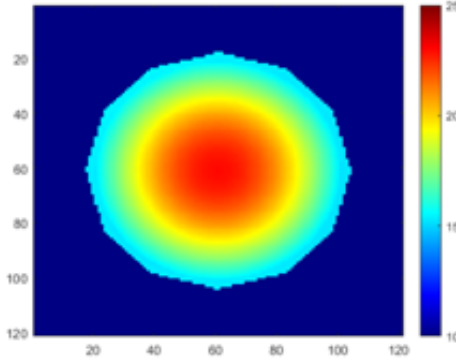


Figure 3.1:  $|B_1^+|$  for a quadrature birdcage coil and a cylindrical phantom with uniform conductivity.

Since this phenomenon is related to the wavelength of the RF pulse, its effect increases when the wavelength is further decreased. The static magnetic field strength of the MRI system is one of the parameters that can affect the wavelength. Higher field strength corresponds to higher RF frequency, resulting in reduced wavelength. Therefore, it is plausible to assume that the central brightness phenomenon will increase in 7T MRI systems.  $\epsilon$  of the imaged object is another parameter that can change the wavelength; higher  $\epsilon$  corresponds to a lower wavelength at the same frequency.

Due to the constant  $|B_1^+|$  assumption, conductivity maps reconstructed using phase-based cr-MREPT suffer from a concave bias. Fig. 3.2 shows an example

of this, where a cylindrical phantom with uniform conductivity is simulated and the resulting conductivity map, reconstructed with phase-based cr-MREPT, is presented. The central region of the conductivity map gives the correct values, where the values start to increase as we move away from the central region. Clearly, this is a crucial error that requires some form of correction.

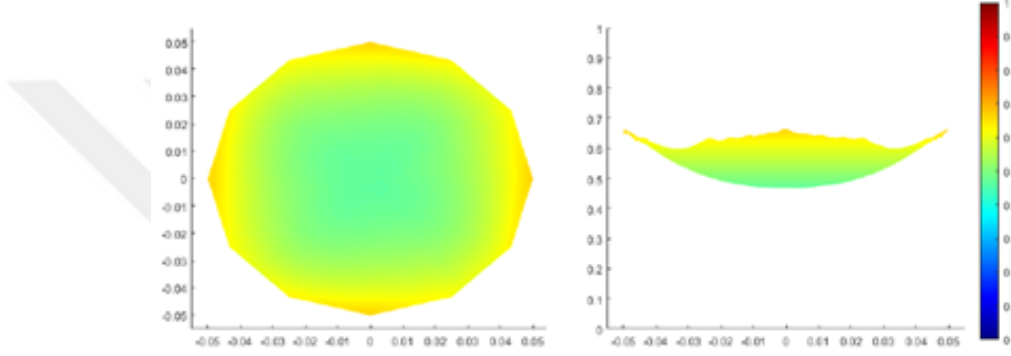


Figure 3.2: Phase-based cr-MREPT reconstruction for cylindrical phantom with uniform conductivity of  $0.5s/m$ . Concave bias is visible, and conductivity values are increased up to  $0.65s/m$  (30%) around the edges of the Region-of-Interest (ROI). Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases.

## 3.2 Theory

Relationship between EPs and  $B_1$  magnetic field can be written as:

$$-\nabla^2 \mathbf{B} = \frac{\nabla \gamma}{\gamma} \times (\nabla \times \mathbf{B}) - i\omega\mu_0\gamma\mathbf{B} \quad (3.1)$$

Here,  $\gamma = \sigma + i\omega\epsilon$ . After defining  $\beta^+$  as

$$\beta^+ = \begin{bmatrix} \beta_x^+ \\ \beta_y^+ \\ \beta_z^+ \end{bmatrix} = \begin{bmatrix} \frac{\partial B_1^+}{\partial x} - i \frac{\partial B_1^+}{\partial y} + \frac{1}{2} \frac{\partial B_1^+}{\partial z} \\ i \frac{\partial B_1^+}{\partial x} + \frac{\partial B_1^+}{\partial y} + i \frac{1}{2} \frac{\partial B_1^+}{\partial z} \\ -\frac{1}{2} \frac{\partial B_z}{\partial x} - i \frac{1}{2} \frac{\partial B_z}{\partial y} + \frac{\partial B_1^+}{\partial z} \end{bmatrix} \quad (3.2)$$

Eq. 3.1 can be rearranged such that the logarithmic form of the cr-MREPT [55] is obtained:

$$\beta^+ \cdot \left( \frac{\nabla \gamma}{\gamma} \right) - \nabla^2 B_1^+ - i\omega\mu_0\gamma B_1^+ = 0 \quad (3.3)$$

Using  $B_1^+ = |B_1^+|e^{i\phi^+}$ , we can rewrite the terms  $\beta^+$  as:

$$\beta_x^+ = |B_1^+|e^{i\phi^+} \left[ \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial x} + i \frac{\partial \phi^+}{\partial x} - i \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial y} + \frac{\partial \phi^+}{\partial y} \right] \quad (3.4)$$

$$\beta_y^+ = |B_1^+|e^{i\phi^+} \left[ \frac{i}{|B_1^+|} \frac{\partial |B_1^+|}{\partial x} - \frac{\partial \phi^+}{\partial x} + \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial y} + i \frac{\partial \phi^+}{\partial y} \right] \quad (3.5)$$

$$\beta_z^+ = |B_1^+|e^{i\phi^+} \left[ \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial z} + i \frac{\partial \phi^+}{\partial z} \right] \quad (3.6)$$

Similarly, the term  $\nabla^2 B_1^+$  can also be rewritten as:

$$\begin{aligned} \nabla^2 B_1^+ = |B_1^+|e^{i\phi^+} & - \left[ \left( \frac{\partial \phi^+}{\partial x} \right)^2 + \left( \frac{\partial \phi^+}{\partial y} \right)^2 + \left( \frac{\partial \phi^+}{\partial z} \right)^2 + i \nabla^2 \phi^+ \right. \\ & \left. + \frac{1}{|B_1^+|} \nabla^2 |B_1^+| + i 2 \nabla \ln |B_1^+| \cdot \nabla \phi^+ \right] \end{aligned} \quad (3.7)$$

We then define  $\Omega$  as:

$$\Omega = \begin{bmatrix} i\frac{\partial\phi^+}{\partial x} + \frac{\partial\phi^+}{\partial y} + \frac{\partial\ln|B_1^+|}{\partial x} - i\frac{\partial\ln|B_1^+|}{\partial y} \\ -\frac{\partial\phi^+}{\partial x} + i\frac{\partial\phi^+}{\partial y} + i\frac{\partial\ln|B_1^+|}{\partial x} + \frac{\partial\ln|B_1^+|}{\partial y} \\ \frac{1}{|B_1^+|}\frac{\partial|B_1^+|}{\partial z} + i\frac{\partial\phi^+}{\partial z} \end{bmatrix} \quad (3.8)$$

Combining all results and rewriting Eq. 3.3 gives:

$$\begin{aligned} \Omega \cdot \nabla \ln \gamma + \left[ \left( \frac{\partial\phi^+}{\partial x} \right)^2 + \left( \frac{\partial\phi^+}{\partial y} \right)^2 + \left( \frac{\partial\phi^+}{\partial z} \right)^2 \right] - i\nabla^2 \phi^+ \\ - \frac{1}{|B_1^+|} \nabla^2 |B_1^+| - i2\nabla \ln |B_1^+| \cdot \nabla \phi^+ + i\omega\mu_0\gamma = 0 \end{aligned} \quad (3.9)$$

Assuming that  $\sigma \gg i\omega\epsilon$ , we can write  $Re\left\{\frac{\nabla\gamma}{\gamma}\right\} \approx \frac{\nabla\sigma}{\sigma} = -\frac{\nabla\rho}{\rho}$  where  $\sigma = \frac{1}{\rho}$ . Also neglecting the real part of the equation and using only the imaginary part, then multiplying by  $\rho$ :

$$\begin{bmatrix} \frac{\partial\phi^+}{x} + \frac{1}{|B_1^+|\frac{\partial|B_1^+|}{\partial y}} \\ \frac{\partial\phi^+}{y} - \frac{1}{|B_1^+|\frac{\partial|B_1^+|}{\partial x}} \\ \frac{\partial\phi^+}{\partial z} \end{bmatrix}^T \begin{bmatrix} \frac{\partial\rho}{\partial x} \\ \frac{\partial\rho}{\partial y} \\ \frac{\partial\rho}{\partial z} \end{bmatrix} + \left[ \nabla^2 \phi^+ + \frac{2}{|B_1^+|} \nabla |B_1^+| \cdot \nabla \phi^+ \right] \rho = \omega\mu_0 \quad (3.10)$$

Following the same derivation steps for  $|B_1^-|$ , we obtain a similar equation:

$$\begin{bmatrix} \frac{\partial\phi^-}{x} - \frac{1}{|B_1^-|\frac{\partial|B_1^-|}{\partial y}} \\ \frac{\partial\phi^-}{y} + \frac{1}{|B_1^-|\frac{\partial|B_1^-|}{\partial x}} \\ \frac{\partial\phi^-}{\partial z} \end{bmatrix}^T \begin{bmatrix} \frac{\partial\rho}{\partial x} \\ \frac{\partial\rho}{\partial y} \\ \frac{\partial\rho}{\partial z} \end{bmatrix} + \left[ \nabla^2 \phi^- + \frac{2}{|B_1^-|} \nabla |B_1^-| \cdot \nabla \phi^- \right] \rho = \omega\mu_0 \quad (3.11)$$

Finally, adding Eq. 3.10 and Eq. 3.11 while making the assumption that  $\frac{1}{|B_1^+|} \nabla |B_1^+| \approx \frac{1}{|B_1^-|} \nabla |B_1^-|$ , and adding an artificial diffusion term for additional regularization, the final form of the bias-corrected phase-based cr-MREPT equation can be obtained as:

$$-c \nabla^2 \rho + \nabla \phi \cdot \nabla \rho + \left[ \nabla^2 \phi + \frac{2}{|B_1^+|} \nabla |B_1^+| \cdot \nabla \phi \right] \rho = 2\omega\mu_0 \quad (3.12)$$

Note that  $\phi$  in Eq. 3.12 is defined as the transceive phase, i.e.:

$$\phi = \phi^{tr} \triangleq \phi^+ + \phi^-$$

An important point to note is that Eq. 3.12 can be used in both 2D and 3D cases, depending on the dimensions of the operators. In this section, the main purpose is to demonstrate the utilization of the bias correction term; hence the equation is employed in 2D. In this case, a single slice of interest is reconstructed while all z-dependent terms in Eq. 3.12 are assumed to be zero. The 3D case in which all slices are reconstructed simultaneously is discussed in Chapter 4. Such 3D reconstructions are very time and memory demanding, and require other methods to reconstruct. There are two cases of 2D reconstructions that are discussed in this chapter:

- When cylindrical simulation and experimental phantoms with z-independent electrical properties are used, the gradient and Laplacian of resistivity were simplified to omit the z-derivatives, i.e.  $\frac{\partial \rho}{\partial z} = \left(\frac{\partial \rho}{\partial z}\right)^2 = 0$ , and  $\frac{\partial B_1^+}{\partial z} = 0$ .
- When using the brain simulation phantom, to reconstruct the slice of interest, we have also used the z-independence assumption for the resistivity, i.e.  $\frac{\partial \rho}{\partial z} = \left(\frac{\partial \rho}{\partial z}\right)^2 = 0$ , but we have calculated  $\frac{\partial B_1^+}{\partial z}$  using slices one above and below of the slice of interest.

Eq. 3.12 can be simplified to obtain the other well-known MREPT equations. Making the assumption that  $|B_1^+|$  is constant, or in other words,  $\nabla|B_1^+| = 0$ , we get the phase-based cr-MREPT [55] equation:

$$-c\nabla^2\rho + \nabla\phi \cdot \nabla\rho + \nabla^2\phi\rho = 2\omega\mu_0 \quad (3.13)$$

It is also structurally similar to the full-form cr-MREPT equation [53], which uses both the magnitude and the phase of  $B_1^+$ . However, this equation involves complex valued variables and is able to obtain both conductivity and permittivity of the tissues.

$$-c\nabla^2\gamma + \beta^+ \cdot \nabla\gamma - \nabla^2 B_1^+ \gamma = i\omega\mu_0 B_1^+ \quad (3.14)$$

Finally, Eq. 3.12 can be simplified to obtain the phase-based Helmholtz MREPT equation [51] with a bias correction term. The phase-based Helmholtz MREPT assumes that the gradients of EPs are zero. Applying this assumption in Eq. 3.12, and also removing the artificial diffusion term, we get the bias-corrected phase-based Helmholtz MREPT equation:

$$\sigma = \frac{\left[ \nabla^2\phi + \frac{2}{|B_1^+|} \nabla|B_1^+| \cdot \nabla\phi \right]}{2\omega\mu_0} \quad (3.15)$$

In the rest of the chapter, the conductivity maps labeled as “uncorrected” are the maps obtained using Eq. 3.13, i.e., the previously developed phase-based cr-MREPT method. The maps labeled as “corrected” are obtained using Eq. 3.12, and those labeled as “full” are obtained using the full-form cr-MREPT method (Eq. 3.14). Reconstructions obtained using Eq. 3.15 are labeled as “corrected phase-based Helmholtz MREPT”.

The complete derivation with all steps and with more details can be found in App. A.

### 3.3 Methods

Various simulation and experimental data are used to show the effectiveness of the proposed bias correction method. Conductivity maps are obtained using the equations given in Section 3.2. The quality of the reconstructed conductivity distributions is evaluated both visually and numerically.

#### 3.3.1 Simulations

Electromagnetic simulations of various phantoms and MRI coils are performed using COMSOL Multiphysics Software (COMSOL AB, Stockholm, Sweden). Three different simulation phantoms are used:

- a uniform cylindrical phantom ( $\sigma = 0.5s/m, \epsilon = 83$ ) with a height of 20-cm and a radius of 6-cm
- a cylindrical phantom of the same size with two conductivity anomalies ( $\sigma = 0.75s/m$  and  $\sigma = 0.85s/m$  for anomalies,  $\sigma = 0.5s/m$  for background,  $\epsilon = 83$ )
- a human head model [1]

For all phantoms, RF excitations are applied using a 16-rung birdcage coil with a height of 20-cm and a radius of 15-cm. Fig. 3.3 shows the phantom and coil geometries used. Simulations are performed at 3T (127.74MHz).

#### 3.3.2 Experiments

2 different phantom experiments are conducted with Siemens Tim Trio 3T MR Scanner (Erlangen, Germany) in UMRAM (National Magnetic Resonance Research Center) in Bilkent University. During experiments, both the phase and

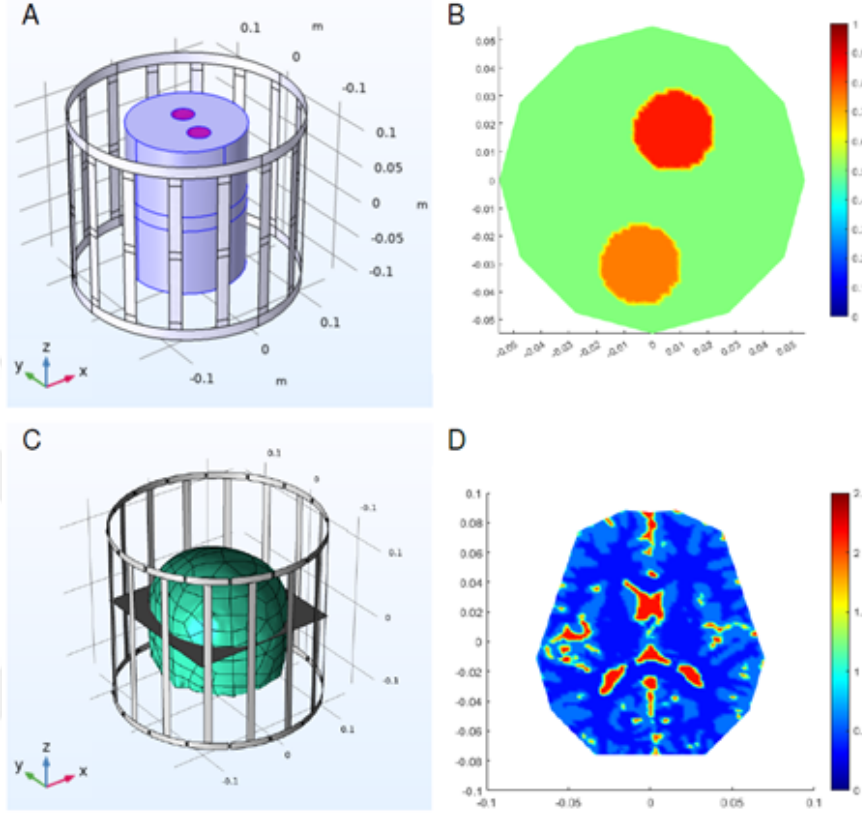


Figure 3.3: Phantom and RF coil geometries. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) Cylindrical phantom with two conductivity anomalies, placed inside a birdcage coil. (B) Conductivity distribution of the cylindrical phantom with two conductivity anomalies. (C) Human head model [1], placed inside a birdcage coil. (D) Conductivity distribution of human head model for the slice shown in (C).

the magnitude of  $B_1$  are measured. To obtain the transceive phase, the 3D bSSFP pulse-sequence is used. The double angle method ([53], [88]) with flip angles  $60^\circ$  and  $120^\circ$  is used for  $|B_1^+|$  mapping. The same pulse sequences with different parameters are used for the experiments. Table 3.1 shows the pulse sequence parameters for all experiments. Complete k-space data are measured during experiments. A bird cage body coil is used for the RF transmit signal, and a 4-channel head coil array is used for the receive signal. Data from different channels of the coil is combined using coil manufacturers combine method.

For the first experiment, a cylindrical phantom with two cylindrical anomalies,

similar to the one used in the simulations, is prepared using Agar jel ( $20gr/l$  Agar,  $2gr/l$  NaCl,  $0.2gr/l$  CuSO<sub>4</sub>) for background and  $4 - 6gr/l$  NaCl,  $0.2gr/l$  CuSO<sub>4</sub> water solution for the two anomalies. The dimensions of the phantom and the anomalies are the same as those of the simulation phantom. A more complex cylindrical phantom is prepared with the same dimensions for the second experiment. This phantom has multiple small diameter conductivity anomalies. The first phantom is referred as "2-anomaly phantom", and the second phantom is referred as the "spatial resolution phantom" throughout the text.

Table 3.1: Pulse sequence parameters for MRI experiments.

|                            | Pulse Sequence      | Resolution(mm) | FOV(mm)      | FA(deg) | TR/TE(ms) | NEX | Duration     |
|----------------------------|---------------------|----------------|--------------|---------|-----------|-----|--------------|
| 2-Anomaly Phantom          | bSSFP               | 1.17x1.17x1.56 | 150x150x31.2 | 40      | 4.88/2.44 | 32  | $\sim 6min$  |
|                            | Double-Angle Method | 1.17x1.17x3.00 | 150x150x3.0  | 60/120  | 5000/5.00 | 1   | $\sim 22min$ |
| Spatial Resolution Phantom | bSSFP               | 1.56x1.56x1.56 | 150x150x31.2 | 40      | 4.70/2.70 | 32  | $\sim 6min$  |
|                            | Double-Angle Method | 1.17x1.17x3.00 | 150x150x3.0  | 60/120  | 1500/5.00 | 1   | $\sim 7min$  |

Fig. 3.4 shows the magnitude views of the experimental phantoms to give a better understanding of the phantoms employed.

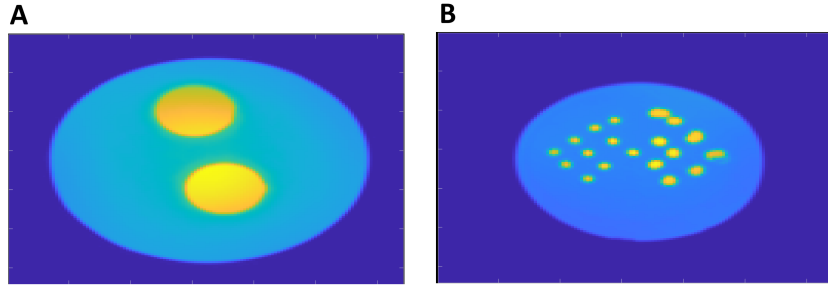


Figure 3.4: Experimental phantoms. (A) 2-anomaly phantom. (B) Resolution phantom.

### 3.3.3 Implementation

All data are exported to Matlab (The Mathworks, Natick, MA, USA) in a Cartesian grid with cell size =  $1.5mm$ , and interpolated into a triangular mesh with maximum triangle size =  $1.5mm$ . Conductivity reconstructions are obtained on a triangle-based finite difference approximation of the related PDE [56]. The resulting system of equations is solved using the backslash operator of Matlab in

the minimum norm least squares sense, without enforcing any boundary conditions. A Gaussian low-pass filter with kernel size of 3 and standard deviation of 0.5 is applied to both the magnitude and phase of the data. For regularization, the nonzero diffusion constant is used in all reconstructions:  $c = 0.001$  for simulation cases,  $c = 0.01$  for experimental cases,  $c = 0.005$  for full-form solution. Uniform noise with standard deviation of 0.02 radians (corresponding to MRI SNR of 50 [40]) is added to the  $B_1^+$  transceive phase in noisy simulations cases.

The  $L^2$ -Norm mean squared error, as given in Eq. 3.16, is calculated for the numerical evaluation of the simulation results.  $\sigma_i^a$  corresponds to the actual conductivity values and  $\sigma_i^c$  represents the calculated conductivity values of the  $i^{th}$  node of the triangular mesh. Since actual conductivity values in experimental phantoms are unknown, the MSE values are calculated only for simulation cases.

$$MSE = 100 \times \sqrt{\frac{\sum_i (\sigma_i^a - \sigma_i^c)^2}{\sum_i (\sigma_i^a)^2}} \quad (3.16)$$

Helmholtz MREPT is known to have artifacts around the internal tissue boundaries, where conductivity distributions are discontinuous. Similarly, in cr-MREPT, sharp conductivity transitions are blunted and widened because of the low-pass filtering of the data and the artificial diffusion based regularization. These well-known conditions create a large difference between the actual and the calculated conductivity values around these regions. As this study focuses on correcting the bias in reconstruction and not the internal boundary artifacts, the “boundary” nodes, that is, the nodes within  $2.5mm$  proximity to the anomaly and tissue boundaries, are not included in the MSE calculations. Toward this a more accurate evaluation of the bias correction was aimed. For all phantoms, the “non-boundary” region is defined as the nodes in the ROI except the “boundary” nodes.

One of the purposes of this study is to show that a low resolution  $|B_1^+|$  is sufficient to be used in the bias correction of phase-based MREPT methods. To do this, simulated  $|B_1^+|$  images are transformed into k-space and part of the

complete  $(121 \times 121)$  k-space is truncated to emulate a low resolution  $|B_1^+|$  map. 2 different truncation options were used:

- Option 1: only the first  $N$  lines in the phase encoding direction
- Option 2:  $N \times N$  central region of the k-space data

For both cases,  $N$  is named the “truncation size”. Option-1 aims to simulate the truncation of the k-space in a Cartesian grid during an MRI experiment. Option-2 aims to resemble a single-shot spiral trajectory focused on the central region of the k-space. The Optimum truncation size is determined by gradually reducing the resolution of the data and calculating the MSE ( $N$  is changed in steps of 1, from 121 to 1).  $N = 11$  is found to be the smallest number that can still provide a reasonable bias correction and MSE, hence is used for the remainder of the study. A Hamming window of proper size, depending on the truncation size, is applied after reducing the k-space data to prevent ringing artifacts. The rest of the k-space is filled with zeros in order to maintain the image size.

A 3<sup>rd</sup> option, Option-3, is the utilization of electromagnetic simulations to obtain  $|B_1^+|$  instead of MRI measurements. Clearly, obtaining an exact  $|B_1^+|$  is not possible with this method, as the EP distribution of the object to be imaged is unknown. However, one can determine the outer boundary of the object using the magnitude of bSSFP image. Using the outer object boundary and assuming a homogeneous EP distribution inside, EM simulations can be conducted in 3 different methods;

- Using a full 3D model of the object, and performing a 3D simulation
- Using a slice of the object to create a 3D cylinder, uniform in z-direction, by simply extruding the slice in z-direction and then performing a 3D simulation
- Using a slice of the object and performing a simple 2D EM simulation of the slice, using a generic 2D model of the MRI coils

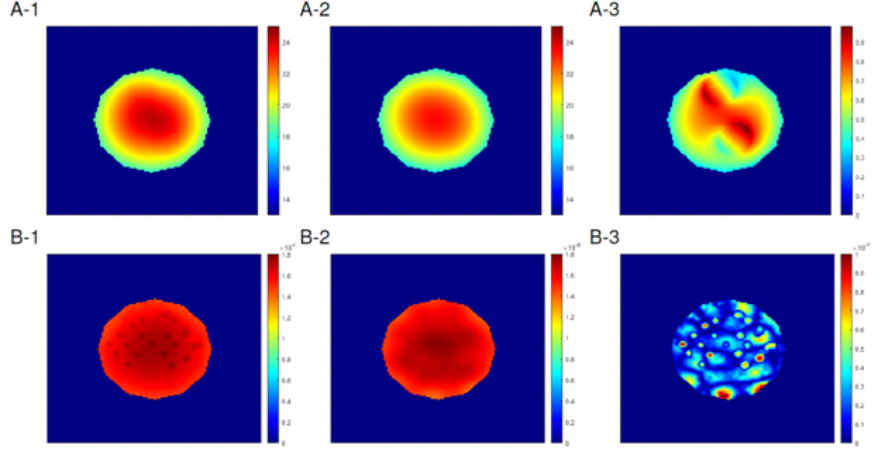


Figure 3.5:  $|B_1^+|$  maps for full k-space (Column-1) and k-space reduced using Option 2 (Column-2), as given in Sec. 3.3.3. (A) Two anomaly simulation phantom, and (B) Spatial resolution experimental phantom. Column-3 shows the difference between Column-1 and -2, for respective rows. Important to note that the scales in Column-3 are much smaller than the scales in the other columns.

It is clear that Method-1 would give the most accurate results, while Method-3 provides the fastest simulation times. During these simulations,  $\sigma = 0.5s/m$  and  $\epsilon_r = 60$  were used for the head model, and  $\sigma = 0.5s/m$  and  $\epsilon_r = 83$  were used for all other cases.

### 3.4 Results

As described in Sect. 3.3.3, data (either simulation or experimental) obtained in full resolution are transformed into k-space, and the k-space data are truncated to lower the resolution. To give a more intuitive feeling of this operation, Fig. 3.5 presents the  $|B_1^+|$  maps that correspond to the full k-space, and the reduced k-space using Option-2 for the 2-anomaly simulation phantom and the spatial resolution experimental phantom. In addition, differences between reduced and non-reduced  $|B_1^+|$  maps are given. It is noticeable that the difference between  $|B_1^+|$  before and after the reduction in the k-space is quite small in magnitude, around 5% of the initial values and is located mainly around conductivity anomalies. It is observed that the reduction of the k-space smoothed the map  $|B_1^+|$ , but it

keeps its overall shape. It may be argued that it is the general low resolution (low frequency) shape of the  $|B_1^+|$  map that is the essential information to achieve bias correction.

Fig. 3.6 shows the k-space data and reconstruction results of a uniform cylindrical phantom. The uncorrected reconstruction results clearly show the bias due to the constant  $|B_1^+|$  assumption as increased conductivity values around the phantom edges. Two different correction methods are employed; correction with full resolution  $|B_1^+|$  and reduced resolution  $|B_1^+|$ , where resolution is reduced using Option-2. For both cases, similar results are obtained and the concave bias disappears. When bias correction is applied using either full or reduced k-space, MSE is reduced to less than 2% compared to 10% of the uncorrected case.

The results of the conductivity reconstruction for the cylindrical phantom with 2 conductivity anomalies are presented in Fig. 3.7. Uncorrected case, correction with full resolution  $|B_1^+|$  and cases where Option-1, -2 and -3 are used for correction is given, as well as the related k-space data for each case when applicable. It can be seen that significant bias correction and almost identical conductivity maps are achieved for all correction cases. Option-1 provides approximately 10 times acceleration of the  $|B_1^+|$  mapping process. In theory, a spiral k-space trajectory can be employed to acquire data similar to Option-2, and even higher acceleration rates can be achieved. For Option-3,  $|B_1^+|$  mapping is completely discarded, as a simple EM simulation is sufficient for correction, and required MRI data can be acquired with a single bSSFP sequence.

Fig. 3.8 presents the conductivity distributions for the same phantom, when uniform noise with standard deviation of 0.02 radians is added to the simulation data. The effect of added noise is clearly visible for all cases as minor disturbances in the conductivity values. However, the proposed bias correction method is still effective and the concave bias disappears when bias correction is applied.

Experimental MRI data from a cylindrical phantom with 2 conductivity anomalies, quite similar to the simulated phantom, are used to calculate conductivity distributions and demonstrate that the proposed bias correction method is

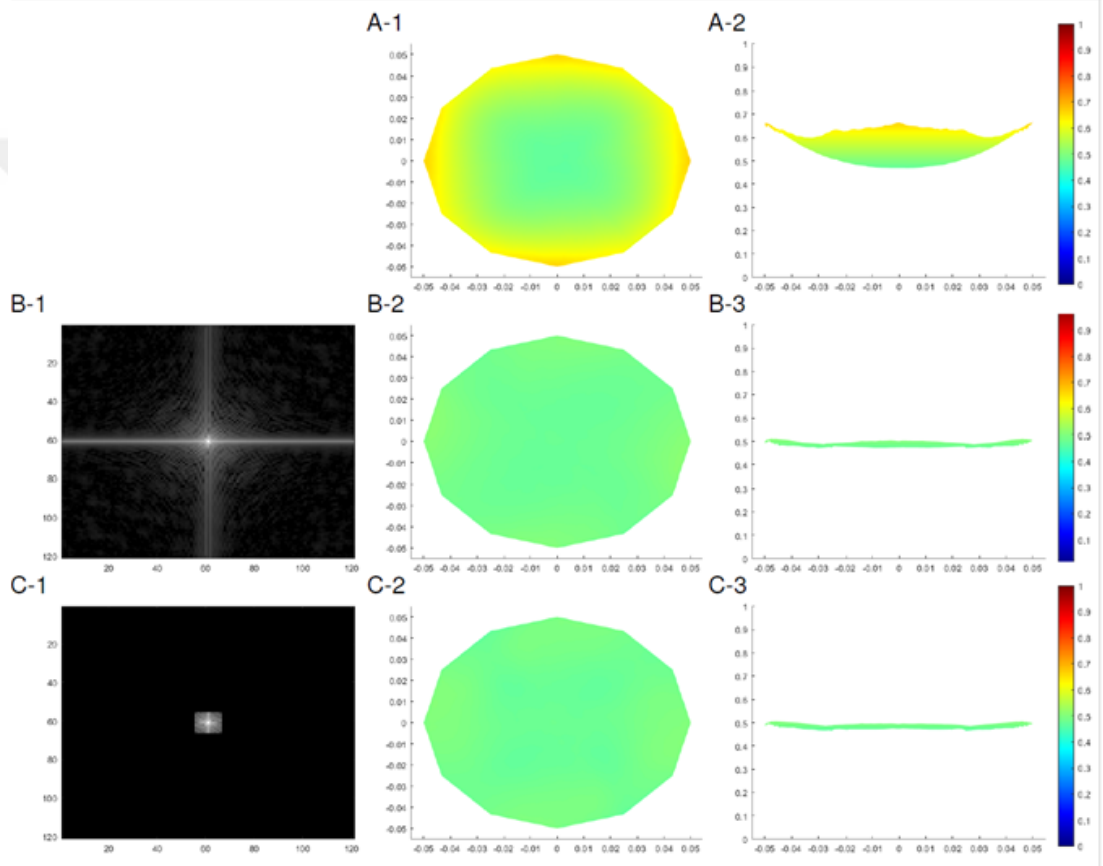


Figure 3.6: Reconstructed conductivity map of the slice, and side views of the conductivity distribution, for the uniform phantom with  $\sigma = 0.5s/m$ . Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A-1,2) No bias correction is applied. (B-1) Full k-space used for bias correction. (B-2,3) Conductivity distribution of the slice, and side view of the conductivity distribution when full k-space is used for correction. (C-1) Reduced k-space (Option-2) used for bias correction. (C-2,3) Conductivity distribution of the slice, and side view of the conductivity when Option-2 is used for correction

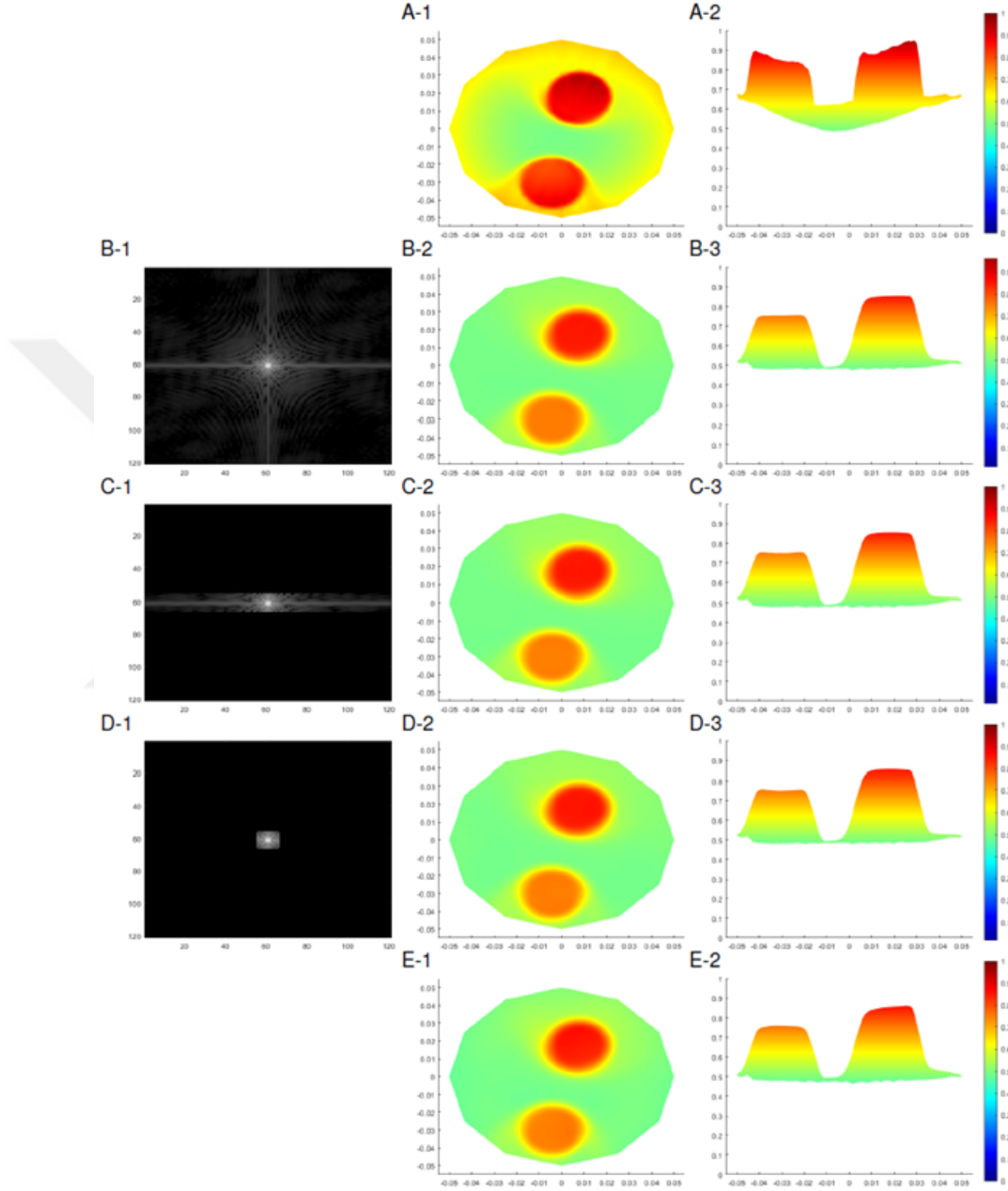


Figure 3.7: Reconstructed conductivity maps of cylindrical phantom with 2 conductivity anomalies, when bias correction is applied for all proposed correction options. Column-1 shows the related k-space data of the  $|B_1^+|$  used in reconstruction. Columns-2 and -3 show the conductivity distribution of the slice, and the side view of the conductivity distribution, respectively. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) No correction is applied. (B) Complete k-space data is used for correction, i.e. reference case. (C) Correction Option-1, where 11 lines in phase-encoding direction is used. (D) Correction Option-2, where an  $11 \times 11$  square in center of k-space is used. (E) Correction Option-3, where  $|B_1^+|$  from homogeneous object simulation is used.

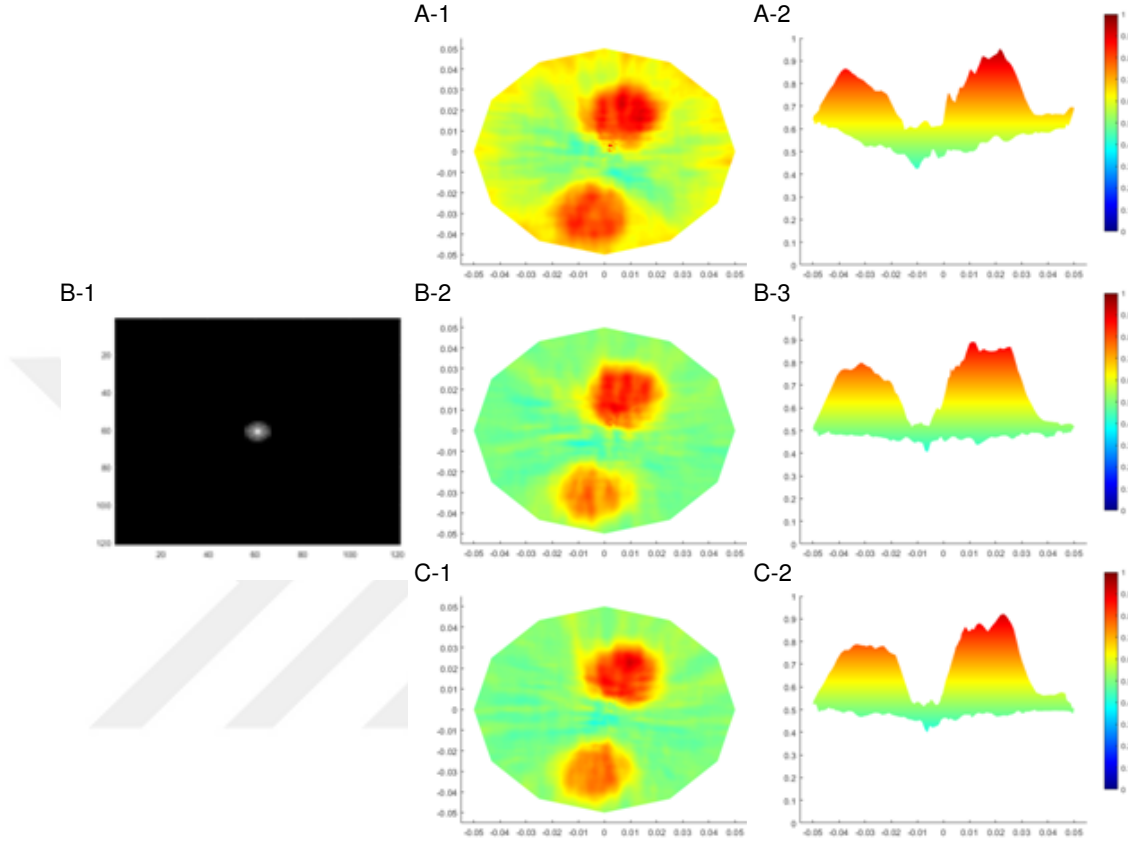


Figure 3.8: Conductivity results and side views of the conductivity distribution, for cylindrical phantom with 2 conductivity anomalies with added noise to  $B_1$  phase and magnitude. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (Row-A) No bias correction is applied. (Row-B) Reduced k-space using Option-2. (Row-C)  $|B_1^+|$  from homogenous object simulations.

also effective in actual MRI images. The results are given in Fig. 3.9, and are quite similar to the simulations; a low resolution  $|B_1^+|$  map, or  $|B_1^+|$  map obtained from homogeneous EP simulations is sufficient to correct the concave background bias.

Another experimental result is given in Fig. 3.10, of the resolution phantom. This phantom consists of multiple small conductivity anomalies such that the resolution limits of the reconstruction methods can be evaluated more accurately. Reconstruction results for bias correction using Option-2 and -3 are given, in addition to the uncorrected case. Similarly to the previous cases, concave bias is

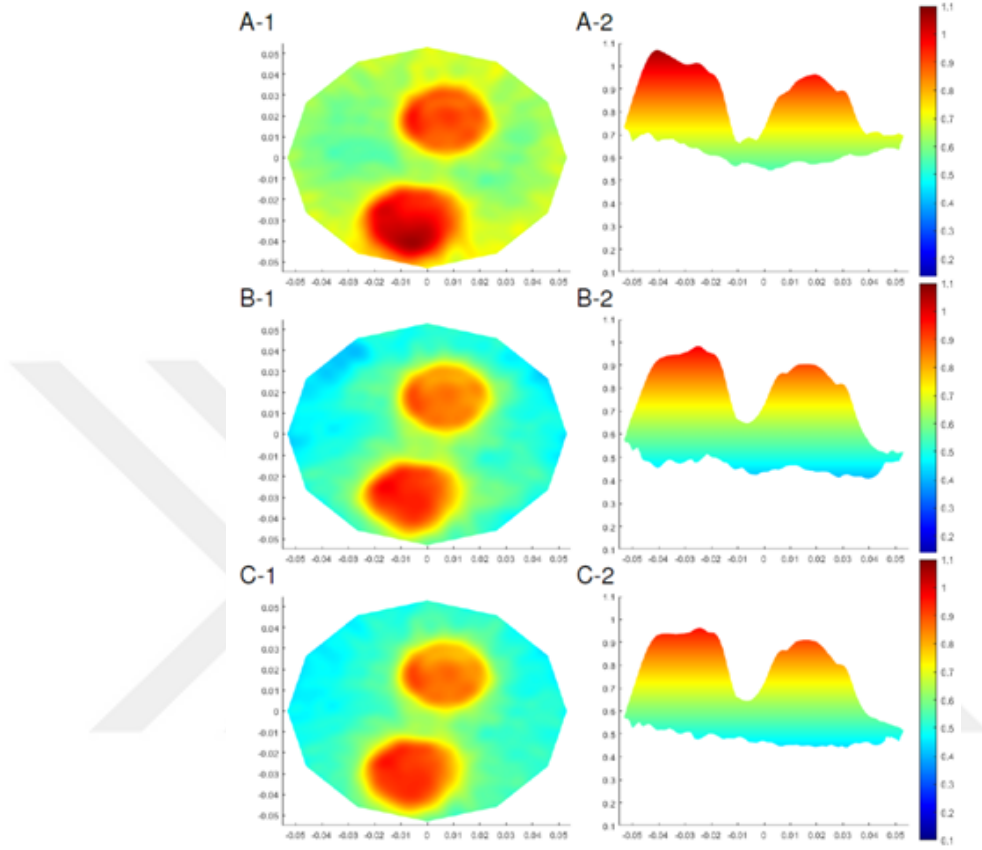


Figure 3.9: Reconstructed conductivity maps and side view of the conductivity distribution for experimental phantom, a cylinder with two conductivity anomalies. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (Row-A) No bias correction is applied. (Row-B) Reduced k-space using Option-2. (Row-C)  $|B_1^+|$  from homogeneous object simulations.

successfully corrected with both options. In addition to the top and side views of the conductivity distributions, a cross-sectional view is given in the  $y$ -direction (at  $x = 0$ ) to present the effect of bias correction more clearly. The conductivity values at the side of the phantom are curved upward for the uncorrected case, where this bias is removed when bias correction is applied. Moreover, inspecting the conductivity distributions, one can see that spatial resolution is also improved in the corrected cases.

Fig. 3.11 shows the results for the human head model. Uncorrected and bias corrected results are presented. The full resolution map  $|B_1^+|$  is used for bias correction, as well as Option-2 and -3. Since the phantom is more complicated

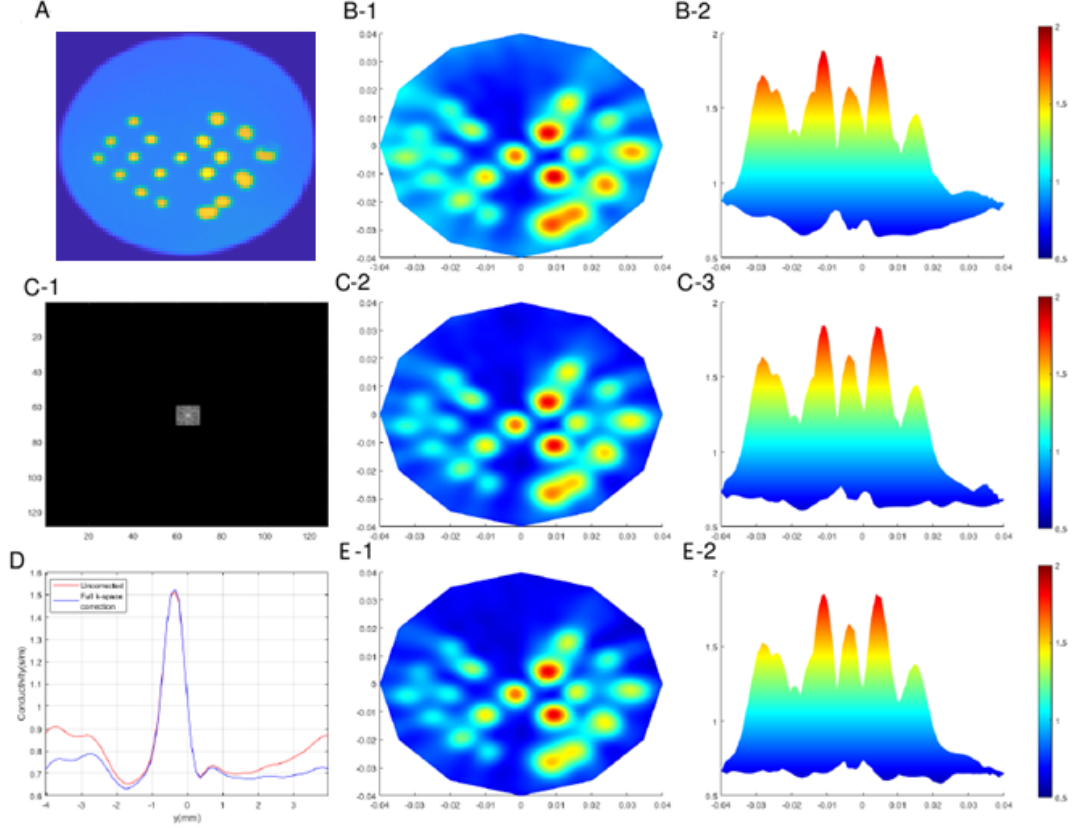
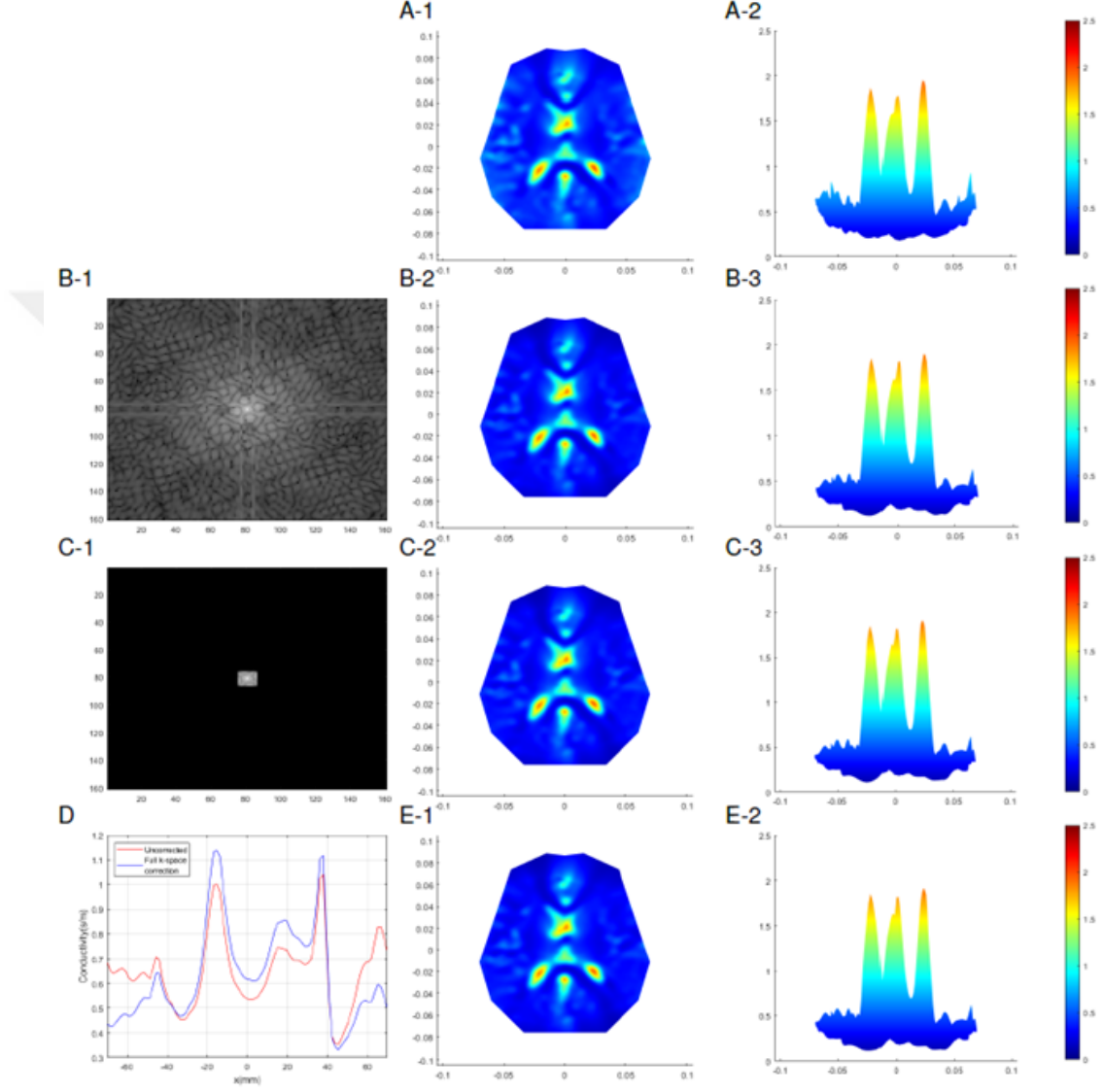


Figure 3.10: Experimental results of the spatial resolution phantom when bias correction is applied. Column-2 and -3 show the conductivity distribution of the slice, and the side view of the conductivity distribution, respectively. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) Magnitude of the bSSFP data. (B) No correction is applied. (C) Correction Option 2, where an  $11 \times 11$  square in center of k-space is used. (D) Cross section ( $x = 0$ ) view of conductivity values when no correction or full k-space correction is applied. (E) Correction Option-3, where  $|B_1^+|$  from homogeneous object simulation is used.

compared to previous ones, the effect of bias correction is not as clear. However, it can be seen that the proposed bias correction method is effective for all correction cases. The effect of bias correction can be easily noticed around the edges of elevated views of the conductivity distribution (Fig. 3.11, Column-3), and even more so in the cross-sectional view of the conductivity distributions (Fig. 3.11, D).

Finally, Fig. 3.12 shows the results of the conductivity distribution for the 2-anomaly simulation phantom when phase-based Helmholtz MREPT is used. Both uncorrected and corrected cases are shown. Option-2 is used for the reduction in resolution of  $|B_1^+|$  when bias correction is applied. The concave bias can be seen in Fig. 3.12 for the uncorrected case, where it is successfully removed when correction is applied. This is also indicated by the MSE values; 35.5% for the non-boundary regions in the uncorrected case and 3.6% for the non-boundary regions in the corrected case. For both uncorrected and corrected cases, boundary artifacts around the anomaly boundaries are also clearly visible.

Table 3.2 shows the MSE values for the reconstructed conductivity distributions of simulation phantoms, for uncorrected cases, and various correction methods. The numerical evaluation results are consistent with the visual results given in the figures, and bias correction methods improve the conductivity map reconstructions in each case. For the uniform phantom, the uncorrected conductivity distribution has an MSE of 10.1 due to the concave bias. However, when correction is applied, the MSE becomes less than 1.56 for all correction cases. Note that Option-3 is not applicable to this phantom, as it is already homogeneous. For phantom with 2 anomalies, MSE decreases from 14.7 to less than 5.62. The relatively high MSE values compared to the uniform phantom case is mostly due to the errors in the internal boundaries. When only the non-boundary regions are considered, MSE is higher for the uncorrected case as the concave bias is more dominant in these regions, but correction is also more effective in non-boundary regions, and MSE decreases to less than 3.41 after correction. This is also similar in the human head phantom case. In addition, corrections with full resolution or either of the 3 correction options have very similar MSE values.



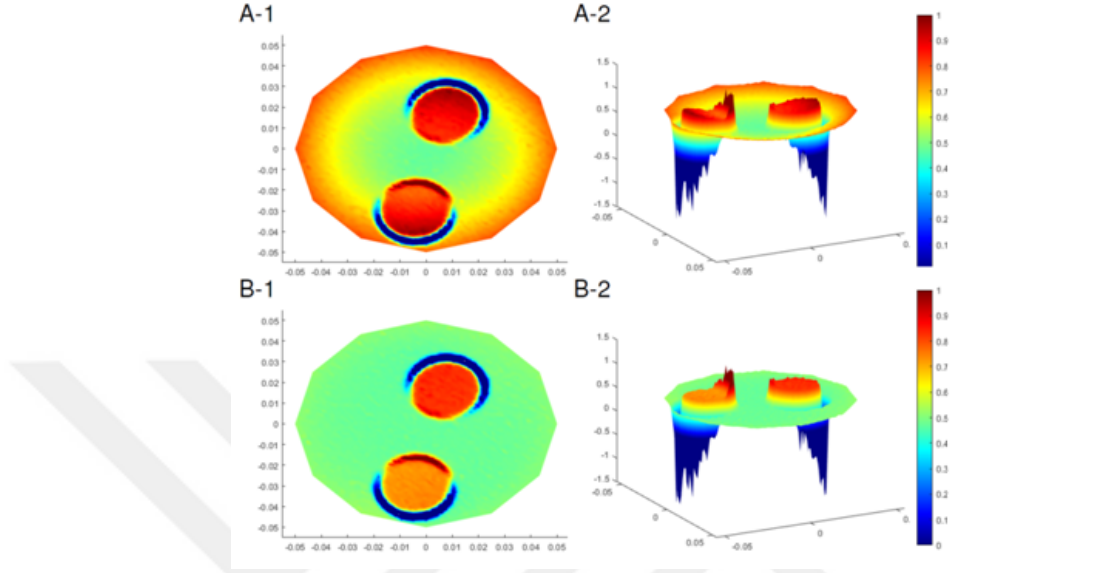


Figure 3.12: Conductivity distributions obtained using phase-based Helmholtz MREPT equation. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) Uncorrected case. (B) Corrected (Option-2) case. Internal boundary artifacts that are common in Helmholtz MREPT is clearly visible in both cases.

Table 3.3 shows the MSE values when bias correction is applied using Option-3. In EM simulations, different simulation methods are described as in Sect. 3.3.3 are used. Unsurprisingly, the smallest error is obtained using 3D simulation, i.e. Method-1, which is also the most computationally heavy method to use. However, Method-3, a simple 2D simulation, showed a similar performance in terms of MSE.

### 3.5 Extension to Full-Form cr-MREPT

The full-form cr-MREPT method has a couple of advantages compared to phase-based methods. First, it can provide the permeability of the tissue as well as conductivity, in contrast to the phase-based methods that can only reconstruct the conductivity distributions. Moreover, since it does not use the assumption that  $|B_1^+|$  is constant, the concave bias that we discuss in this section is not observed in reconstructions. However, full-form methods require both phase and

Table 3.2: MSE values for various phantoms and cases.

|                                   | Uncorrected | Full k-space<br>Correction | 11 k-space<br>Lines<br>(Option-1) | 11x11 square<br>in k-space<br>(Option-2) | Homogeneous Simulation<br>Correction<br>(Option-3) |
|-----------------------------------|-------------|----------------------------|-----------------------------------|------------------------------------------|----------------------------------------------------|
| Uniform                           | 10.1        | 1.54                       | 1.56                              | 1.55                                     | -                                                  |
| 2-Anomalies                       | 14.7        | 5.62                       | 5.61                              | 5.55                                     | 5.75                                               |
| 2-Anomalies<br>Non-Boundary       | 17.8        | 3.40                       | 3.39                              | 3.35                                     | 3.41                                               |
| Head                              | 22.4        | 17.2                       | 17.3                              | 17.3                                     | 17.4                                               |
| Head<br>Non-Boundary              | 25.7        | 8.12                       | 8.13                              | 8.12                                     | 9.7                                                |
| 2-Anomalies<br>Full-Form cr-MREPT | 3.72        | -                          | 8.81                              | 8.79                                     | 11.4                                               |

Table 3.3: MSE values when correction Option-3 is used with different methods employed for EM simulations.

|          | Head | Head<br>Non-Boundary |
|----------|------|----------------------|
| 3D       | 17.4 | 9.74                 |
| Cylinder | 17.6 | 10.95                |
| 2D       | 17.5 | 10.07                |

magnitude of  $B_1^+$ , which makes long imaging times necessary. Then, it is clear that it would be beneficial to see if the k-space reduction methods we have utilized for bias correction are also applicable to full-form cr-MREPT.

Fig. 3.13 shows the results of the cr-MREPT reconstruction in full-form for the noiseless simulation of the cylindrical phantom with 2 anomalies, where Fig. 3.14 presents the noise addition case. For both cases, it can be seen that the full-form cr-MREPT method, applied using the full resolution  $B_1^+$  map, is able to perfectly reconstruct the conductivity map of the simulation phantom, apart from a slight blunting of the conductivity variation across the anomaly boundaries. When low resolution  $|B_1^+|$ , reduced using Option-2, is utilized for reconstruction, the reconstruction quality is not as good as the reconstruction quality obtained with the bias corrected phase-based method using the same  $|B_1^+|$  resolution. The result may still be deemed acceptable (MSE=8.79). As shown in Part C of Fig. 3.13, the image quality further decreases when  $|B_1^+|$  maps obtained using homogeneous EP simulations are used (MSE=11.4). Increased non-uniformity in the non-boundary

regions and diffuse boundary artifacts are observed. Noise added results are also quite similar to this, with the same effects observed when low resolution  $|B_1^+|$  map is used.

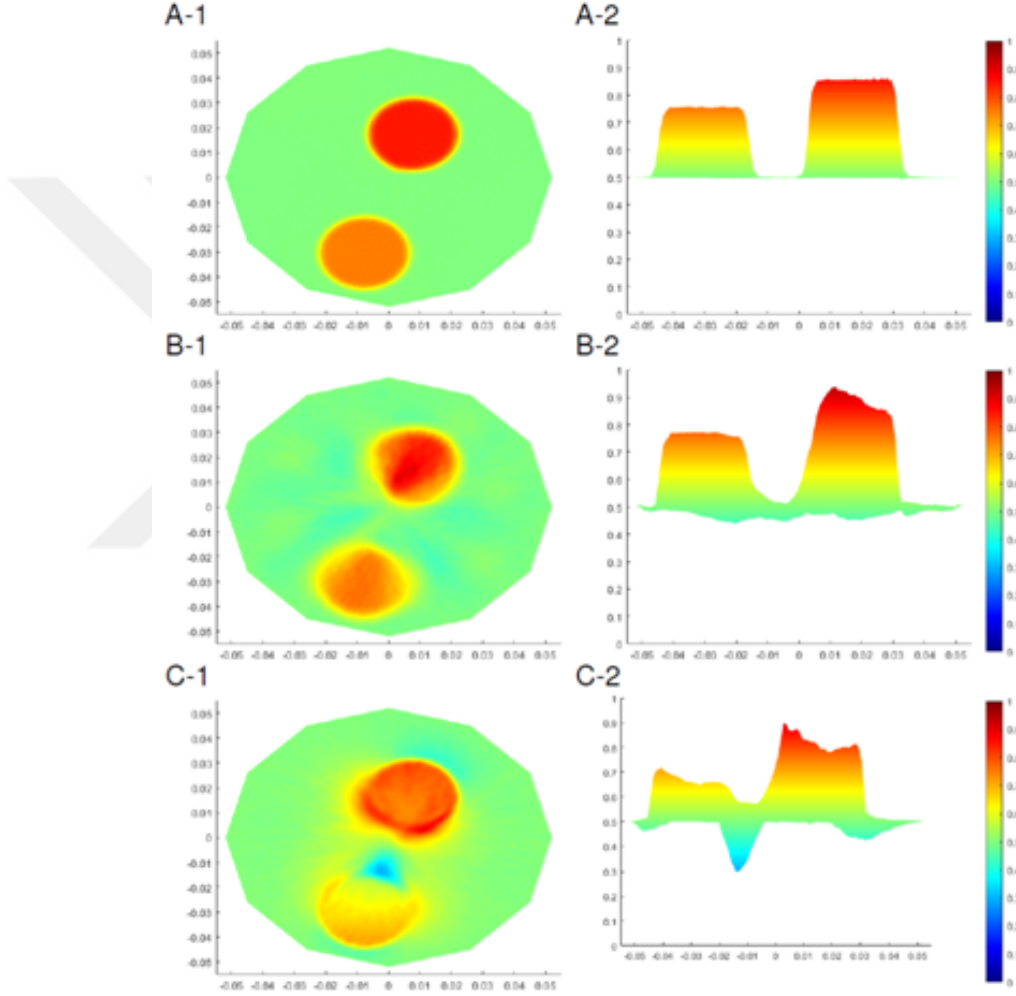


Figure 3.13: Conductivity maps obtained using full-form cr-MREPT method for the simulation phantom with 2 anomalies. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) Complete  $|B_1^+|$  data is used, reference case. (B) Correction Option-1, where 11 lines in phase-encoding direction is used. (C) Correction Option-3, where  $|B_1^+|$  from homogeneous object simulation is used.

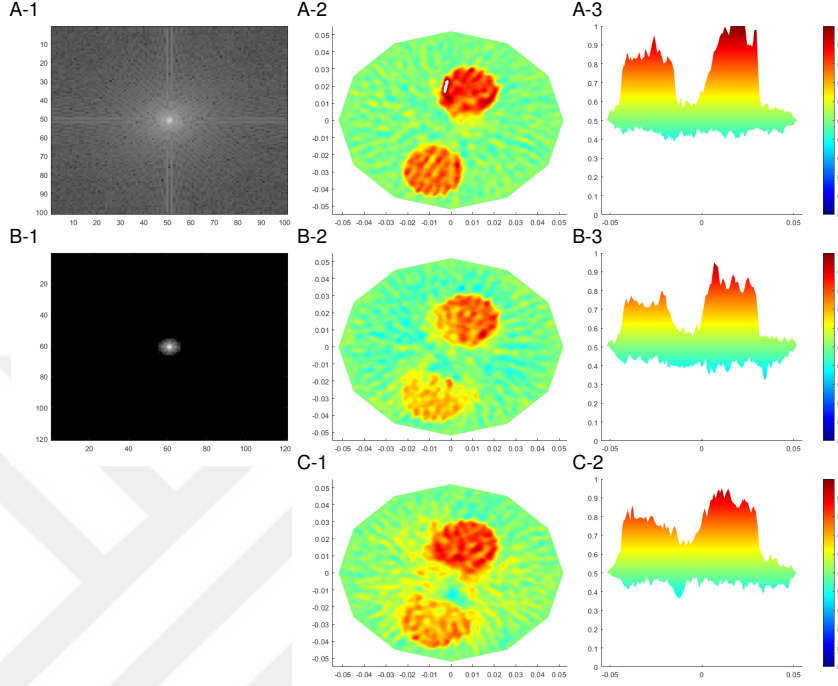


Figure 3.14: Conductivity maps obtained using full-form cr-MREPT method, when noise is added to the simulation data from phantom with 2 anomalies. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) Complete  $|B_1^+|$  data is used, reference case. (B) Correction Option-1, where 11 lines in phase-encoding direction is used. (C) Correction Option-3, where  $|B_1^+|$  from homogeneous object simulation is used.

### 3.6 Discussion

All in all, a bias correction method is developed in order to overcome the concave bias problem observed in phase-based MREPT methods. Although the proposed method relies on the  $|B_1^+|$  maps, a very low resolution map is sufficient for bias correction even for noise added simulations and experimental data. Furthermore, simulations of phantoms with the outer shape of the imaged object and homogeneous conductivity values can be used to obtain the required  $|B_1^+|$  maps. Significant reduction in imaging times can be achieved using the proposed bias correction method, as high resolution  $|B_1^+|$  maps are no longer necessary to obtain good conductivity maps. For simpler phantoms, with bias correction and artificial diffusion coefficient, almost perfect conductivity maps are obtained without

requiring boundary conditions. However, for a more complicated phantom (i.e. the head model and the spatial resolution phantom), the effect of bias correction is not as visible. This can be explained with the concave bias itself not being as visible in these cases because of the complicated conductivity distribution with many spatially small conductivity variations. Indeed, for real in-vivo applications, noise artifacts and other imperfections caused by the MRI system will also be effective. However, when conductivity cross-sections and MSE values are inspected, it can be seen that all bias correction options provide some improvement in quality of the conductivity maps. Moreover, when only the error in the non-boundary regions is considered, the effectiveness of the correction becomes clearer even in a complicated head phantom.

When deriving the main equation for bias correction in phase-based cr-MREPT, it is assumed that  $\frac{1}{|B_1^+|} \nabla |B_1^+| \approx \frac{1}{|B_1^-|} \nabla |B_1^-|$ . Inspecting this in detail, this assumption means that the spatial distribution of sensitivity of transmit and receive coils over the object to be imaged is similar. This is already the case when a single coil, for example, a Quadrature Birdcage Coil (QBC), is used for both transmit and receive. In case when different coils are utilized for transmit and receive operations, for example, when a multichannel coil array is used for the receive side instead of a QBC, it is plausible to assume that data from all channels of the multichannel coil array will be combined, using the MRI device manufacturer's method or another coil-combine algorithm [72], so that the resulting receive sensitivity will resemble the volume transmit sensitivity of the QBC, and therefore the given assumption will hold again.

It was previously mentioned in this Section that obtaining the magnitude of  $B_1^+$  with high SNR takes quite a long time. In this study, MRI scan times of  $\sim 22min$  and  $\sim 7min$  were used, for single slice  $B_1^+$  magnitude mapping, for experimental phantoms of 2-anomaly and spatial resolution. The TR values used in the experiments are 5 seconds and 1.5 seconds, respectively [53, 88]. Another popular method that is faster compared to the double angle method is the Actual Flip Angle Imaging (AFI) [89]. However, since a high SNR is an important factor for successfully reconstructing conductivity maps, the TR values are longer than usual. For example, Voigt et al have used an AFI based method that takes 10

minutes for 11 slices [50]. The proposed bias correction method can shorten the data acquisition time ten-fold, by using k-space reduction using Options 1 or 2. Then, a 3D, i.e. multi-slice mmapping can be possible under 1 minute when AFI-based methods are used. There is also an ultrafast mapping method, DREAM [90] that is basically designed for quick  $B_1$  shimming. However, this method is known to have a low SNR, and hence is not suitable for MREPT. In the DREAM method, it may be necessary to have long averaging repetitions to be acceptable for MREPT purposes, again increasing the total imaging times.

Another important point to consider for obtaining the phase and magnitude of  $B_1^+$  is that simultaneous acquisition of magnitude and phase is necessary to avoid registration errors in practice. Recently, there have been attempts for fast spiral acquisition for phase imaging [91] achieving total head coverage with multiple averages in less than a minute. However, similar spiral magnitude mapping methods have not been developed. An approach to simultaneous acquisition is based on Carr-Purcell Spin echoes [92]. However, their method has to be further developed for high fidelity results. In summary, there is a need for innovative fast mapping techniques, but as of now the k-space reduction method that we have proposed provides a practical and viable solution.

Option-3 that is used for bias correction in this study relies on EM simulations that are performed using the outer shape of the imaged object and homogeneous generic EP values. The outer shape of the object can be determined using the bSSFP magnitude image, where the phase of the acquired data is already used for phase mapping. Then, it is straightforward to perform a simulation with the obtained geometry using homogenous, generic electrical property values. It is also shown that a simple 2D simulation is sufficient for bias correction. Hence, the EM simulation can be performed rather quickly and in the matter of seconds. Although this seems like an additional step, the time required by the patient to spend in the MR machine is significantly reduced, since it is not required to be obtained. Moreover, any error due to co-registering separate images from different sequences is prevented, since a single pulse sequence is sufficient to obtain the data. This topic is investigated in more detail in Chapter 5, where such simulations are integrated in the cr-MREPT algorithm in Matlab.

In addition to cr-MREPT, it is shown in Fig. 3.12 that the proposed bias correction method can also be applied to phase-based Helmholtz MREPT. Since Helmholtz MREPT is extremely easy to implement, it is the most popular and widely used MREPT method even though it has well-known limitations. The most significant of these limitations are concave bias and internal boundary artifacts. The proposed bias correction method therefore solves one of the most important problems related to phase-based Helmholtz MREPT. Algorithms have been developed to mitigate the internal boundary artifacts of phase-based Helmholtz EPT by using nonlinear filtering techniques such as in [93, 94]. The method proposed in this section can be easily coupled to these algorithms simply by adding the bias correction term in Eq. 3.12.

After showing that a low resolution  $|B_1^+|$  is sufficient for bias correction in phase-based MREPT, it is a natural process to assume that the same is true for full-form MREPT. However, after applying the same k-space reduction methods in the full-form cr-MREPT solution, it is concluded that low resolution maps are not as useful in the full-form cr-MREPT solution. Homogeneous EP simulations are also utilized for reconstruction, and even worse results are obtained. For both cases, an overall pattern of conductivity distribution is satisfactorily obtained but with very distinct artifacts.

Even though somewhat successful reconstructions are obtained using low resolution magnitude maps, the results are clearly inferior compared to the full resolution case and significant artifacts all around the conductivity map are observed. The most significant problem is that there is a clear artifact at the internal boundary in the central region of the map. Moreover, the shapes of the anomalies are far from the original shapes, and boundaries of the anomalies seem to have values higher than the actual ones. Finally, conductivity values at non-boundary regions of the phantom, where actual conductivity values are relatively constant, have radially located artifacts. Combining these, it is reasonable to say that full-form cr-MREPT requires a higher resolution map compared to bias correction for phase-based cr-MREPT. Full-form cr-MREPT requires second derivatives of the while bias corrected phase-based method requires only the first derivatives. As the resolution for the map is reduced, the second derivatives become more

inaccurate. Due to this, the full-form cr-MREPT method is more prone to error when map resolution is reduced because more errors in internal boundaries are observed, and these errors are spread into the non-boundary regions.



## Chapter 4

# 3D Implementation and Acceleration of phase-based cr-MREPT

### 4.1 Motivation

Helmholtz MREPT, by nature, is a point-wise method; meaning that the conductivity reconstruction on a given node is dependent only on the  $B_1$  field and its derivatives on that node. Hence, the solution time increases linearly with the number of nodes to solve for. However, in cr-MREPT, a partial differential equation (PDE) involving all nodes in the ROI is solved to obtain all conductivity values simultaneously. While this provides regularization and helps with internal boundary artifacts, especially in 3D applications very large matrix inversions are encountered and computation time is increased exponentially with respect to the number of nodes in ROI. As a result, most of the previous studies in cr-MREPT involve obtaining conductivity in a single slice in the XY-plane. Multi-slice reconstructions where each slice is reconstructed independently result in conductivity offsets across the slices. Some studies employ cr-MREPT in 3D ( [58, 59] where iterative matrix inversion is used to combat the memory problem,

but the problem of long computation time is not yet solved.

Even a simple cylindrical phantom with conductivity anomalies can be used as an example that ignoring z-dependency indeed affects the obtained conductivity values. Fig. 4.1 shows conductivity values calculated using the 2D and 3D MREPT algorithms for the same phantom. There is a significant difference between the resulting conductivity values, with the 3D implementation giving more accurate values.

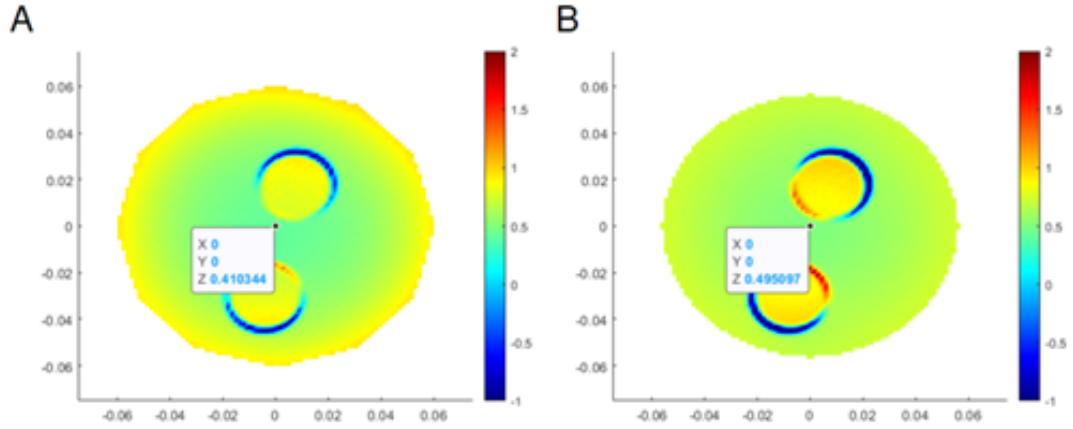


Figure 4.1: Conductivity reconstructions for the same z-independent phantom. Phantom has a cylindrical shape, and has 2 conductivity anomalies that are also cylindrical. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes. (A) 2D reconstruction results. (B) 3D reconstruction results.

Table 4.1: Solution time for cr-MREPT for various ROI sizes. Mesh resolution is  $1.5mm$  for all cases.

| ROI size (mm)            | Number of Nodes | Number of Elements | Solution Time (sec) |
|--------------------------|-----------------|--------------------|---------------------|
| $20 \times 20 \times 20$ | 5036            | 24893              | 13                  |
| $30 \times 30 \times 30$ | 12201           | 64377              | 303                 |
| $40 \times 40 \times 40$ | 28609           | 24893              | 2252                |
| $50 \times 50 \times 50$ | 53946           | 299199             | 7467                |
| $60 \times 60 \times 60$ | 93251           | 523016             | 24045               |

In this study, we implement bias corrected phase-based cr-MREPT [95] in 3D tetrahedral mesh, and propose dividing the ROI into smaller 3D regions for faster reconstruction of the conductivity distributions. By using cr-MREPT in small regions, more manageable sized PDEs are obtained, and solutions for all of

the regions can be done in parallel. After the conductivity distributions for each region were obtained separately, the results of each individual solution are collaged to obtain a conductivity distribution for the whole ROI. This approach assumes that the reconstruction of conductivity at a certain voxel is not affected by phase measurements in voxels beyond a certain distance from the voxel of interest. To determine a proper size for the small regions, the sensitivities of the reconstructed conductivity values to the  $B_1$  phase values in the nearby voxels are calculated and the minimal region for which the sensitivity is sufficiently significant is selected. The selected regions are large enough so that the cr-MREPT method can provide a stable solution and gives correct conductivity values. By working on small volumes, the memory requirements and solution times are significantly reduced. Solutions of individual small volumes can be done in parallel, further accelerating the solution.

## 4.2 Theory

In Sect. 3.2, we have started from the relationship between EPs and  $B_1$  field in Eq. 3.1 as:

$$-\nabla^2 \mathbf{B} = \frac{\nabla \gamma}{\gamma} \times (\nabla \times \mathbf{B}) - i\omega\mu_0\gamma\mathbf{B} \quad (4.1)$$

Where  $\gamma = \sigma + i\omega\epsilon$ . Then we have reached the final form of the bias corrected phase-based cr-MREPT:

$$-c\nabla^2 \rho + \nabla \phi \cdot \nabla \rho + \left[ \nabla^2 \phi + \frac{2}{|B_1^+|} \nabla |B_1^+| \cdot \nabla \phi \right] \rho = 2\omega\mu_0 \quad (4.2)$$

The complete derivation can also be found in App. A. In Chapter 4, we employed this equation in 2D and omitted the dependence of  $z$  for both conductivity and magnetic field, since we were only interested in the reconstitution of

a single slice at a time. Here, however, our interest is to obtain the reconstruction in 3D, i.e. obtaining all conductivity values for all slices simultaneously. Hence, z-dependence is also taken into account, and all derivatives are calculated accordingly.

## 4.3 Methods

Different simulation phantoms are utilized to develop the 3D cr-MREPT solution method, with noiseless and noise added EM simulations. Sensitivity maps of the conductivity reconstructions with respect to the change in  $B_1^+$  phase are calculated, as well as with respect to the boundary conditions enforced while solving the PDE. The volume where we want to obtain conductivity is divided into smaller regions, solved separately and in parallel for acceleration of the solution, then the results are combined to get the complete conductivity distributions.

### 4.3.1 Simulations

COMSOL Multiphysics Software (COMSOL AB, Stockholm, Sweden) is used to perform electromagnetic simulations with different RF coil and phantom geometries. Three different simulation phantoms are used:

- a cylindrical phantom with a height of 20-cm and a radius of 6-cm with two z-independent conductivity anomalies ( $\sigma = 0.75s/m$  and  $\sigma = 0.85s/m$  for anomalies,  $\sigma = 0.5s/m$  for background,  $\epsilon = 83$ )
- a smaller cylindrical phantom with a height of 5-cm and a radius of 2-cm with two z-dependent conductivity anomalies ( $\sigma = 0.65s/m$  and  $\sigma = 0.75s/m$  for anomalies,  $\sigma = 0.5s/m$  for background,  $\epsilon = 83$ )
- a human head model [1]

RF excitations are applied using a 16-rung birdcage coil with a height of 20-cm and a radius of 15-cm. Fig. 4.2 shows the phantom and coil geometries used, and the conductivity distributions on constant x-, y- and z-planes. Simulations are performed at 3T (127.74MHz).

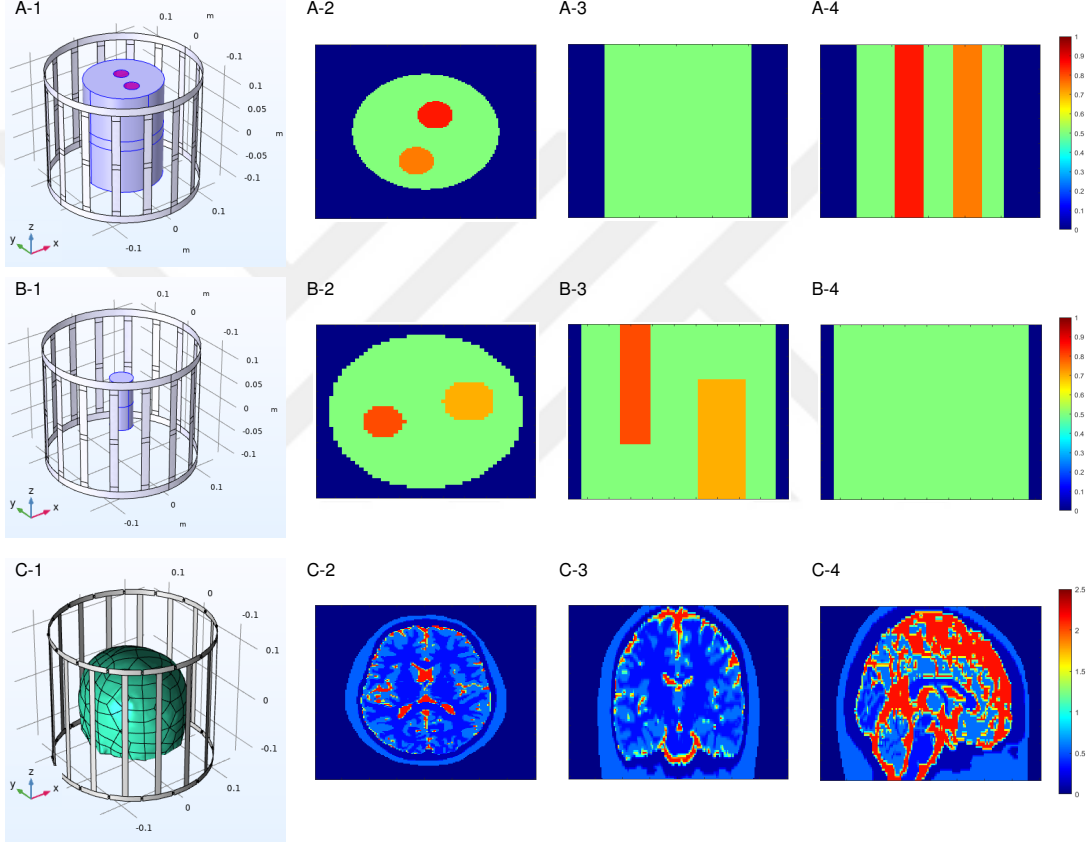


Figure 4.2: Coil and phantom geometries used in the study. Column 1 shows the coil and phantom geometries, and Columns 2-4 present conductivity distributions of the phantoms in constant z-, y-, and x-planes, respectively. (A) Cylindrical phantom with height of 20-cm and radius of 6-cm with two z-independent conductivity anomalies. (B) Cylindrical phantom with height of 5-cm and radius of 2-cm with two z-dependent conductivity anomalies. (C) Human head model [1].

### 4.3.2 Implementation

The simulation data are exported to Matlab (The Mathworks, Natick, MA, USA) in a Cartesian grid (grid cell size =  $1.5mm$ ) and interpolated into a triangular/tetrahedral mesh. The maximum triangle/tetrahedral size is  $1.5mm$  for all cases. Conductivity reconstructions are obtained on a triangle-based finite difference approximation of the related PDE [56]. The resulting system of equations is solved using the backslash operator of Matlab in the minimum norm least squares sense. A Gaussian low pass filter (kernel size = 3, std. dev. = 0.5) is applied to both the magnitude and phase of data and non-zero diffusion constant ( $c = 0.001$ ) is used in all reconstructions. Uniform noise with standard deviation of 0.02 radians (corresponding to MRI SNR of 50 [40]) is added to the  $B_1^+$  transceive phase in noisy simulation cases.

### 4.3.3 ROI Definitions

As the ROI size increases, the number of nodes to solve for increases exponentially. Due to this, especially in 3D problems, solution times can get quite long and solution procedure gets more demanding in terms of computational power. To overcome this problem, we divide the object to be imaged into smaller regions. However, as mentioned earlier, cr-MREPT is not a point-wise method, and the solution at a given node depends on the volume around the node. Therefore, in order to obtain the correct conductivity distribution on a given volume, cr-MREPT should be applied on a larger volume covering it. To avoid any confusion, let us first define the terms to be used in the rest of the thesis;

- Object: The large volume in which the final conductivity map is obtained.
- Local ROI: The small volume for which the conductivity map is obtained in a single reconstruction.
- Solution ROI: The volume around the local ROI that is used in a single reconstruction.

Solution ROI is defined to obtain the correct conductivity values in the local ROIs, since solving for the exact local ROI may give incorrect conductivity distributions, especially on the boundaries of the target ROI. This is more dominant when boundary conditions are applied, as the values we enforce on boundaries are constant, generic values, and not the actual conductivities.

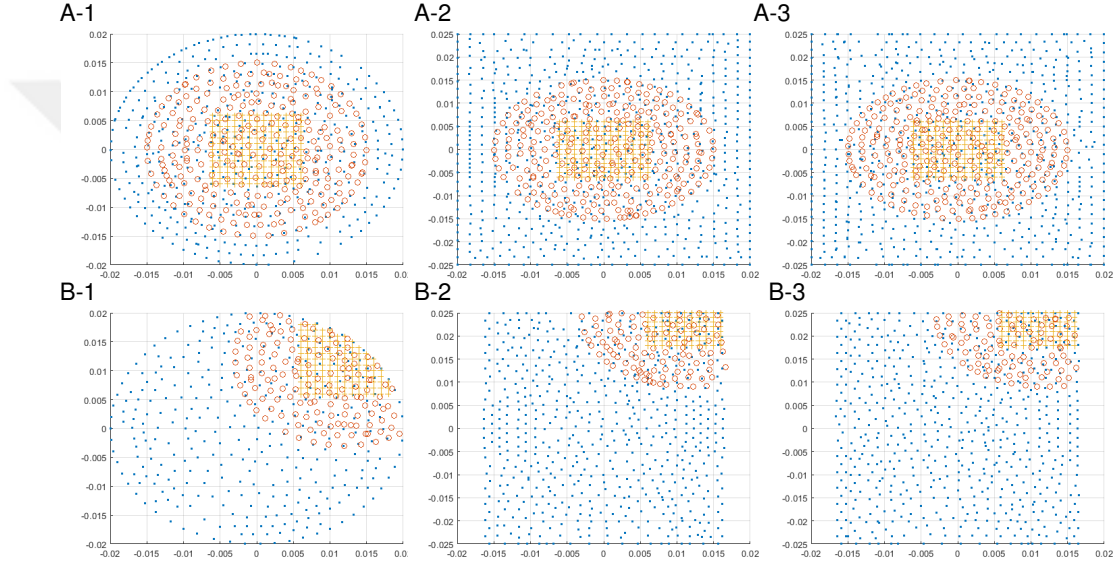


Figure 4.3: Whole object (blue dots), Local ROI (red circles) and Solution ROI (orange pluses) for the 3D case. Line A shows where local ROI is at the center of the object, where Line B shows where it is located at the edge of the object. Columns 1, 2 and 3 correspond to axial, sagittal and coronal cross sections, respectively.

The local ROI and its corresponding solution ROI are moved around in space in order to cover the whole object. Since there are no magnetic resonance data outside the object, the regions of segments outside the object are cut accordingly. The boundary conditions are not enforced on the boundaries of local ROI even if the solution ROI is cut and the local ROI is on the edge of the solution ROI.

After the conductivity values for each local ROI are obtained, they are combined to obtain the conductivity distribution for the object. When solutions of separate PDEs are combined, some variation is expected since the PDEs of interest are ill-conditioned and do not have a single solution. To improve combining and prevent any artifacts around local ROI boundaries, the constant boundary

condition ( $\sigma = 0.5s/m$ ) is enforced on the solution ROI boundaries. This also helps to obtain a more stable solution, especially when a small solution ROI is used.

There are a couple of factors that are used for this decision. First of all, the size of the solution ROI should be large enough that we obtain a stable solution to the PDE system. Moreover, the dependence of the reconstructed conductivity values should be low enough to the region outside of the solution ROI. In other words, the sensitivity of the conductivity values with respect to the phase of  $B_1^+$  should be low enough for the nodes that we do not use in the solution. The last factor is that the solution ROI should be large enough that the boundary conditions that we apply on the solution ROI boundaries do not significantly disturb the reconstructed conductivity values in the local ROI. For the remaining of this thesis, for 2D reconstructions, local ROIs are  $15mm \times 15mm$  squares with  $1.5mm$  resolution, and solution ROIs are circles with  $30mm$  radius. For 3D cases, local ROI size is  $12mm \times 12mm \times 12mm$  with  $1.5mm$  resolution, and solution ROIs are spheres with  $20mm$  radius. The details of how these values are selected are discussed in the following sections.

#### 4.3.4 Sensitivity Maps

To determine segment sizes, sensitivity maps of the reconstructed conductivity values, depending on the phase of  $B_1^+$ , are calculated. For this, a random point is selected in the object, which corresponds to a local ROI with a single node. Solution ROIs of different sizes are defined around this node. To calculate the sensitivity of the solution at the initial node with respect to each node in the solution ROI, the phase of  $B_1^+$  in that node is modified by 0.1% and the conductivity at the initial node is calculated. Then, conductivity at the initial node is calculated again without any modifications to the phase data, and sensitivity is calculated using the following equation:

$$S_n = \frac{\frac{(\sigma_n - \sigma_r)}{\sigma_r}}{\frac{(\phi_{nf} - \phi_{ni})}{\phi_{ni}}} \quad (4.3)$$

Where:

$\sigma_r$ : Reference conductivity, which is the conductivity of the initial node calculated without modifying any phase data.

$\sigma_n$ : Conductivity of the initial node, calculated after modifying the phase of the node n.

$\phi_{ni}$ : Original phase data of node n.

$\phi_{nf}$ : Modified phase data of node n.

The same operation is repeated for Helmholtz MREPT, cr-MREPT, and cr-MREPT with a boundary condition value  $\sigma = 0.5s/m$  at the solution ROI boundaries, for 2D and 3D. In order to better emphasize the change of sensitivity with distance, 2 different representations of sensitivity are given; (i) 2D sensitivity maps, where  $S_n$  values are plotted in the local ROI, and (ii) normalized sensitivity values, which are cross-sectional views of the 2D sensitivity distributions divided by the maximum sensitivity value for each case, to avoid the effect of different MREPT methods.

### 4.3.5 Boundary Condition Analysis

Another condition for determining the solution ROI size is that the solution ROI should be large enough so that the constant boundary condition we apply during the solution of the PDE does not affect the reconstruction result for the local ROI. This condition is not applicable for Helmholtz MREPT, which is a point-wise method anyway.

To see the effect of the enforced boundary condition, a process similar to the sensitivity map calculation is applied; a random point is selected in the object, and a solution ROI of different sizes are defined around this node. This time, the

constant boundary condition of  $\sigma = 0.5s/m$  is enforced. The resulting conductivity value at the initial node is then compared to the actual conductivity value by calculating the percentage, using the following formula;

$$S_{bc} = 100 \times \frac{(\sigma_n - \sigma_a)}{\sigma_a} \quad (4.4)$$

Where:

$\sigma_a$ : Actual conductivity, which is the true conductivity used in EM simulations.  
 $\sigma_n$ : Calculated conductivity, after enforcing constant boundary conditions on solution ROI boundaries.

#### 4.3.6 Parallelization

After dividing the object into smaller volumes, we end up with many smaller equation systems instead of a one large system. This has two advantages:

- Memory requirement for solving the system is significantly less demanding
- The solution of smaller equation systems can be parallelized

The first advantage means that conductivity maps can be obtained even for large volumes, which is not possible with a direct solution because of hardware limitations. Moreover, it is expected that the solution time can be decreased even without parallelization, since solving for individual local ROI can be quite fast.

With parallelization, the theoretic limit for the solution time becomes equal to the solution time for an individual solution ROI plus the time required to combine the results. This is, of course, the case when an adequate computer with enough computational power is available to work on each solution ROI at the same time. Although many different methods can be used for parallelization, we used the

built-in parallel for loop of Matlab, “parfor”, to solve for different segments at the same time during the study.

A Unix-based server (Ubuntu OS) is used with an Intel Xeon Phi 7290 @1.50GHz processor with 72 cores with 4 threads per core and 384GB of RAM for the solutions. Parallelization of up to 64 was implemented. Matlab version 2025b is employed for implementation of the proposed methods.

## 4.4 Results

### 4.4.1 Sensitivity Analysis

Fig. 4.4 shows the sensitivity results in 2D, for a uniform simulation phantom for Helmholtz MREPT, cr-MREPT and cr-MREPT with boundary condition value  $\sigma = 0.5s/m$  at the solution ROI boundaries, for different solution ROI size. Fig. 4.5 presents the normalized cross-section views of sensitivity values shown in Fig. 4.4, for a solution ROI is of  $30mm$  radius.

For the Helmholtz MREPT method, the sensitivity depends only on a couple of nodes around the target node, which are used to calculate the first- and second-order derivatives. This result is expected since Helmholtz MREPT is a point-wise method. Similarly, Helmholtz MREPT is able to give the correct conductivity values, even with the smallest solution ROI size. For cr-MREPT without any boundary conditions, the solution of the PDE becomes unstable for the solution ROI size smaller than  $25mm$  radius. For these cases, the sensitivity values are significantly high as the PDE system is highly sensitive to variations in the  $B_1^+$  phase data. When the solution ROI is large enough to obtain a stable solution, it can be seen that the solution is mostly dependent on nodes that are closer to the target node, but the region to which the solution is sensitive is larger compared to Helmholtz MREPT. When cr-MREPT is implemented with constant boundary conditions, it can be seen that the sensitivity of the solution is significantly reduced, even for a quite small (radius =  $10mm$ ) solution ROI. However, for such a

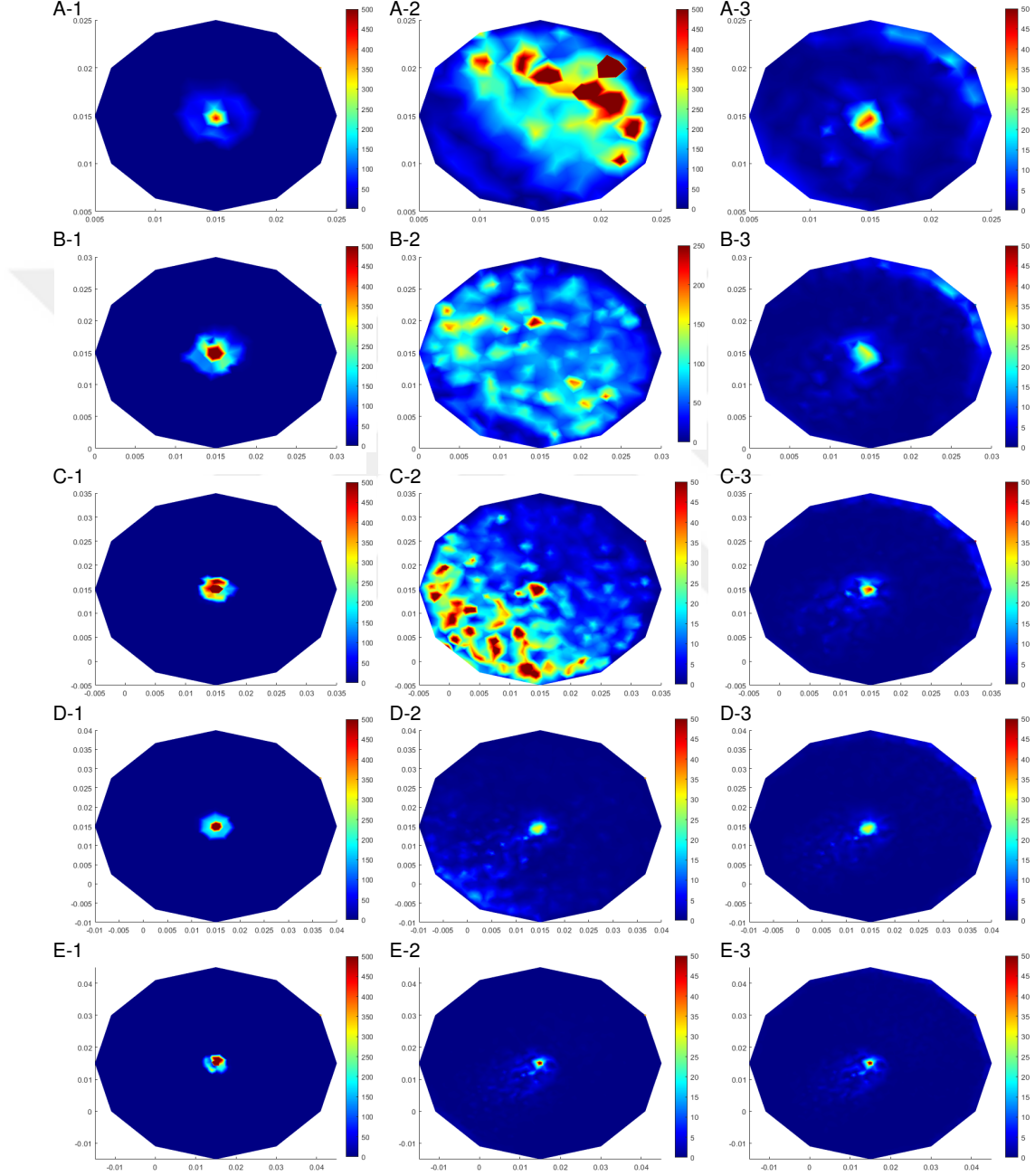


Figure 4.4: Sensitivity distributions for different MREPT methods and different ROI sizes, for a uniform phantom. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition. Lines A-E corresponds to different solution ROI radii; 10, 15, 20, 25 and 30 mm respectively.

small ROI the constant boundary condition dominates the obtained conductivity values, which will be discussed later.

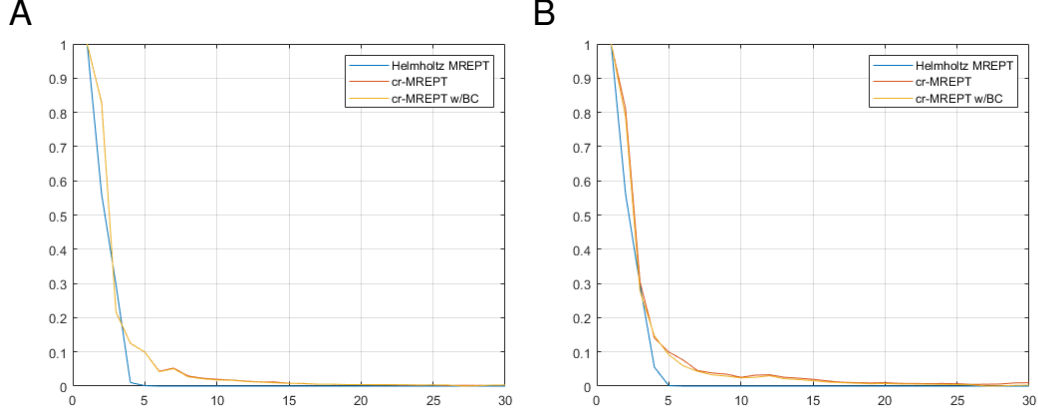


Figure 4.5: Normalized sensitivity results for different MREPT methods in 2D, for a uniform phantom. X-Axis corresponds to the distance from the initial node in mm. Different curves represent Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition. (A) Noiseless case. (B) Noise added case.

Fig. 4.5 shows the normalized sensitivity results for Helmholtz MREPT, cr-MREPT and cr-MREPT with boundary condition value  $\sigma = 0.5s/m$  at the solution ROI boundaries, with respect to distance from the initial node. Since Helmholtz MREPT is a point-wise method, sensitivity is non-zero for only couple of nodes, which are used for calculating second order derivatives. Since the maximum mesh size we employ is  $1.5mm$ , the normalized sensitivity becomes almost zero after  $3 - 4mm$ . For MREPT cases, the sensitivity also depends on the nodes that are further away and becomes zero after approximately  $20mm$ . For noise added cases, the region to which the solution is sensitive is slightly larger and expands to approximately  $25mm$ . It is also important to note that for cr-MREPT, there is no significant difference in sensitivity with or without enforcing constant boundary condition.

Fig. 4.6 shows the sensitivity results in 2D for a simulation phantom with 2 conductivity anomalies for Helmholtz MREPT, cr-MREPT, and cr-MREPT with boundary condition value  $\sigma = 0.5s/m$  at the solution ROI boundaries, for different solution ROI size. For Helmholtz MREPT and cr-MREPT without boundary

conditions, the sensitivity results are quite similar. For Helmholtz MREPT, the sensitivity is high only around the target node, and successful reconstructions can be achieved without dependence on the ROI size of the solution. When no boundary condition is applied, the cr-MREPT method requires an ROI radius larger than  $20mm$ . For an ROI smaller than that, the solution becomes unstable and highly dependent on the  $B_1^+$  phase data. When cr-MREPT is applied with boundary conditions, sensitivity analysis shows that the solution is more stable even for smaller ROI. However, when the reconstruction results are examined, it is seen that the applied boundary condition is quite dominant for smaller ROI and an ROI radius larger than  $20mm$  is required for a successful reconstruction.

Fig. 4.7 shows the sensitivity distributions in constant x-, y- and z-planes for 3D case for Helmholtz MREPT, cr-MREPT and cr-MREPT with boundary condition value  $\sigma = 0.5s/m$  at the solution ROI boundaries. Since the results are quite similar to the 2D cases, only the case for selected solution ROI size ( $r = 20mm$ ) is given. Fig. 4.8 shows the normalized cross-section views of the sensitivity values shown in Fig. 4.7.

Sensitivity distributions in 3D are quite similar to 2D cases. The sensitivity of Helmholtz MREPT is limited to a radius of 3-4 mm of the initial node, where for cr-MREPT it extends to a range of 20 mm. Moreover, in 3D cases, it is found that applying boundary conditions in cr-MREPT enlarges the region that significantly affects the solution for a given node, unlike in 2D reconstructions where enforcing boundary condition does not affect sensitivity. It is also important to note that the sensitivity in the z-direction is quite similar to the x- and y-directions, although the cr-MREPT equation is not spherically symmetric.

As mentioned earlier, another condition for determining the solution ROI size is that a stable conductivity reconstruction can be obtained, and the solution ROI should be large enough so that the constant boundary condition we apply during the solution of the PDE does not affect the reconstruction result for the local ROI. Fig. 4.9 shows the percentage error for the simulation phantom with 2 conductivity anomalies for Helmholtz MREPT, cr-MREPT, and cr-MREPT with boundary condition ( $\sigma = 0.5s/m$ ) enforced, for different solution ROI size

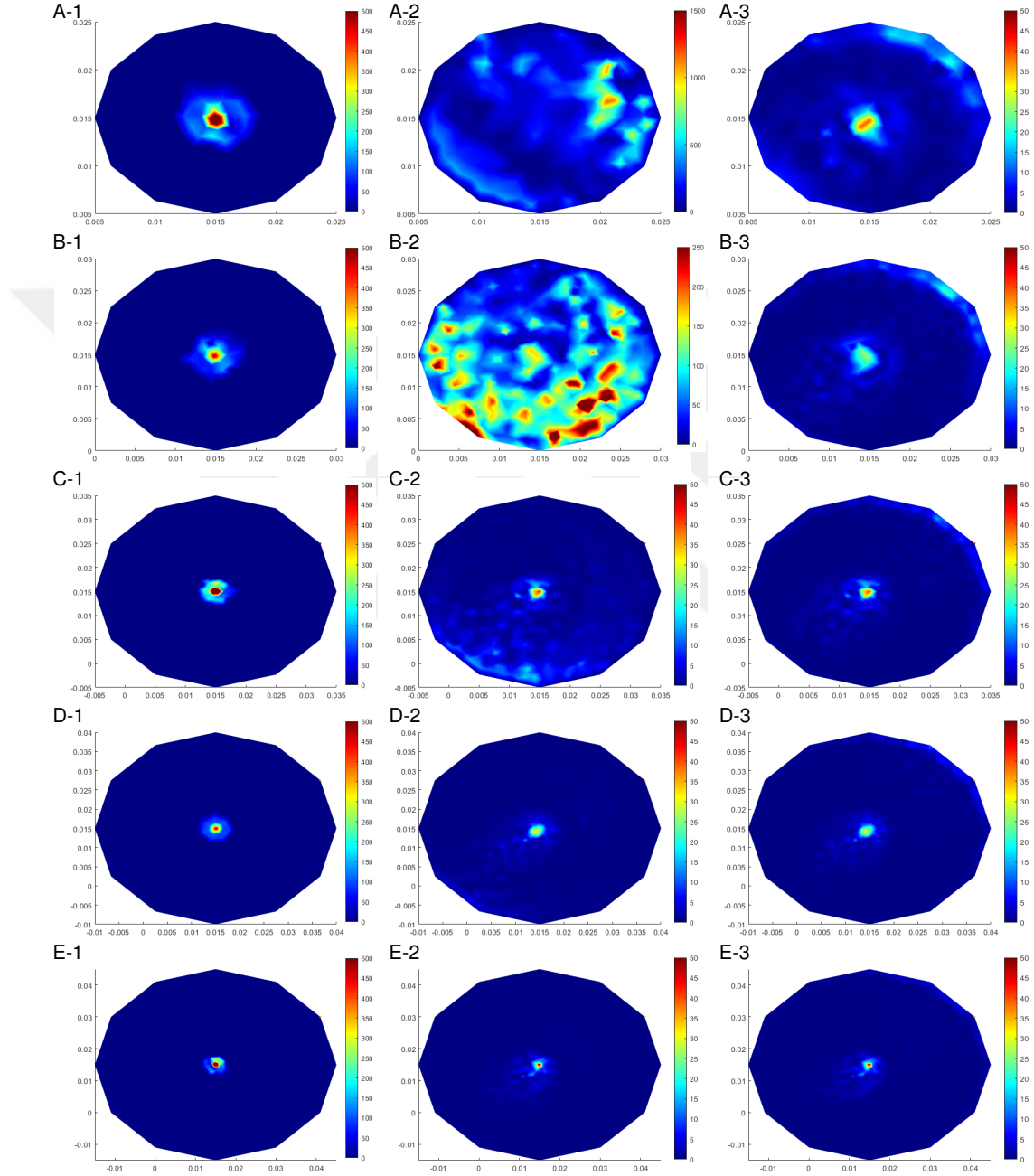


Figure 4.6: Sensitivity distributions for different MREPT methods and different ROI sizes, for a cylindrical phantom with 2 conductivity anomalies. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition. Lines A-E corresponds to different ROI radii; 10, 15, 20, 25 and 30 mm respectively. Distance unit is  $m$ , unless specified in the plot axes.

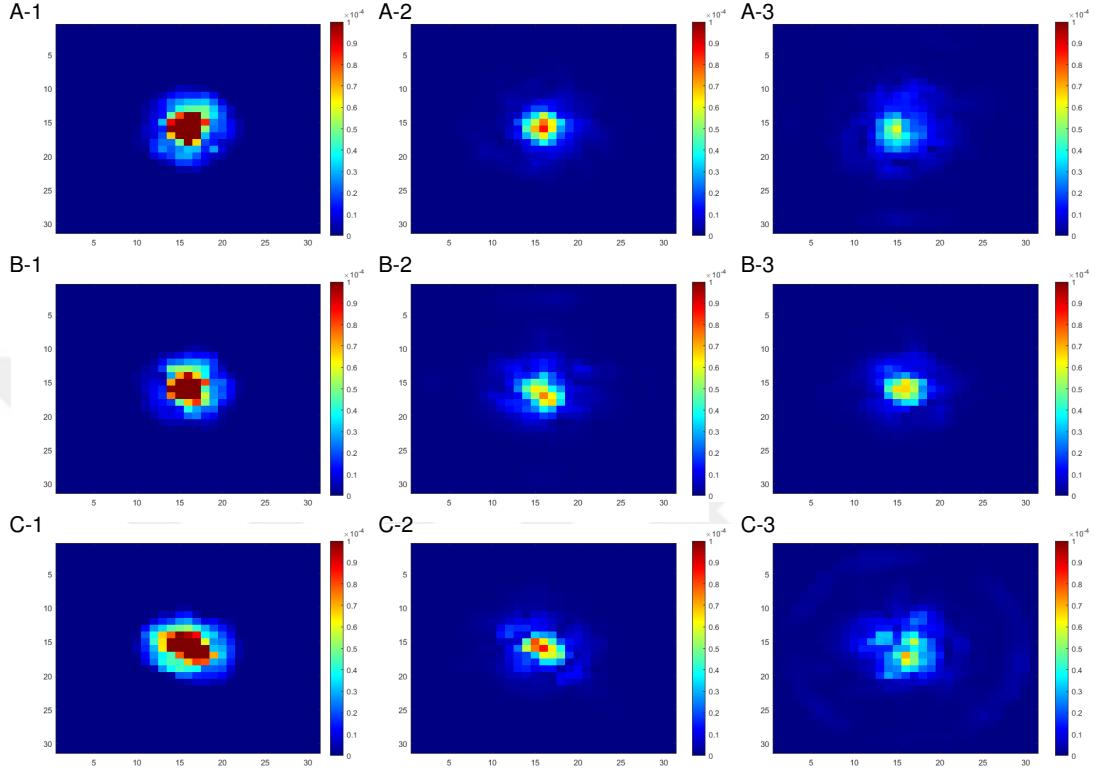


Figure 4.7: Sensitivity results in 3D for different MREPT methods and different ROI sizes, for a cylindrical phantom with 2 conductivity anomalies. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition. Lines A-C corresponds to z-, y- and x-cross-sections, respectively.

and both 2D and 3D solutions. For Helmholtz MREPT, the results are quite similar to the sensitivity results; percentage error becomes almost zero after 3 – 4mm for both 2D and 3D cases. For cr-MREPT with no boundary conditions assigned, the error is high until the ROI is large enough to obtain a stable solution. When boundary conditions are applied, the error is relatively low for a small ROI compared to the case without boundary conditions, since the boundary conditions stabilize the solution. However, the reconstructed value is not correct until the ROI is large enough that the effect of boundary conditions is negligible.

To give a better intuition of ROI size selection and how it affects the reconstruction results, Figs 4.10 and 4.11 show the results of conductivity reconstructions for the cases given in Figs 4.4, 4.6 and 4.7, respectively.

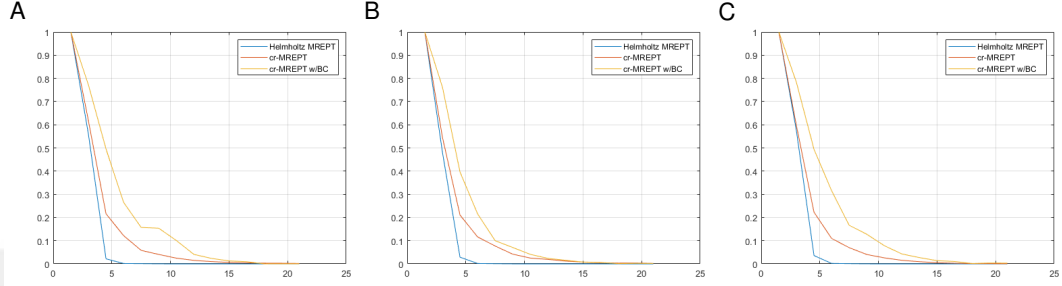


Figure 4.8: Sensitivity results for different MREPT methods applied in 3D and in different directions, for a cylindrical phantom with 2 conductivity anomalies. Distance unit is  $m$ , unless specified in the plot axes. (A) X-direction. (B) Y-direction. (C) Z-direction

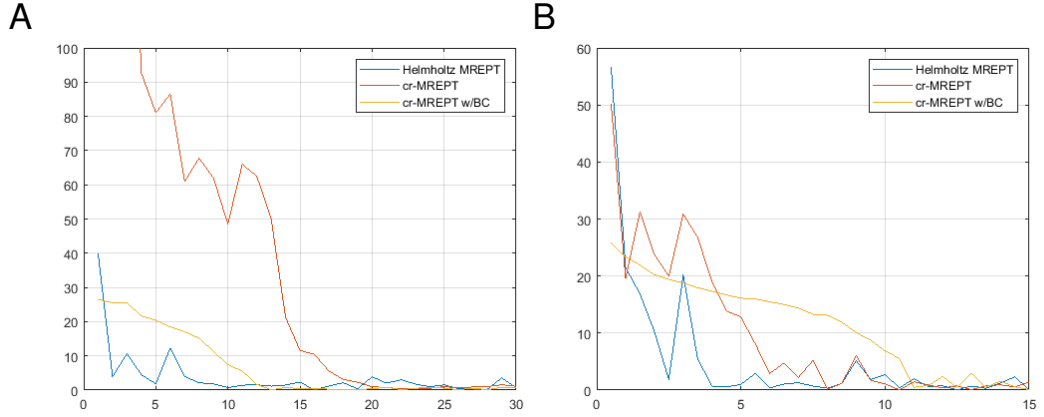


Figure 4.9: Percentage error for different MREPT methods, for phantom with 2 conductivity anomalies. (A) 2D solution. (B) 3D solution. X-Axis corresponds to the solution ROI radius. Different curves represent Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition. The initial node is selected close to the anomalies so that the applied boundary condition affects the solution. Note that the scales are different for plots.

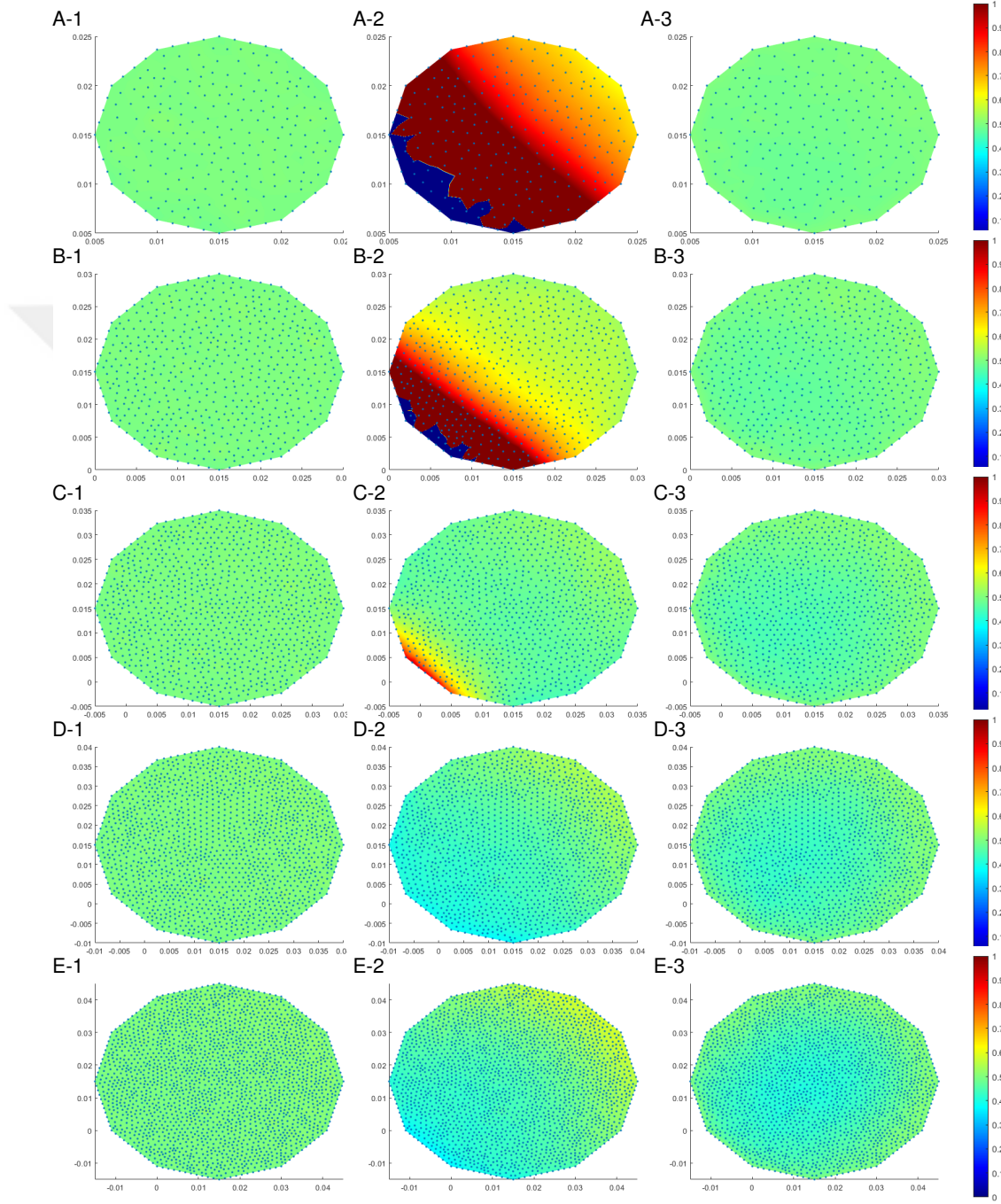


Figure 4.10: Conductivity reconstruction results for different MREPT methods and different ROI sizes, for a uniform phantom. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition. Lines A-E corresponds to different ROI radii; 10, 15, 20, 25 and 30 mm respectively. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes.

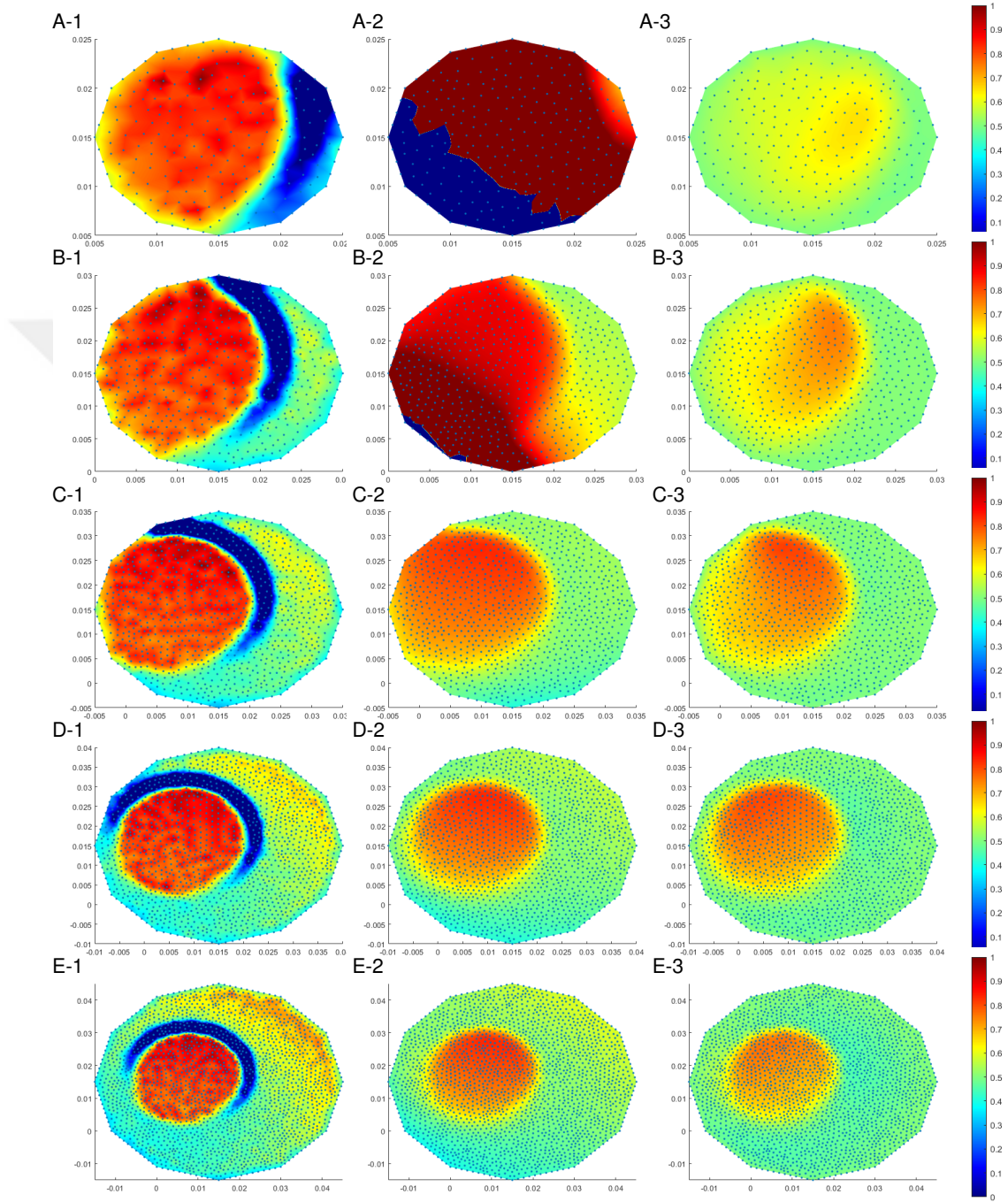


Figure 4.11: Conductivity reconstruction results for different MREPT methods and different ROI sizes, for a cylindrical phantom with 2 conductivity anomalies. Solution ROI is selected to be around one of the conductivity anomalies. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition. Lines A-E corresponds to different ROI radii; 10, 15, 20, 25 and 30 mm respectively. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes.

For both uniform phantom and phantom with 2-anomalies, it can be seen that Helmholtz MREPT is able to successfully reconstruct the conductivity values, barring the internal boundary artifacts. For cr-MREPT when no boundary conditions are enforced, the solution of the PDE is not stable. The correct conductivity values are obtained only when a relatively large ROI of the solution is chosen. The solution becomes stable even for a small solution ROI when boundary conditions are enforced. However, it is clear from Fig. 4.11 that the boundary conditions significantly affect the reconstruction results.

#### 4.4.2 Reconstruction Results

Fig. 4.12 shows the conductivity results obtained with the proposed method for the cylindrical phantom with 2 conductivity anomalies. Similarly to the previous figures, results obtained using 3 different methods are presented; Helmholtz MREPT, cr-MREPT, and cr-MREPT with boundary condition value  $\sigma = 0.5s/m$  at the solution ROI boundaries. Since it is a point-wise method, Helmholtz MREPT is not affected when local ROIs are used, and the reconstruction result is the same when the proposed method is used or not. However, for cr-MREPT, the results are not so straightforward when no boundary conditions are applied. Although the conductivity reconstructions of each individual local ROI are stable and generally correct, there is a significant offset between different local ROI, resulting in a “pixelated” conductivity map. Implementing boundary conditions, however, overcomes the offset between local ROIs and almost perfect conductivity maps are obtained. Fig. 4.12 also shows the reconstruction results when noise is added to the simulation data, and quite similar results are obtained compared to the noiseless cases.

Fig. 4.13 presents the results of the conductivity reconstruction for 3 slices in the XY-plane, for  $z = -16mm/0mm/+16mm$ , for the cylindrical phantom with z-dependent conductivity values, obtained in 3D. Fig. 4.14 shows the cross section views in each direction, for the same phantom. Similarly to the 2D case, Helmholtz MREPT and cr-MREPT with constant boundary conditions are able

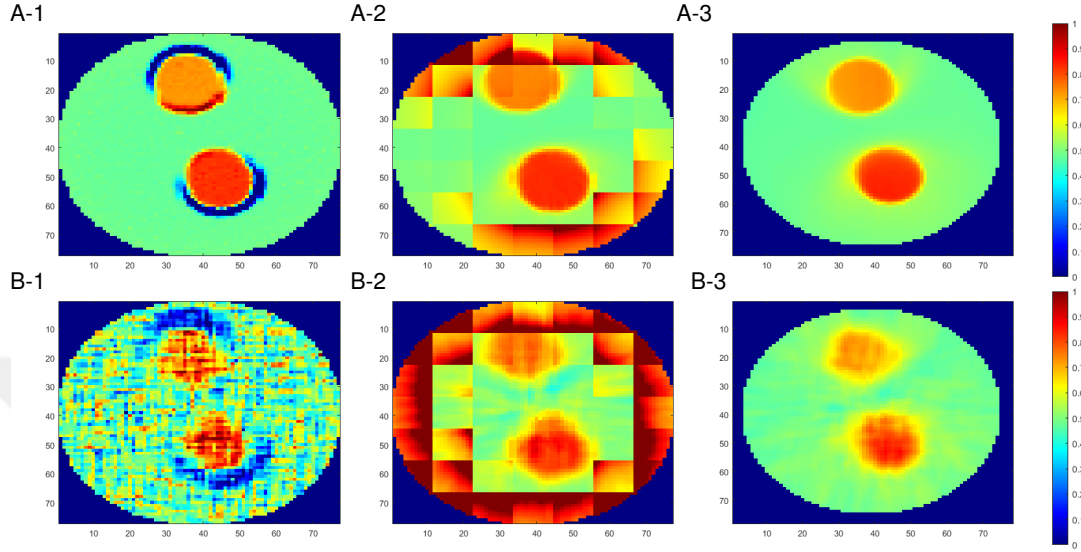


Figure 4.12: Conductivity reconstruction results for different MREPT methods, for a cylindrical phantom with 2 conductivity anomalies. Line A shows the noiseless case, and Line B shows the noise-added simulations. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition, respectively. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes.

to obtain almost perfect conductivity reconstruction, where clear offsets are observed when no boundary conditions are applied in cr-MREPT.

Fig. 4.16 shows the reconstructed conductivity maps for a 3D brain phantom. The top, middle and bottom rows correspond to  $xy$ -( $z = 0$ ),  $xz$ -( $y = 0$ ) and  $yz$ -planes( $x = 0$ ), respectively. The columns correspond to reconstructions obtained using Helmholtz MREPT, cr-MREPT, and cr-MREPT with boundary condition value  $\sigma = 0.5s/m$  at the local ROI boundaries. Although the phantom is much more complicated than in the previous cases, the results are, in general, quite similar. Helmholtz MREPT is able to obtain the reconstruction results with no effect of using a smaller ROI and combining, while for cr-MREPT it requires a constant boundary condition applied to successfully obtain the conductivity maps.

Table 4.2 shows the reconstruction computation times for the cylindrical phantom with  $z$ -dependent conductivity anomalies and the human head model, for

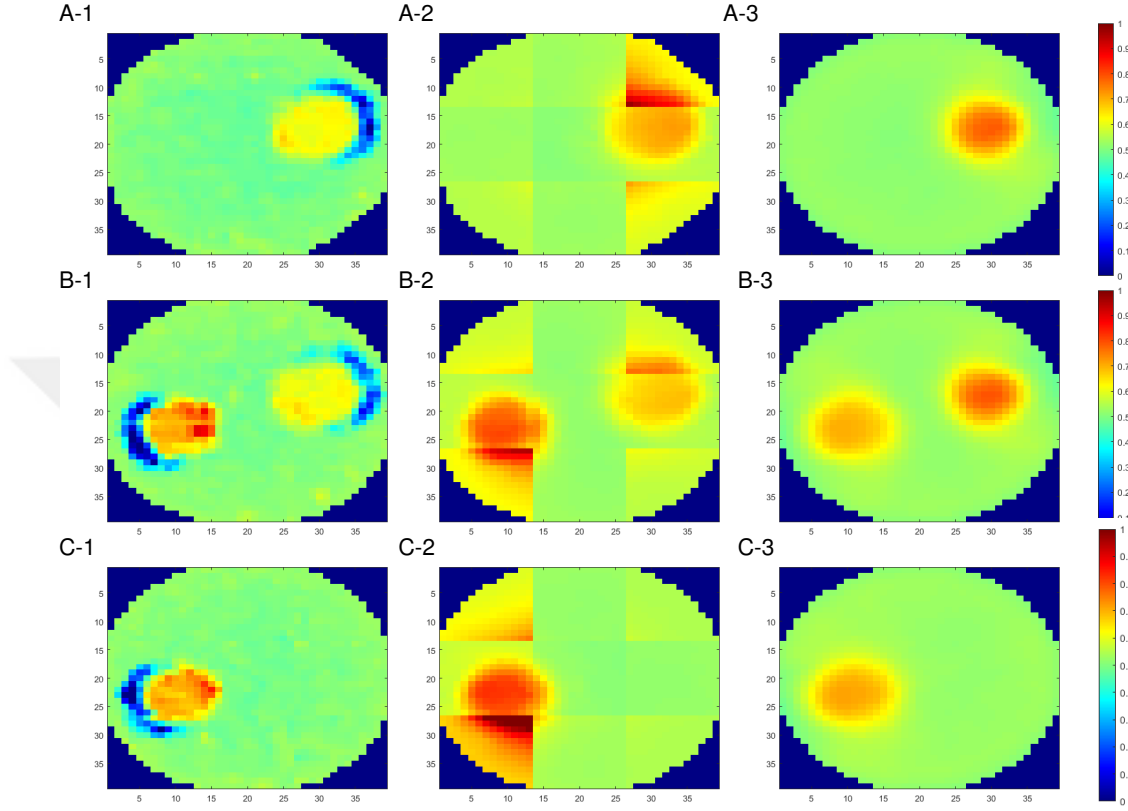


Figure 4.13: Conductivity reconstruction results obtained in 3D for different MREPT methods, for a cylindrical phantom with  $z$ -dependent conductivity anomalies. Row A shows the  $z = -16mm$  slice, Row B shows the  $z = 0mm$  slice and Row C shows  $z = +16mm$  slice. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition, respectively. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes.

various parallelization cases. Direct solution means when the PDEs are constructed and solved for the entire solution ROI without partitioning into local ROIs. It corresponds to the straight-forward case where the cr-MREPT method is applied in a global 3D tetrahedral mesh. For both phantoms, this method gives the longest solution time as expected, though solution time for human head model is significantly longer because this phantom has a larger size. When the proposed method is applied, cylindrical phantom with  $z$ -dependent conductivity anomalies is divided into 45 local ROIs, where the human head model is divided into 180 local ROIs of the same size. The case where the solution ROI is divided

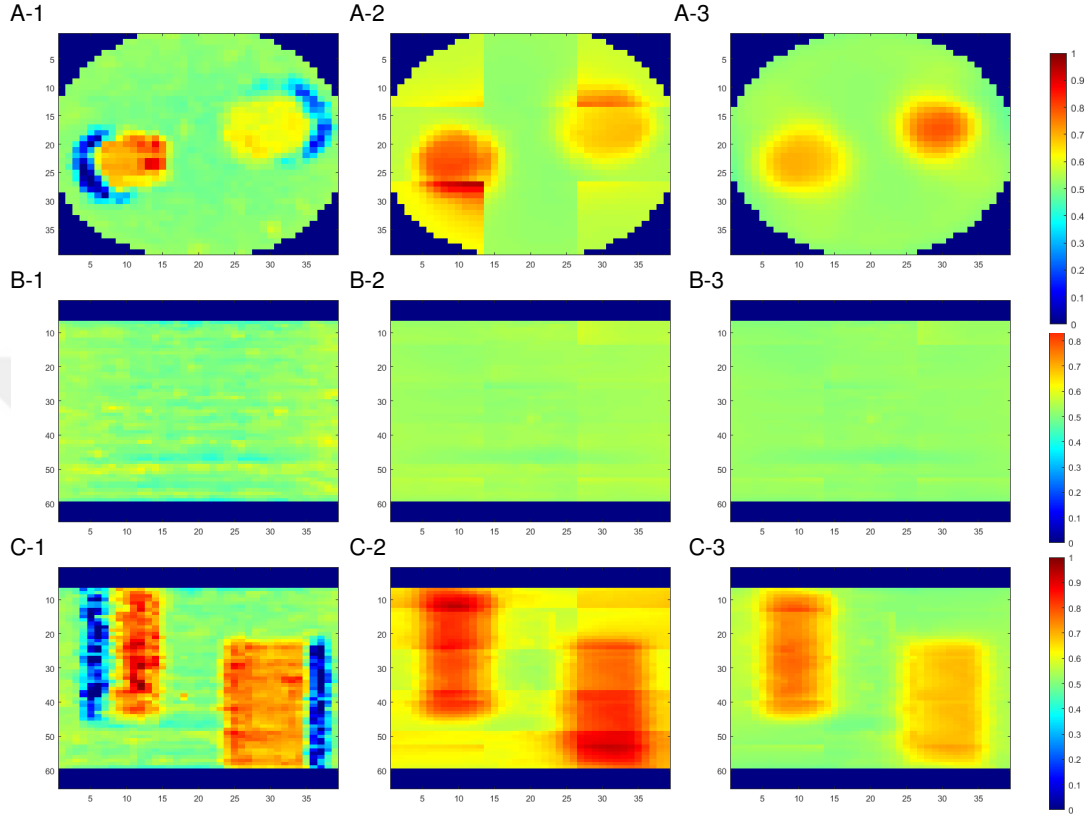


Figure 4.14: Conductivity reconstruction results obtained in 3D for different MREPT methods, for cylindrical phantom with z-dependent conductivity anomalies. Row A shows the  $x = 0mm$  slice, Row B shows the  $y = 0mm$  slice and Row C shows  $z = 0mm$  slice. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition, respectively. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes.

into smaller local ROIs but the solutions are achieved sequentially (without parallelization) is given in Line 4 of Table 4.2. It can be seen that, even without any parallelization, the solution time is significantly reduced with the proposed method, since solving multiple smaller problems is computationally less demanding compared to a single, much larger problem. Increasing the number of parallel solvers further decreases the solution time almost linearly.

Finally, in the last line of Table 4.2, the solution time for a single local ROI is given. Since the local ROI size is the same for both phantoms, the solution times are also the same for a single local ROI. It can be concluded that, with proper

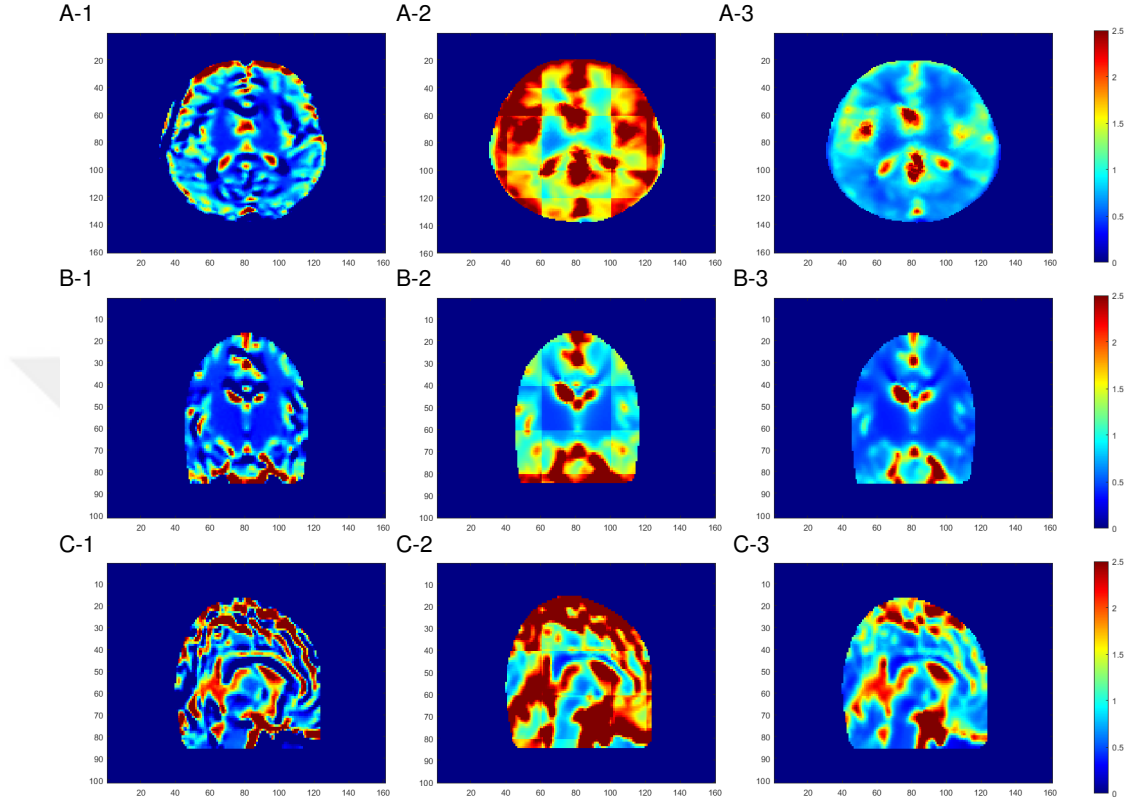


Figure 4.15: Conductivity reconstruction results for different MREPT methods, for human head phantom. Row A shows  $z = 0$ , Row B shows  $y = 0$  and Row C shows  $x = 0$  slices. Columns 1, 2 and 3 corresponds to Helmholtz MREPT, cr-MREPT and cr-MREPT with constant ( $\sigma = 0.5s/m$ ) boundary condition, respectively.

hardware, parallelization rate can be increased and solution time for a single local ROI would be the limiting factor for the overall solution time. However, there is some overhead time involved in the total solution time for setting up the PDEs and combining the results after parallel solutions are completed. For example, with 64 parallel solvers, which is larger than the number of local ROIs ( $= 45$ ) for the cylindrical phantom, the total solution time is 57 s, indicating that the overhead is 27 s. For human head model, each parallel solver works 3 times since there are 180 local ROIs and 64 parallel solvers. This takes approximately 90 seconds, 3 times the solution time for a single local ROI, and the overhead is approximately 45 seconds for this case.

Table 4.2: Solution times for various phantoms and methods. Direct solution corresponds to the case where no segmentation or parallelization is applied, and the PDEs are solved for the whole object. Acceleration rate is given with respect to direct solution. When number of parallel solvers is 1, segmentation is applied but parallelization is not used.

|                                        | 3D Cylinder            |                   | 3D Brain Phantom       |                   |
|----------------------------------------|------------------------|-------------------|------------------------|-------------------|
| Number of Parallel Solvers             | Computation Time (sec) | Acceleration Rate | Computation Time (sec) | Acceleration Rate |
| Direct Solution                        | 2595                   | -                 | 14043                  | -                 |
| 1                                      | 1393                   | 1.86              | 5443                   | 2.58              |
| 2                                      | 728                    | 3.56              | 2748                   | 5.11              |
| 4                                      | 384                    | 6.75              | 1397                   | 10.05             |
| 8                                      | 229                    | 11.33             | 735                    | 19.11             |
| 16                                     | 157                    | 16.53             | 405                    | 34.67             |
| 32                                     | 91                     | 28.52             | 197                    | 71.30             |
| 64                                     | 57                     | 45.53             | 133                    | 105.58            |
| Maximum time for single reconstruction | $\sim 30$              | -                 | $\sim 30$              | -                 |

## 4.5 Discussion

The sensitivity of the reconstructed conductivity value for a single node is calculated with respect to the phase of  $B_1^+$  of the nodes at a distance to determine the minimum ROI size that can be used to successfully employ different MREPT methods. Since Helmholtz MREPT is a point-wise method, it was expected that the solution can be obtained even for a single node, and the solution is only sensitive to the region where second order derivatives are calculated. The results demonstrated this, as it was shown that the solution is only sensitive to the  $B_1^+$  phase data of neighboring nodes, since the derivative calculations use only these. Since the mesh we used has a maximum size of  $1.5mm$ , this corresponds to  $3 - 4mm$  around the node of interest, as consistent with the sensitivity cross section plots (Fig. 4.5 and Fig. 4.8). Successful reconstructions were achieved even for the smallest ROI ( $r = 10mm$ ). On the other hand, cr-MREPT has a more complicated equation, and it is not clear how sensitive the solution is to the  $B_1^+$  phase value of any given node in ROI. Our hypothesis was that a

fairly small region would be enough to obtain the correct conductivity values, and the results have shown that this hypothesis holds. Although a relatively large ROI is required when no boundary condition is applied compared to the constant boundary condition, for both cases, a small ROI was sufficient to obtain the conductivity maps. Moreover, it is shown that the sensitivity is independent of the object to be imaged, or if reconstruction is done in 2D or 3D as sensitivity and conductivity results in local ROI are pretty similar for all cases. It is also interesting that the sensitivity in the z-direction is almost identical to that in other directions.

Two main factors for determining the local ROI radius was; (i) sensitivity is small enough that the  $B_1^+$  phase data outside of the selected region does not affect the conductivity calculation, and (ii) constant boundary conditions that were enforced on the solution ROI boundaries to increase solution stability do not significantly affect the reconstruction results in the nodes we are interested in, namely the local ROI. Inspecting the results from Fig. 4.4 to Fig. 4.12, it is determined that the smallest solution ROI should have at least  $20mm$  radius in 2D cases to obtain the correct conductivity value at a single node at the center of the circle. However, it is more desirable to have a larger local ROI instead of a single point to decrease the number of individual local ROIs, so that the number of calculations is fewer. Because of this, the local ROI is defined as a square  $15mm \times 15mm$  square and solution ROI radius is selected as  $30mm$  so that the node closest to the side of the solution ROI boundary has a distance of approximately  $20mm$ . For 3D cases, a smaller solution ROI was found to be sufficient to obtain more stable solutions. In this case, the limiting factor for the smallest solution ROI size is the minimum region where boundary conditions do not significantly affect the conductivity values in the target ROI. Hence, a spherical solution ROI radius of  $20mm$  is selected for a local ROI of a  $12mm \times 12mm \times 12mm$  cube.

Combining the conductivity results of each individual local ROI and obtaining a high quality conductivity map for the whole solution ROI was another challenging part of the study. When no boundary conditions are applied, the overall structure/shape of the conductivity can be obtained successfully. However, clear

offsets are observed between different solution ROIs, causing artifacts along the local ROI boundaries in the final conductivity maps. This effect is clearer on the outer local ROI sections, where some of the nodes are eliminated since they correspond to points outside of the object. This phenomenon can be explained as the PDE systems we are solving are ill-conditioned and do not have a unique solution. Although a stable solution is obtained for each local ROI, it is reasonable to expect the offset we have observed in the results. However, enforcing boundary conditions further decreases the degree of freedom of the solution and removes the offset between local ROIs. This can be observed for both 2D and 3D, and for all phantoms.

The reconstruction results are found to be satisfactory for all cases in which the proposed method is used. Conductivity maps that are obtained by solving the PDE in solution ROIs and combined after are identical when conductivity is obtained for the whole object in a single PDE system. Moreover, solutions obtained using both methods are quite close to the true conductivity values of the phantoms. Fig. ?? shows the reconstruction results obtained with the standard direct solution and the proposed method. The numerical evaluation also shows that the results are very similar; the direct solution has an MSE of 5.75, while the proposed method has an MSE of 5.58.

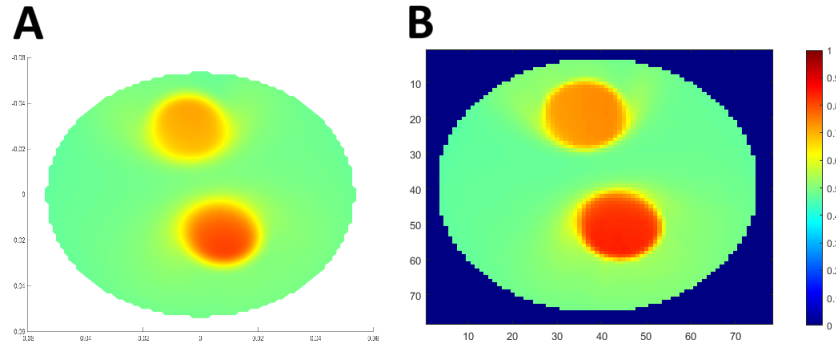


Figure 4.16: Conductivity reconstruction results for 2-anomaly phantom, obtained using the standard direct solution and the proposed method. (A) Standard direct solution method. (B) Proposed method.

As mentioned above and as can be seen in Table 4.2, using smaller solution

ROIs to obtain the solution significantly decreases the solution time and memory requirement. Compared to the direct solution method, even if partitioning to smaller ROIs but no computation parallelization is implemented, the solution time is approximately decreased to half. In this study, maximum parallelization of up to 64 is employed. The solution time for a single solution ROI is found to be around 30 seconds for a full, central solution ROI, which would also be the theoretical limit for the shortest computation time. This, and the overhead time for additional operations such as setting up PDEs and combining the parallel results can be improved by using a faster CPU. In addition, a very simple parallelization method, “parfor” function of Matlab, is used in this work. This method basically makes use of the availability of a multi-core computer architecture. With more optimized methods for parallelization and with use of GPUs, the acceleration rate may be further increased.

# Chapter 5

## Phase-based cr-MREPT Library

### 5.1 Motivation

MREPT is a relatively new and developing imaging technique, and the number of people working on the topic is limited. The method, in all forms, requires calculation of derivatives and solution of a partial differential equation, which may quickly become complicated to implement. It might be especially discouraging for an interested researcher that is new to the MREPT, since they would have to start with implementing the existing methods, such as cr-MREPT, since it can take a lot of time and effort.

In addition to this, MREPT research groups around the world are developing their own MREPT variants. These variants, while based on the same principals, employ different equations and are usually required to be implemented from scratch. Implementing different methods can be tricky and time consuming, even for experienced researchers in the field. On the other hand, understanding the working principles of other MREPT methods could be very beneficial in obtaining more information and overcoming the problems related to ones own method.

Helmholtz MREPT, especially the phase-based Helmholtz MREPT, depends

on a relatively simple equation. Despite its well-known problems, such as internal boundary artifacts and concave bias, it is widely used among various research groups due to ease of implementation and can be considered the most popular MREPT method. cr-MREPT (or methods developed by other researchers) is able to provide significantly improved conductivity maps, but has a more complicated main equation to solve. Simply because of the difficulties of implementation, Helmholtz MREPT is usually preferred over cr-MREPT, even though the obtained conductivity maps are worse compared to the ones obtained with cr-MREPT. For either drawing attention of new researchers or increasing the collaboration of various MREPT research groups, it is crucial to have common, easy-to-use implementations of the existing methods. For this purpose, a database called EPTLib is created [96]. However, this database is not complete and has significant problems in implementing cr-MREPT, especially the full-form version.

Part of this thesis work is therefore dedicated to creating a tool for researchers new to the MREPT applications or cr-MREPT method, so that they can have a quick start working on the actual problems of the method instead of implementation related problems.

## 5.2 Methods

### 5.2.1 Implementation

As discussed in the previous section, the main motivation of this part of the thesis is to create a user friendly library for MREPT researchers. The library employs bias-corrected phase-based cr-MREPT as the main method, but Helmholtz MREPT is also included. To make the library easy to use, all related work is implemented in Matlab (The Mathworks, Natick, MA, USA), and the main purpose is that the user will be able to load any data and obtain the conductivity distributions without any additional step.

In order to apply bias correction for the phase-based Helmholtz or cr-MREPT,

we require the  $|B_1^+|$  distribution. Although a low resolution map is sufficient for this purpose, obtaining  $|B_1^+|$  distribution is problematic as discussed in detail in Chapter 3. It is also discussed in Chapter 3 that EM simulations can be performed using generic and uniform EP values ( $\epsilon = 60, \sigma = 0.5$ ) to obtain a  $|B_1^+|$  distribution that can be used in bias correction. Performing such a simulation requires to know the outer shape of the object to be imaged. Two separate cases were considered during implementation to obtain the outer shape information:

- Simulation data: It is assumed that the user has the true conductivity values used in the simulation in addition to the magnetic field phase distribution. True conductivity values will be used to determine the outer shape of the imaged object.
- Experimental data: The user will only need to load complex MRI data that is suitable to calculate the magnetic field phase distribution, such as a complex image obtained using the bSSFP sequence. The magnitude of these data will be used to determine the outer shape of the imaged object.

For the simulation case, it is safe to assume that the user already has the true conductivity distribution since it has already been used to obtain the  $B_1^+$  distribution, during the initial simulations. For an experimental case, obtaining the complex data does not require any additional imaging steps, as the data are already collected this way. Parameters related to the imaging sequence, such as ROI size and resolution, are also critical for successful applications.

After loading the related data and starting the reconstruction process, the outer boundary of the object is determined using “edge” and “bwboundaries” functions of Matlab automatically. Then, the outer boundary is used for harmonic EM simulation at Larmor Frequency. Generic and uniform EP values ( $\epsilon = 60, \sigma = 0.5$ ) are assumed through the object. The simulations are performed using ”PDE” and ”EM model” tools of Matlab. The magnitude of the magnetic field obtained in this simulation is then utilized for bias correction. Finally, the code calculates the conductivity map for Helmholtz and cr-MREPT with bias correction also applied for both cases.

The library includes various simulation and experimental phantoms as built-in examples, but the user is also given the option to load their own data. In addition to this, various parameters and options can be modified in the script.

### 5.2.2 Simulation Phantoms

EM simulations are conducted in COMSOL Multiphysics Software (COMSOL AB, Stockholm, Sweden) for different RF coil and phantom geometries. In order to increase samples, all previously used simulation phantoms are included in the library. These are:

- a uniform cylindrical phantom ( $\sigma = 0.5s/m, \epsilon = 83$ ) with a height of 20-cm and a radius of 6-cm
- a cylindrical phantom of the same size with two conductivity anomalies ( $\sigma = 0.75s/m$  and  $\sigma = 0.85s/m$  for anomalies,  $\sigma = 0.5s/m$  for background,  $\epsilon = 83$ )
- a cylindrical phantom with the same size and four conductivity anomalies ( $\sigma = 1.25s/m, 1s/m$  and  $0.75s/m$  for anomalies,  $\sigma = 0.5s/m$  for background,  $\epsilon = 83$ )
- a cylindrical phantom with the same size and multiple conductivity anomalies ( $\sigma = 1s/m$  anomalies,  $\sigma = 0.5s/m$  for background,  $\epsilon = 83$ )
- a smaller cylindrical phantom with a height of 5-cm and a radius of 2-cm with two z-dependent conductivity anomalies ( $\sigma = 0.65s/m$  and  $\sigma = 0.75s/m$  for anomalies,  $\sigma = 0.5s/m$  for background,  $\epsilon = 83$ )
- a human head model [1]

For all simulations, a 16-rung birdcage coil with a height of 20-cm and a radius of 15-cm is used for RF excitations. The smaller cylindrical phantom has z-dependent conductivity anomalies. Hence, different slices of this phantom

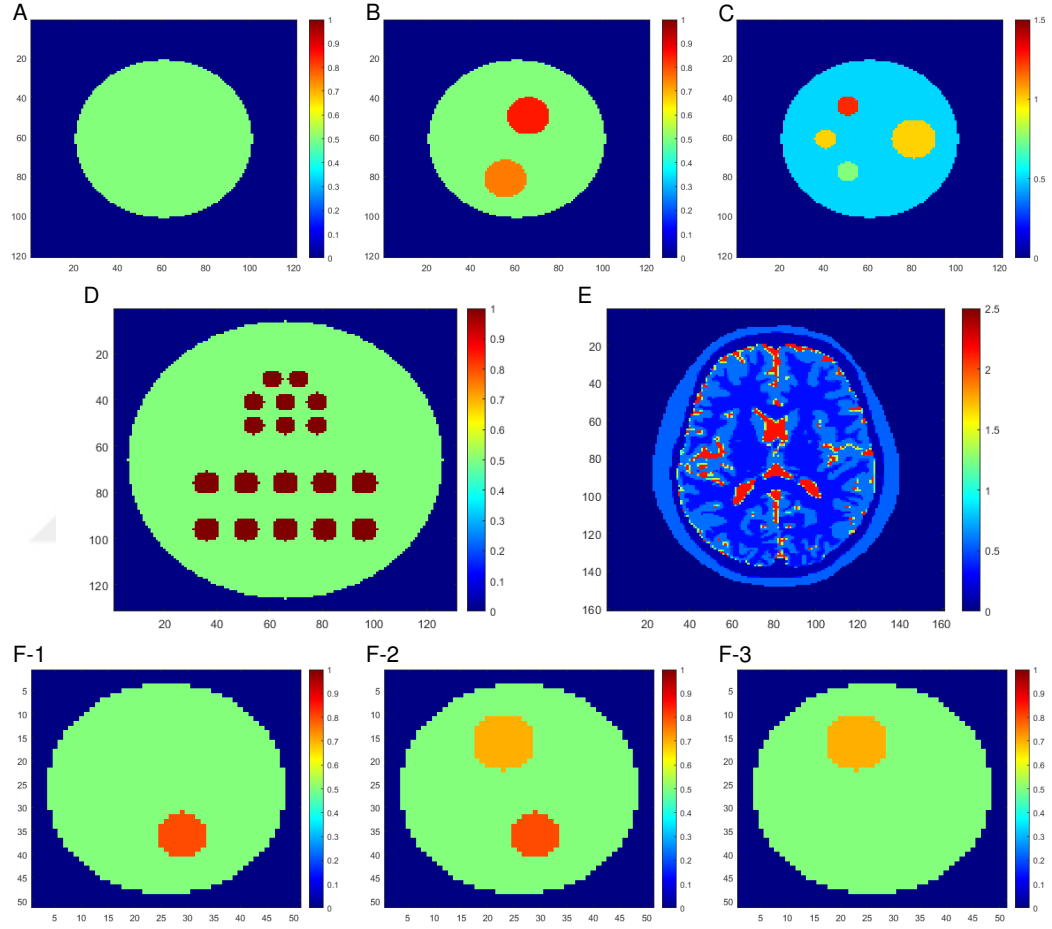


Figure 5.1: True conductivity values of simulation phantom geometries used in the study. Conductivity unit is  $S/m$ , distance unit is m for all cases. (A) Uniform cylindrical phantom. (B) Cylindrical phantom with two z-independent conductivity anomalies. (C) Cylindrical phantom with four z-independent conductivity anomalies. (D) Cylindrical phantom with multiple z-independent conductivity anomalies. (E) Human head model. [1] (F) Cylindrical phantom with height of 5-cm and radius of 2-cm with two z-dependent conductivity anomalies. 1-3 corresponds to top, middle and bottom slices, respectively.

are also included in the prepared library. The true conductivity values of the simulation phantoms are given in Fig. 5.1.

### 5.2.3 Experimental Phantoms

3 different experimental phantoms are included in the prepared cr-MREPT library:

- 2-Anomaly Phantom: A cylindrical phantom with two cylindrical anomalies. Agar jel (20gr/l Agar, 2gr/l NaCl, 0.2gr/l CuSO<sub>4</sub>) is used for the background, and the water solution of 4 – 6gr/l NaCl, 0.2gr/l CuSO<sub>4</sub> is used for the two anomalies.
- 4-anomaly Phantom: A cylindrical phantom with four cylindrical anomalies. Agar jel (20gr/l Agar, 2gr/l NaCl, 0.2gr/l CuSO<sub>4</sub>) is used for the background, and the water solution of 6gr/l NaCl, 0.2gr/l CuSO<sub>4</sub> is used for the two anomalies.
- Resolution Phantom: A cylindrical phantom with multiple small diameter conductivity anomalies.

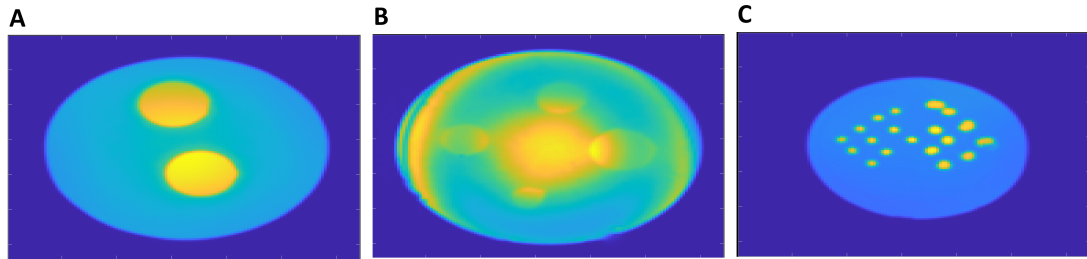


Figure 5.2: Experimental phantoms. (A) 2-anomaly phantom. (B) 4-anomaly phantom. (C) Resolution phantom.

The experiments were conducted in UMRAM (National Magnetic Resonance Research Center) in Bilkent University with a Siemens Tim Trio 3T MR Scanner (Erlangen, Germany). To obtain  $B_1$  phase, 3D bSSFP pulse-sequence is used.

Table 5.1 shows the pulse sequence parameters for the experiments. Fig. 5.2 shows the magnitude views of the MRI data for the experimental phantoms. A bird cage body coil is used for the RF transmit signal, and a 4-channel head coil array is used for the receive signal. Data from different channels of the coil is combined using coil manufacturers combine method.

Table 5.1: Pulse sequence parameters for MRI experiments. 3D bSSFP pulse sequence is employed for each case.

|                    | Resolution(mm) | FOV(mm)      | FA(deg) | TR/TE(ms) | NEX | Duration    |
|--------------------|----------------|--------------|---------|-----------|-----|-------------|
| 2-Anomaly          | 1.17x1.17x1.56 | 150x150x31.2 | 40      | 4.88/2.44 | 32  | $\sim 6min$ |
| 4-Anomaly          | 1.17x1.17x1.56 | 150x150x31.2 | 40      | 10/5      | 20  | $\sim 4min$ |
| Spatial Resolution | 1.56x1.56x1.56 | 150x150x31.2 | 40      | 4.70/2.70 | 32  | $\sim 6min$ |

### 5.3 Results

Fig. 5.3 shows the outputs of the prepared cr-MREPT library, when the human head model simulation is selected as the phantom. The conductivity distribution used in the EM simulations is given. Using this, outer boundary of the phantom is determined. The outer boundary is then used in the EM simulations, where uniform and generic EP values,  $\sigma = 0.5s/m$  and  $\epsilon = 83$ , are used to obtain  $|B_1^+|$ . The obtained  $|B_1^+|$  is also given in Fig. 5.3, as well as the conductivity distributions calculated using Helmholtz and cr-MREPT. The figures to be plotted can be chosen by the user using a single input. In this case, only figures representing an important step of the reconstruction process are selected. More steps, such as calculated partial derivatives of the  $B_1^+$  phase, can also be plotted for debugging purposes.

Another option that the user can choose is to apply bias correction or leave the concave bias uncorrected. Fig. 5.4 presents the Helmholtz and cr-MREPT conductivity reconstruction results for uncorrected and bias corrected cases. It can be seen again that bias correction is highly effective for both Helmholtz and cr-MREPT, and concave bias is removed completely.

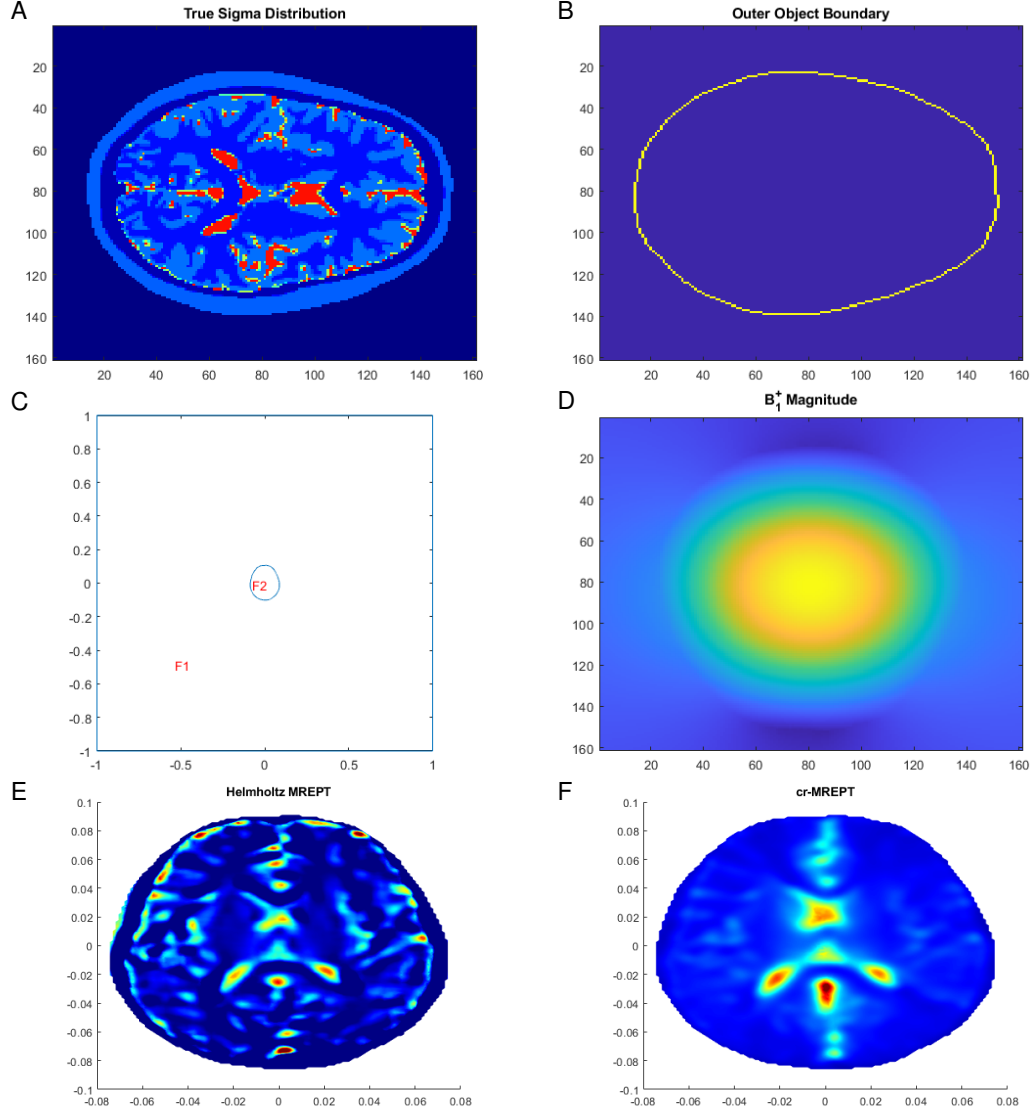


Figure 5.3: Outputs of the cr-MREPT library, showing all calculation steps and obtained conductivity maps for the brain simulation phantom. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes. (A) True conductivity values of the phantom. (B) Outer boundaries of the phantom, detected by the library. (C) Simulation setup for EM simulations to calculate  $|B_1^+|$ . (D) Simulated  $|B_1^+|$  map for uniform EPs. (E) Conductivity distribution obtained using bias corrected phase-based Helmholtz MREPT. (F) Conductivity distribution obtained using bias corrected phase-based cr-MREPT.

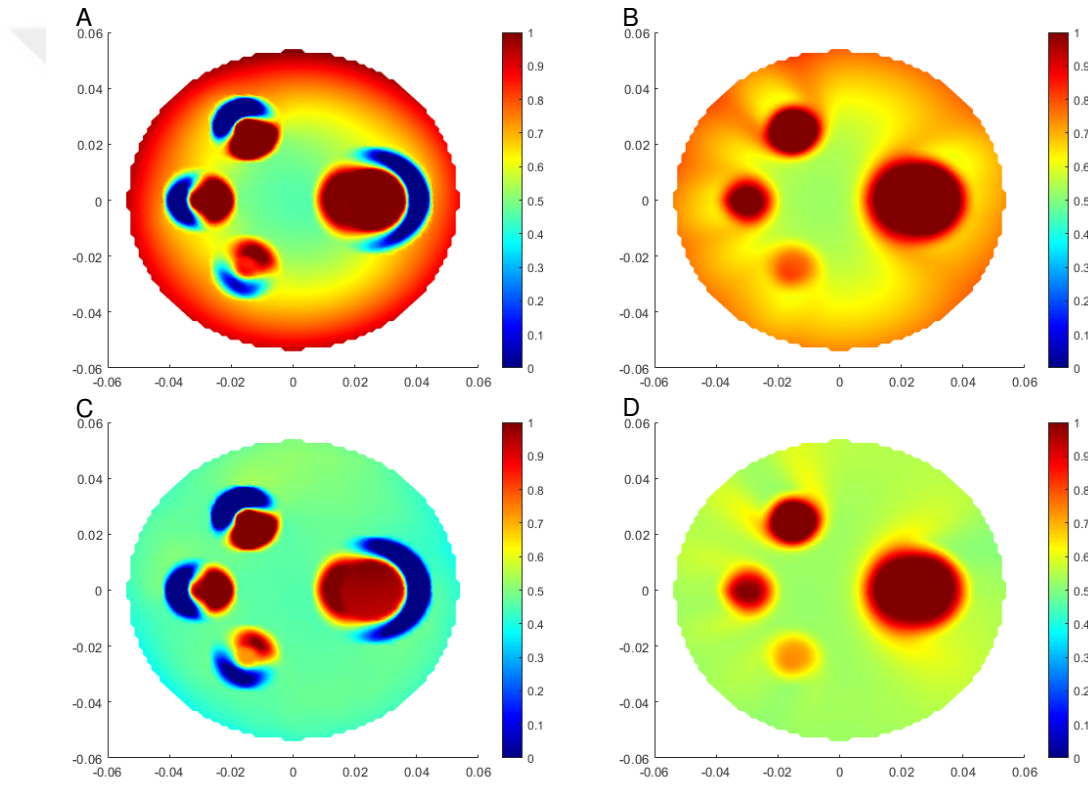


Figure 5.4: Conductivity reconstruction results for 4-anomaly phantom. (A) Helmholtz MREPT, uncorrected case. (B) cr-MREPT, uncorrected case. (C) Helmholtz MREPT, bias correction applied. (D) cr-MREPT, bias correction applied.

Fig. 5.5 shows the conductivity distributions obtained for all simulation phantoms. It can be seen from the figure that conductivity maps are successfully reconstructed in all cases. Bias correction is also effective, since the concave bias completely disappears.

The calculation steps for experimental data are quite similar to the simulation case, but there are some minor differences. Fig. 5.6 shows the output of each step of the library code. Similarly to the simulation case, the outer boundary of the object is determined in the first step. However, instead of using true conductivity values, we here use the magnitude of the data we obtained during the MRI experiment. This is plausible since the bSSFP sequence already provides the complex data. After this, EM simulation is performed in Matlab in order to calculate a rough  $|B_1^+|$  map. Then, in the final step, conductivity reconstruction is performed using either Helmholtz or cr-MREPT, both in phase-based form. The bias correction is also applied in the results shown in Fig. 5.6, but can be omitted if the user wishes.

Finally, Fig. 5.7 shows the conductivity distributions obtained for all experimental phantoms. Once again, conductivity maps are successfully reconstructed in all 3 cases. Bias correction is also effective, since the concave bias completely disappears.

## 5.4 Discussion

MREPT and conductivity imaging is a relatively new and promising imaging technique that still requires some research to be clinically useful. To increase researcher interest in MREPT and provide resources to accelerate the learning curve for novice researchers of the topic, part of this thesis was dedicated to creating an MREPT library with step by step explanations in the implementation and built in examples to be reconstructed, both simulations and experiments.

Since they are advantageous in various ways compared to full-form methods,

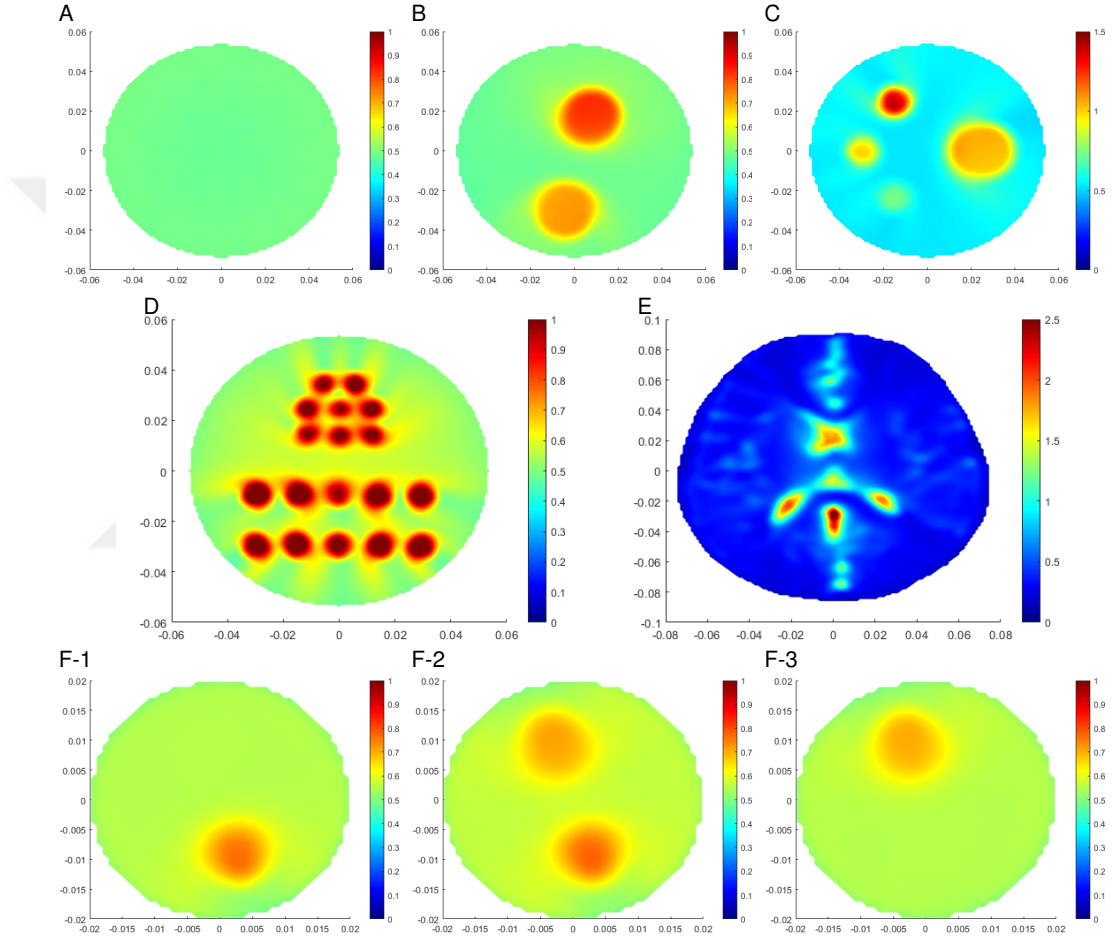


Figure 5.5: Conductivity reconstruction results for all simulation phantoms. Conductivity unit is  $s/m$ , distance unit is m for all cases. (A) Uniform cylindrical phantom. (B) Cylindrical phantom with two z-independent conductivity anomalies. (C) Cylindrical phantom with four z-independent conductivity anomalies. (D) Cylindrical phantom with multiple z-independent conductivity anomalies. (E) Human head model. (F) Cylindrical phantom with height of 5-cm and radius of 2-cm with two z-dependent conductivity anomalies. 1-3 corresponds to top, middle and bottom slices, respectively.

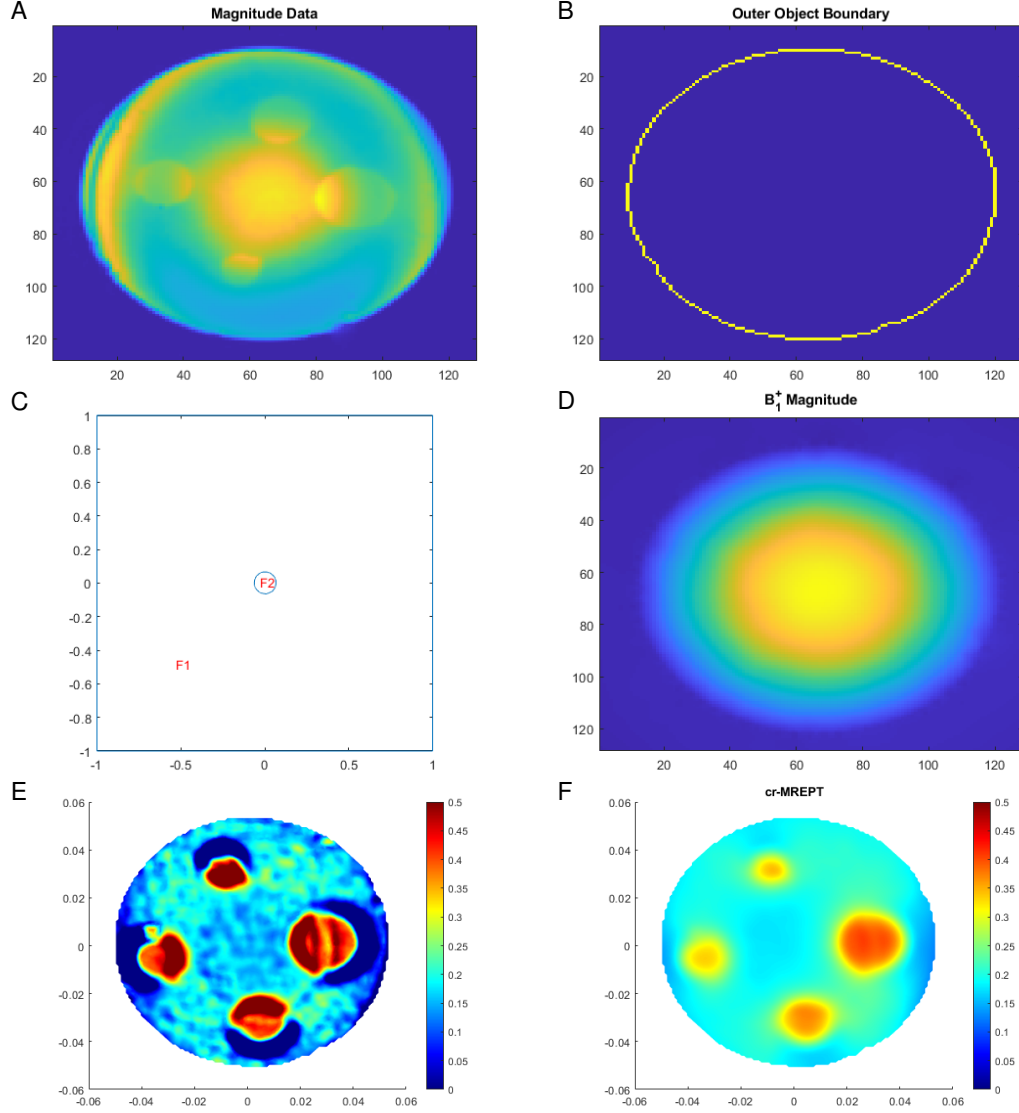


Figure 5.6: Outputs of the cr-MREPT library, showing all calculation steps and obtained conductivity maps for the experimental phantom with four conductivity anomalies. Conductivity unit is  $s/m$ , distance unit is  $m$ , unless specified in the plot axes. (A) Magnitude of the MRI image. (B) Outer boundaries of the phantom, detected by the library. (C) Simulation setup for EM simulations to calculate  $|B_1^+|$ . (D) Simulated  $|B_1^+|$  map for uniform EPs. (E) Conductivity distribution obtained using bias corrected phase-based Helmholtz MREPT. (F) Conductivity distribution obtained using bias corrected phase-based cr-MREPT.

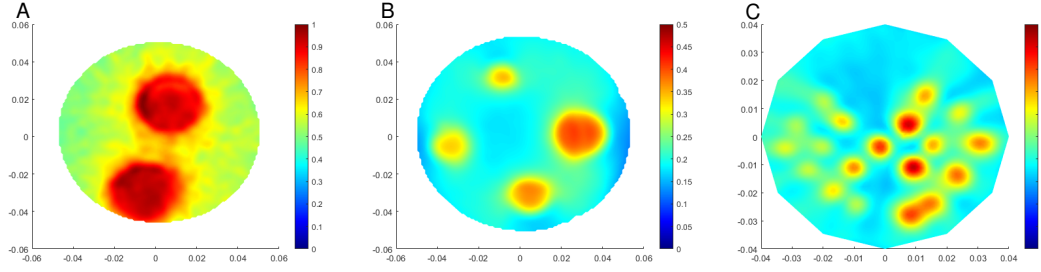


Figure 5.7: Conductivity reconstruction results for all experimental phantoms. Conductivity unit is  $s/m$ , distance unit is  $m$  for all cases. (A) Cylindrical phantom with two z-independent conductivity anomalies. (B) Cylindrical phantom with four z-independent conductivity anomalies. (C) Cylindrical resolution phantom.

the library is mainly dedicated to phase-based methods. One of the most important advantages of phase-based methods is that only phase of  $B_1^+$  is required for calculations, so actual imaging times can be shortened in the MR device. Moreover, since the number of unknowns to solve is halved compared to full-form methods, the reconstruction is usually faster and less computationally heavy. One serious problem with phase-based methods that affect image quality is the concave bias. However, this problem is solved by bias correction discussed in Chapter 3. Since the bias correction method can work with a simulated  $|B_1^+|$  map, no additional imaging time is required. During the development of the MREPT library, the required EM simulations are also implemented in Matlab. Hence, the user can apply bias corrected phase-based MREPT methods, either Helmholtz or cr-MREPT, without any extra manual steps. In the end, by just using data from a single imaging sequence that takes less than 10 minutes in most cases, high quality conductivity maps can be obtained without any manual work by using the developed MREPT library.

The library aims to be easy to use and understand the details of the operations, and the user will be able to modify the provided Matlab code in order to develop their own methods and improvements. Developing a graphical user interface was also considered, but decided against for couple of reasons. Most importantly, the library is developed for researchers working on MREPT, not for end users with no engineering background to reconstruct conductivity distributions of actual

patients. Hence, it is considered more important to actually see and understand the method and calculation steps and to modify if necessary, instead of having a pretty interface to work on. Useful tips and tricks to improve image quality are also provided in the related parts of the code, especially for different options like filtering, determining diffusion constants, or ROI selection.

There are 8 simulation phantoms and 3 experimental phantoms included in the library. The detail level of the phantoms varies in order to test different aspects of the newly developed methods. Starting from a uniform simulation phantom to a human head model, simulation phantoms offer different levels of complexity to test the user's own method. There is also an option to add noise to simulated data, which is quite helpful to see how the solution method behaves under different amounts of noise. In addition to the simulation phantoms mentioned above, 3 different experimental phantoms are included in the library, again in various detail levels. One phantom for both simulation and experimental data that has many small and close conductivity anomalies, called a resolution phantom, is particularly useful for determining the resolution of the developed method and comparing it with the Helmholtz or cr-MREPT.

Finally, all conductivity results are presented in the Sect. 5.3 shows that the proposed bias corrected phase-based cr-MREPT method is able to successfully reconstruct conductivity distributions for all simulation and experimental phantoms. The conductivity maps are of similar quality to the full-form solutions, without the need of  $|B_1^+|$  data.

# Chapter 6

## Conclusion

Estimating electrical properties of tissues has been a point of interest for many years as EPs can be quite useful for anatomical imaging, diagnosis, monitoring, and treatment of various diseases and RF safety. MREPT is the most promising method to obtain conductivity distributions as it relies only on standard MRI equipment, is non-invasive and non-ionizing. While previously proposed MREPT methods like Helmholtz MREPT are generally able to estimate conductivity distributions, they suffer from some well known problems such as internal boundary artifacts, transceive phase approximation, concave bias in phase-based variants, and long imaging times due to high SNR requirements. cr-MREPT was proposed to overcome internal boundary artifacts, and phase-based form of cr-MREPT does not use the transceive phase approximation. However, it still suffers from concave bias and high SNR requirements.

In this thesis, the motivation is to develop a method that overcomes the mentioned problems and implement it in 3D tetrahedral mesh such that the reconstruction takes a reasonable time. Moreover, as the number of MREPT methods increases, it becomes harder to follow and to implement each MREPT method. Therefore, it is crucial to provide an easy to use tool in order to increase the number of researchers that the proposed methods reach. All these aims are achieved and discussed in detail in the respective sections of the thesis.

Chapter 3 presents the bias correction method developed for phase-based cr-MREPT. The motivation here is to develop a method that does not have internal boundary artifacts, does not use transceive phase approximation in the derivation, does not have concave bias, and relies on MRI data that can be obtained relatively fast. For this purpose, we derived a novel central equation and evaluated its performance in simulation and experimental phantoms. The results are quite satisfactory, and bias correction is achieved even for complicated, noise added simulations and experiments. The work done in this chapter is presented in a conference and published as a journal article;

- Çan, M. K. & Ider, Y. Z. (2022) Bias Correction for Phase-Based cr-MREPT Using Low Resolution B1+ Magnitude. Proceedings of QMR-LUCCA: Workshop on MR phase, Magnetic Susceptibility and Electrical Properties Mapping, Lucca, Italy, 16-19 October 2022.
- Çan, M. K., & Ider, Y. Z. (2024). Bias correction for phase-based cr-MREPT using low resolution B1+ magnitude. *Physics in Medicine & Biology*, 69(12), 125020.

Chapter 4 shows the 3D implementation of bias corrected phase-based cr-MREPT in 3D tetrahedral meshes and the acceleration of the solution process. The implementation in 3D is straightforward as the central equation derived in the previous chapter is already in 3D. However, increasing the number of unknowns exponentially increases the memory and computational power requirements. It is not practically possible to obtain a direct solution for a relatively large object such as a human brain. With this motivation, we proposed a method to divide the 3D volume into smaller regions where matrix sizes are more manageable and solution times are much shorter. We have performed sensitivity analysis for determining the smallest region size in which cr-MREPT can estimate conductivity distributions correctly and parallelized the solution of these small regions so that the total solution time decreases significantly. In the end, the 3D conductivity distribution of a human brain was successfully reconstructed without the need for a supercomputer or HPC server. The proceeding of this chapter is submitted for review as a journal article;

- Çan, M. K., & Ider, Y. Z. (2025). An Accelerated Solution Method for 3D phase-based cr-MREPT. [Manuscript submitted for publication]. Physics in Medicine & Biology

Chapter 5 presents the cr-MREPT library developed during the thesis. The library is aimed at being useful for various purposes. Most importantly, EM simulations to estimate  $|B_1^+|$  is implemented in the phase-based cr-MREPT algorithm, for any given phantom, simulation or experimental. Hence, using only the phase of  $B_1^+$ , we achieved a reconstruction method that overcomes all main problems related to MREPT that are discussed previously. Moreover, 8 simulation phantoms and 3 experimental phantoms are included in the library as built in examples. In the library, it is also described in detail how to use the reconstruction algorithm on new data. The motivation here is that new users can use this library to get familiar with cr-MREPT using the example data and apply the method on their own data with ease. This is crucial for further development of the MREPT method and increasing clinical applications, as thus far MREPT is still not very commonly used in practical application, although its quite promising for various purposes. In addition to this, the cr-MREPT library is intended to increase collaboration between various research groups that develop their own MREPT algorithms and help with better performance evaluation between these methods. The Matlab code for the library and related data is shared in the following repository.

- <https://github.com/kaancan/PhaseBasedcrMREPT>

In conclusion, the motivation for this thesis work is to further develop a promising imaging method, cr-MREPT, and increase practical applications. There is still work to be done, but the phase-based cr-MREPT with bias correction and 3D application has the potential to be widely used in the clinical environment.

# Bibliography

- [1] N. Gurler and Y. Ider, “Numerical methods and software tools for simulation, design, and resonant mode analysis of radio frequency birdcage coils used in mri,” *Concepts in Magnetic Resonance Part B: Magnetic Resonance Engineering*, vol. 45, no. 1, pp. 13–32, 2015.
- [2] R. T. L.W. Organ and N. Moody, “Brain tumor localization using an electrical impedance technique,” *Journal of Neurosurgery*, vol. 28, no. 1, pp. 35–44, 1968.
- [3] C. R. D.P. Becker and J. Seelig, “A simplified method for electrical impedance monitoring in brain tumor localization,” *Journal of Neurosurgery*, vol. 32, no. 3, pp. 375–377, 1970.
- [4] A. S. S.S. Chaudhary, R.K. Mishra and J. Thomas, “Dielectric properties of normal and malignant human breast tissues at radiowave and microwave frequencies,” *Indian journal of biochemistry and biophysics*, vol. 21, no. 1, pp. 76–79, 1984.
- [5] J. B. A.J. Surowiec, S.S. Stuchly and A. Swarup, “Dielectric properties of breast carcinoma and the surrounding tissues,” *IEEE Transactions on Biomedical Engineering*, vol. 35, no. 4, pp. 257–263, 1988.
- [6] J. X. Y. Lu, B. Li and J. Yu, “Dielectric properties of human glioma and surrounding tissue,” *International journal of hyperthermia*, vol. 8, no. 6, pp. 755–760, 1992.

- [7] C. L. W.T. Joines, Y. Zhang and R. Jirtle, "The measured electrical properties of normal and malignant human tissues from 50 to 900 mhz," *Medical physics*, vol. 21, no. 4, pp. 547–550, 1994.
- [8] H. C. A. N. L. S. E. Balidemaj, A.L. van Lier and C. van den Berg, "Feasibility of electric property tomography of pelvic tumors at 3t," *Magnetic resonance in medicine*, vol. 73, no. 4, pp. 1505–1513, 2015.
- [9] S. B. I. Hancu, J.C. Roberts and S. Lee, "On conductivity, permittivity, apparent diffusion coefficient, and their usefulness as cancer markers at mri frequencies," *Magnetic resonance in medicine*, vol. 73, no. 5, pp. 2025–2029, 2015.
- [10] D. K. M. K. E. K. H. M. S.Y. Kim, J. Shin and J. Yoon, "Correlation between conductivity and prognostic factors in invasive breast cancer using magnetic resonance electric properties tomography (mrept)," *European radiology*, vol. 26, pp. 2317–2326, 2016.
- [11] S. B. M. M. M.T. Alrashidi, M.A. Nooradean and H. Poptani, "Mr electrical properties tomography (mrept) at 9.4 t to assess treatment response of choline kinase inhibition on gl261 glioblastoma," *Neuro-oncology*, vol. 24, no. 4, 2022.
- [12] A. M. A. T. H. K. E. W. C. Lesbats, N. Katoch and H. Poptani, "High-frequency electrical properties tomography at 9.4 t as a novel contrast mechanism for brain tumors," *Magnetic resonance in medicine*, vol. 86, no. 1, pp. 382–392, 2021.
- [13] D. Holder, "Detection of cortical spreading depression in the anaesthetised rat by impedance measurement with scalp electrodes: implications for non-invasive imaging of the brain with electrical impedance tomography," *Clinical Physics and Physiological Measurement*, vol. 13, no. 1, p. 77, 1992.
- [14] S. D. E. S. K. F. M. J. M.A. Fallert, M.S. Mirotznik and D. Bogen, "Myocardial electrical impedance mapping of ischemic sheep hearts and healing aneurysms," *Circulation*, vol. 87, no. 1, pp. 199–207, 1993.

- [15] N. Gurler and Y. Z. Ider, “Generalized phase based electrical conductivity imaging,” in *Proc. Intl. Soc. Mag. Reson. Med*, vol. 24, p. 2991, 2016.
- [16] A. L. Van Lier, A. J. Raaijmakers, D. O. Brunner, D. Klomp, K. P. Pruessmann, J. Lagendijk, and C. van den Berg, “Propagating rf phase: a new contrast to detect local changes in conductivity,” in *Proceedings of the 18th Annual Meeting of ISMRM, Stockholm, Sweden*, p. 2864, 2010.
- [17] K. J. e. a. Rasanjala O, Nguyen NT, “Application of ept to ischemic stroke: Comparison of conductivity between infarct and contralateral brain,” in *Proceedings of the 31th Annual Meeting of ISMRM, London, UK*, p. 2864, 2022.
- [18] M. L. H. R. S. P. C. R. S. Hong., Y. Choi and G. Jahng, “Increased extraneurite conductivity of brain in patients with alzheimer’s disease: a pilot study,” *Psychiatry Research: Neuroimaging*, vol. 340, 2024.
- [19] H. K. M. L. H. R. S. P. T. Park, Y. Choi and G. Jahng, “Exploring the relationship between larmor-frequency electrical conductivity, diffusivity, and tissue volume in the aging brain,” *Quantitative Imaging in Medicine and Surgery*, vol. 15, no. 5, p. 4669, 2025.
- [20] S. P. S. J. H. R. C. R. G.H. Jahng, M.B. Lee and O. Kwon, “Characteristics of high and low frequency conductivities in patients with alzheimer’s disease,” *International Journal of Bioelectromagnetism*, vol. 24, 2022.
- [21] M. L. G.H. Jahng and O. Kwon, “Gadolinium based contrast agent induced electrical conductivity heterogeneity analysis in the brain of alzheimer’s disease,” *Scientific Reports*, vol. 15, no. 1, p. 10832, 2025.
- [22] U. H. H.D. Lux and I. Dietzel, “Ionic changes and alterations in the size of the extracellular space during epileptic activity,” *Advances in neurology*, vol. 44, pp. 619–639, 1986.
- [23] J. A. M. C. B. D. G. H. K. Tabelow, E. Balteau and S. Mohammadi, “hmri—a toolbox for quantitative mri in neuroscience and clinical research,” *Neuroimage*, vol. 194, pp. 191–210, 2019.

- [24] J. P. H. K. T. O. W. K. H. P. S. Kim, B.K. Choi, "Identification of brain damage after seizures using an mr-based electrical conductivity imaging method," *Diagnostics*, vol. 11, no. 3, p. 569, 2021.
- [25] J. L. P. v. d. M. P. F. X. Zhang, S. Schmitter and B. He, "Local sar estimation for human brain imaging using multi-channel transceiver coil at 7t," *In Proc ISMRM*, p. 288, 2013.
- [26] L. Z. A. Arduino, M. Chiampi and O. Bottauscio, "Alternative approaches to magnetic resonance-based electric properties tomography and local specific absorption rate estimation," *IEEE Transactions on Magnetics*, vol. 53, no. 2, pp. 1–8, 2016.
- [27] G. S. A. v. L. R. R. L. S. E. Balidemaj, H.P. Kok and J. Crezee, "Hyperthermia treatment planning for cervical cancer patients based on electrical conductivity tissue properties acquired in vivo with ept at 3 t," *International Journal of Hyperthermia*, vol. 32, no. 5, pp. 558–568, 2016.
- [28] D. McRae and M. Esrick, "The dielectric parameters of excised emt-6 tumours and their change during hyperthermia," *Physics in Medicine and Biology*, vol. 37, no. 11, p. 2045, 1992.
- [29] H. K. W. J. H. W. T. O. O.I. Kwon, M. Chauhan and E. Woo, "Fast conductivity imaging in magnetic resonance electrical impedance tomography (mreit) for rf ablation monitoring," *International Journal of Hyperthermia*, vol. 30, no. 7, pp. 447–455, 2014.
- [30] S. F. V. R. J. B. S. S. P.R. Krahn, L. Biswas and G. Wright, "Mri-guided cardiac rf ablation for comparing mri characteristics of acute lesions and associated electrophysiologic voltage reductions," *IEEE Transactions on Biomedical Engineering*, vol. 69, no. 8, pp. 2657–2666, 2022.
- [31] J. L. F.S. Salinas and P. Fox, "3d modeling of the total electric field induced by transcranial magnetic stimulation using the boundary element method," *Physics in Medicine and Biology*, vol. 54, no. 12, p. 3631, 2009.
- [32] D. Barber and B. Brown, "Applied potential tomography," *Journal of Physics E: Scientific Instruments*, vol. 17, no. 9, p. 723, 1984.

- [33] D. I. D. G. L.F. Fuks, M. Cheney and J. Newell, "Detection and imaging of electric conductivity and permittivity at low frequency," *IEEE Transactions on Biomedical Engineering*, vol. 38, no. 11, pp. 1106–1110, 1991.
- [34] J. N. P.M. Edic, G.J. Saulnier and D. Isaacson, "A real-time electrical impedance tomography," *IEEE Transactions on Biomedical Engineering*, vol. 42, no. 9, pp. 849–859, 1995.
- [35] Y. I. N.G. Gencer and S. Williamson, "Electrical impedance tomography: Induced-current imaging achieved with a multiple coil system," *IEEE Transactions on Biomedical Engineering*, vol. 43, no. 2, pp. 139–149, 1996.
- [36] L. H. T. O. E. W. A. Romsauerova, A.M. Ewan and D. Holder, "A comparison of multi-frequency eit systems intended for acute stroke imaging," *Medical Physics and Biomedical Engineering*, pp. 3918–3920, 2007.
- [37] H. Griffiths, W. Stewart, and W. Gough, "Magnetic induction tomography: a measuring system for biological tissues," *Annals of the New York Academy of Sciences*, vol. 873, no. 1, pp. 335–345, 1999.
- [38] H. Griffiths, "Magnetic induction tomography," *Measurement science and technology*, vol. 12, no. 8, p. 1126, 2001.
- [39] A. Korjenevsky, V. Cherepenin, and S. Sapetsky, "Magnetic induction tomography: experimental realization," *Physiological measurement*, vol. 21, no. 1, p. 89, 2000.
- [40] R. A. G.C. Scott, M.L.G. Joy and R. Henkelman, "Sensitivity of magnetic resonance current density imaging," *Journal of Magnetic resonance*, vol. 97, pp. 235–254, 1992.
- [41] Y. Ider and Ö. Birgül, "Use of the magnetic field generated by the internal distribution of injected currents for electrical impedance tomography (mr-eit)," *Turkish Journal of Electrical Engineering and Computer Sciences*, vol. 6, no. 3, pp. 215–226, 1998.
- [42] J. K. Seo, J.-R. Yoon, E. J. Woo, and O. Kwon, "Reconstruction of conductivity and current density images using only one component of magnetic

- field measurements,” *IEEE Transactions on Biomedical Engineering*, vol. 50, no. 9, pp. 1121–1124, 2003.
- [43] Y. Z. Ider and S. Onart, “Algebraic reconstruction for 3d magnetic resonance–electrical impedance tomography (mreit) using one component of magnetic flux density,” *Physiological measurement*, vol. 25, no. 1, p. 281, 2004.
  - [44] J. K. Seo, O. Kwon, and E. J. Woo, “Magnetic resonance electrical impedance tomography (mreit): conductivity and current density imaging,” in *Journal of Physics: Conference Series*, vol. 12, p. 140, IOP Publishing, 2005.
  - [45] H. S. Nam, C. Park, and O. I. Kwon, “Non-iterative conductivity reconstruction algorithm using projected current density in mreit,” *Physics in Medicine & Biology*, vol. 53, no. 23, p. 6947, 2008.
  - [46] E. J. Woo and J. K. Seo, “Magnetic resonance electrical impedance tomography (mreit) for high-resolution conductivity imaging,” *Physiological measurement*, vol. 29, no. 10, p. R1, 2008.
  - [47] E. Haacke, L. Petropoulos, E. Nilges, and D. Wu, “Extraction of conductivity and permittivity using magnetic resonance imaging,” *Physics in medicine & biology*, vol. 36, no. 6, p. 723, 1991.
  - [48] U. Katscher, T. Voigt, and C. Findekklee, “Electrical conductivity imaging using magnetic resonance tomography,” in *2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 3162–3164, IEEE, 2009.
  - [49] H. Wen, “Noninvasive quantitative mapping of conductivity and dielectric distributions using rf wave propagation effects in high-field mri,” in *Medical Imaging 2003: Physics of Medical Imaging*, vol. 5030, pp. 471–477, SPIE, 2003.
  - [50] U. K. T. Voigt and O. Doessel, “Quantitative conductivity and permittivity imaging of the human brain using electric properties tomography,” *Magnetic resonance in medicine*, vol. 66, pp. 456–466, 2011.

- [51] D. K. U. Katscher and J. Seo, “Recent progress and future challenges in mr electric properties tomography,” *Computational and Mathematical Methods in Medicine*, 2013.
- [52] J. K. Seo, D.-H. Kim, J. Lee, O. I. Kwon, S. Z. Sajib, and E. J. Woo, “Electrical tissue property imaging using mri at dc and larmor frequency,” *Inverse Problems*, vol. 28, no. 8, p. 084002, 2012.
- [53] N. G. F.S. Hafalir, O.F. Oran and Y. Ider, “Convection-reaction equation based magnetic resonance electrical properties tomography (cr-mrept),” *IEEE transactions on medical imaging*, vol. 33, no. 3, pp. 777 – 793, 2014.
- [54] Y. Z. Ider, G. Ariturk, and G. Yildiz, “Spatial and contrast resolution of phase based mrept,” in *Proceedings 25th Annu. Meeting ISMRM*, p. 3642, 2017.
- [55] N. Gurler and Y. Ider, “Gradient-based electrical conductivity imaging using mr phase,” *Magnetic Resonance in Medicine*, vol. 77, no. 1, pp. 137 – 150, 2015.
- [56] Y. Z. Ider and M. N. Akyer, “Properties and implementation issues of phase based cr-mrept for conductivity imaging,” in *Proceedings of the ISMRM & SMRT Virtual Conference & Exhibition*, pp. 8–14, 2020.
- [57] K. K. Tha, U. Katscher, S. Yamaguchi, C. Stehning, S. Terasaka, N. Fujima, K. Kudo, K. Kazumata, T. Yamamoto, M. Van Cauteren, *et al.*, “Noninvasive electrical conductivity measurement by mri: a test of its validity and the electrical conductivity characteristics of glioma,” *European radiology*, vol. 28, no. 1, pp. 348–355, 2018.
- [58] C. Boga, “Iterative fitting approach to cr-mrept,” Master’s thesis, graduate school of engineering and science of bilkent university, 2019.
- [59] *LCF Artifact Elimination in cr-MREPT using Phased-Array Receive Coil*, 2018.
- [60] J. K. Seo, M.-O. Kim, J. Lee, N. Choi, E. J. Woo, H. J. Kim, O. I. Kwon, and D.-H. Kim, “Error analysis of nonconstant admittivity for mr-based electric

- property imaging,” *IEEE transactions on medical imaging*, vol. 31, no. 2, pp. 430–437, 2011.
- [61] A. L. van Lier, A. Raaijmakers, T. Voigt, J. J. Lagendijk, P. R. Luijten, U. Katscher, and C. A. van den Berg, “Electrical properties tomography in the human brain at 1.5, 3, and 7t: a comparison study,” *Magnetic resonance in medicine*, vol. 71, no. 1, pp. 354–363, 2014.
  - [62] S.-K. Lee, S. Bulumulla, and I. Hancu, “Theoretical investigation of random noise-limited signal-to-noise ratio in mr-based electrical properties tomography,” *IEEE transactions on medical imaging*, vol. 34, no. 11, pp. 2220–2232, 2015.
  - [63] T.-F. Chen, H. A. Levine, and P. E. Sacks, “Analysis of a convective reaction-diffusion equation,” *Nonlinear Analysis: Theory, Methods & Applications*, vol. 12, no. 12, pp. 1349–1370, 1988.
  - [64] G. Ariturk and Y. Z. Ider, “Optimal multichannel transmission for improved cr-mrept,” *Physics in Medicine & Biology*, vol. 63, no. 4, p. 045001, 2018.
  - [65] N. Gurler, O. F. Oran, and Y. Z. Ider, “cr-mrept using multichannel receive coil,” in *Proceedings of the 22nd Annual Meeting ISMRM*, p. 3247, 2014.
  - [66] G. Yıldız, “Low convective field artifact elimination using dielectric padding and multichannel receive in cr-mrept conductivity images,” Master’s thesis, Bilkent Universitesi (Turkey), 2018.
  - [67] G. Yildiz and Y. Z. Ider, “Use of dielectric padding to eliminate low convective field artifact in cr-mrept conductivity images,” *Magnetic Resonance in Medicine*, vol. 81, no. 5, pp. 3168–3184, 2019.
  - [68] Y. Z. Ider, C. Boga, and G. Yildiz, “Spatial resolution of full cr-mrept: 2d and 3d evaluation,” in *Proceedings of the 26th Annual Meeting of ISMRM, Paris, France*, 2018.
  - [69] D. K. Sodickson, L. Alon, C. M. Deniz, R. Brown, B. Zhang, G. C. Wiggins, G. Y. Cho, N. B. Eliezer, D. S. Novikov, R. Lattanzi, *et al.*, “Local

maxwell tomography using transmit-receive coil arrays for contact-free mapping of tissue electrical properties and determination of absolute rf phase,” in *Proceedings of the 20th Annual Meeting of ISMRM, Melbourne, Australia*, p. 387, 2012.

- [70] J. E. Serrallés, I. I. Giannakopoulos, B. Zhang, C. Ianniello, M. A. Cloos, A. G. Polimeridis, J. K. White, D. K. Sodickson, L. Daniel, and R. Lattanzi, “Noninvasive estimation of electrical properties from magnetic resonance measurements via global maxwell tomography and match regularization,” *IEEE Transactions on Biomedical Engineering*, vol. 67, no. 1, pp. 3–15, 2019.
- [71] Y. Wan, M. Negishi, and R. T. Constable, “2d magnetic resonance electrical property tomography based on b1-field mapping,” in *2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, pp. 6060–6063, IEEE, 2014.
- [72] J. S. J. Lee and D. Kim, “Mr-based conductivity imaging using multiple receiver coils,” *Magnetic resonance in medicine*, vol. 76, pp. 530–539, 2016.
- [73] J. P. Marques, D. K. Sodickson, O. Ipek, C. M. Collins, and R. Gruetter, “Single acquisition electrical property mapping based on relative coil sensitivities: a proof-of-concept demonstration,” *Magnetic resonance in medicine*, vol. 74, no. 1, pp. 185–195, 2015.
- [74] E. Balidemaj, C. A. van den Berg, J. Trinks, A. L. van Lier, A. J. Nederveen, L. J. Stalpers, H. Crezee, and R. F. Remis, “Csi-ept: A contrast source inversion approach for improved mri-based electric properties tomography,” *IEEE transactions on medical imaging*, vol. 34, no. 9, pp. 1788–1796, 2015.
- [75] J. Liu, X. Zhang, P.-F. Van de Moortele, S. Schmitter, and B. He, “Determining electrical properties based on b1 fields measured in an mr scanner using a multi-channel transmit/receive coil: a general approach,” *Physics in Medicine & Biology*, vol. 58, no. 13, p. 4395, 2013.

- [76] J. Liu, X. Zhang, S. Schmitter, P.-F. Van de Moortele, and B. He, “Gradient-based electrical properties tomography (g ept): A robust method for mapping electrical properties of biological tissues in vivo using magnetic resonance imaging,” *Magnetic resonance in medicine*, vol. 74, no. 3, pp. 634–646, 2015.
- [77] H. Ammari, H. Kwon, Y. Lee, K. Kang, and J. K. Seo, “Magnetic resonance-based reconstruction method of conductivity and permittivity distributions at the larmor frequency,” *Inverse Problems*, vol. 31, no. 10, p. 105001, 2015.
- [78] L. Guo, J. Jin, C. Liu, F. Liu, and S. Crozier, “An efficient integral-based method for three-dimensional mr-ept and the calculation of the rf-coil-induced  $\{B_z\}$  field,” *IEEE Transactions on Biomedical Engineering*, vol. 65, no. 2, pp. 282–293, 2017.
- [79] A. Borsic, I. Perreard, A. Mahara, and R. J. Halter, “An inverse problems approach to mr-ept image reconstruction,” *IEEE transactions on medical imaging*, vol. 35, no. 1, pp. 244–256, 2015.
- [80] I. I. Giannakopoulos, G. Carluccio, M. B. Keerthivasan, G. Koerzdoerfer, K. Lakshmanan, H. L. De Moura, J. E. Cruz Serrallés, and R. Lattanzi, “Mr electrical properties mapping using vision transformers and canny edge detectors,” *Magnetic resonance in medicine*, vol. 93, no. 3, pp. 1117–1131, 2025.
- [81] X. Yu, J. E. Serrallés, I. I. Giannakopoulos, Z. Liu, L. Daniel, R. Lattanzi, and Z. Zhang, “Pifon-ept: Mr-based electrical property tomography using physics-informed fourier networks,” *IEEE journal on multiscale and multiphysics computational techniques*, vol. 9, pp. 49–60, 2023.
- [82] C. Cui, K.-J. Jung, M. A. Al-Masni, J.-H. Kim, S.-Y. Kim, M. Park, S. Y. Huang, S. Y. Chun, and D.-H. Kim, “Deep network regularization for phasebased magnetic resonance electrical properties tomography with stein’s unbiased risk estimator,” *IEEE Transactions on Biomedical Engineering*, 2024.

- [83] K.-J. Jung, S. Mandija, C. Cui, J.-H. Kim, M. A. Al-masni, T. G. Meerbothe, M. Park, C. A. van den Berg, and D.-H. Kim, “Data-driven electrical conductivity brain imaging using 3 t mri,” *Human Brain Mapping*, vol. 44, no. 15, pp. 4986–5001, 2023.
- [84] R. Leijssen, C. van den Berg, A. Webb, R. Remis, and S. Mandija, “Combining deep learning and 3d contrast source inversion in mr-based electrical properties tomography,” *NMR in Biomedicine*, vol. 35, no. 4, p. e4211, 2022.
- [85] A. J. G. Inda, S. Y. Huang, N. İmamoğlu, R. Qin, T. Yang, T. Chen, Z. Yuan, and W. Yu, “Physics informed neural networks (pinn) for low snr magnetic resonance electrical properties tomography (mrept),” *Diagnostics*, vol. 12, no. 11, p. 2627, 2022.
- [86] N. Hampe, U. Katscher, C. A. Van den Berg, K. K. Tha, and S. Mandija, “Investigating the challenges and generalizability of deep learning brain conductivity mapping,” *Physics in Medicine & Biology*, vol. 65, no. 13, p. 135001, 2020.
- [87] S. Mandija, E. F. Meliadó, N. R. Huttinga, P. R. Luijten, and C. A. van den Berg, “Opening a new window on mr-based electrical properties tomography with deep learning,” *Scientific reports*, vol. 9, no. 1, p. 8895, 2019.
- [88] F. S. S. Akoka, F. Franconi and A. le Pepe, “Radiofrequency map of an nmr coil by imaging,” *Magnetic resonance in medicine*, vol. 11, pp. 437–441, 1993.
- [89] V. Yarnyh, “Actual flip-angle imaging in the pulsed steady state: A method for rapid three-dimensional mapping of the transmitted radiofrequency field,” *Magnetic resonance in medicine*, vol. 57, pp. 192–200, 2007.
- [90] K. Nehrke and P. Bornert, “Dream - a novel approach for robust, ultrafast, multislice b1 mapping,” *Magnetic resonance in medicine*, vol. 68, pp. 1517–1526, 2012.
- [91] J. Z. L. S. S. Ozdemir, E. Ilıcak and F. Zöllner, “Feasibility of undersampled spiral trajectories in mrept for fast conductivity imaging,” *Magnetic resonance in medicine*, vol. 91, pp. 1567–1575, 2024.

- [92] C. G. S. Iyyakkunel, M. Weigel and O. Bieri, “Complex b1+ mapping with carr-purcell spin echoes and its application to electrical properties tomography,” *Magnetic resonance in medicine*, vol. 87, pp. 1250–1260, 2022.
- [93] T. V. M. I. H. A. G. N. U. Katscher, K. Djamshidi and J. Keupp, “Estimation of breast tumor conductivity using parabolic phase fitting,” *Proc. Intl. Soc. Mag. Reson. Med*, vol. 20, 2012.
- [94] A. Karsa and K. Shmueli, “New approaches for simultaneous noise suppression and edge preservation to achieve accurate quantitative conductivity mapping in noisy images,” *Proc. Intl. Soc. Mag. Reson. Med*, vol. 29, 2021.
- [95] M. K. Çan and Y. Z. Ider, “Bias correction for phase-based cr-mrept using low resolution b1+ magnitude,” *Physics in Medicine & Biology*, vol. 69, no. 12, p. 125020, 2024.
- [96] A. Arduino, “Eptlib: An open-source extensible collection of electric properties tomography techniques,” *Applied Sciences*, vol. 11, no. 7, p. 3237, 2021.

## Appendix A

# Complete Derivation of Bias-Corrected cr-MREPT

Starting from the logarithmic form of the cr-MREPT equation, as given in [55]:

$$\beta^+ \cdot \left( \frac{\nabla \gamma}{\gamma} \right) - \nabla^2 B_1^+ - i\omega\mu_0\gamma B_1^+ = 0 \quad (\text{A.1})$$

Here,  $\beta^+$  is defined as;

$$\beta^+ = \begin{bmatrix} \beta_x^+ \\ \beta_y^+ \\ \beta_z^+ \end{bmatrix} = \begin{bmatrix} \frac{\partial B_1^+}{\partial x} - i \frac{\partial B_1^+}{\partial y} + \frac{1}{2} \frac{\partial B_1^+}{\partial z} \\ i \frac{\partial B_1^+}{\partial x} + \frac{\partial B_1^+}{\partial y} + i \frac{1}{2} \frac{\partial B_1^+}{\partial z} \\ -\frac{1}{2} \frac{\partial B_z}{\partial x} - i \frac{1}{2} \frac{\partial B_z}{\partial y} + \frac{\partial B_1^+}{\partial z} \end{bmatrix} \quad (\text{A.2})$$

Using  $B_1^+ = |B_1^+|e^{i\phi^+}$  and  $\gamma = \sigma + i\omega\epsilon$ , we can rearrange  $\beta_x$  as:

$$\beta_x^+ = \frac{\partial B_1^+}{\partial x} - i \frac{\partial B_1^+}{\partial y} + \frac{1}{2} \frac{\partial B_1^+}{\partial z} \quad (\text{A.3})$$

$$= \frac{\partial |B_1^+|}{\partial x} e^{i\phi^+} + i |B_1^+| \frac{\partial \phi^+}{\partial x} e^{i\phi^+} - i \left( \frac{\partial |B_1^+|}{\partial y} e^{i\phi^+} + i |B_1^+| \frac{\partial \phi^+}{\partial y} e^{i\phi^+} \right) \quad (\text{A.4})$$

$$= |B_1^+| e^{i\phi^+} \left[ \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial x} + i \frac{\partial \phi^+}{\partial x} - i \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial y} + \frac{\partial \phi^+}{\partial y} \right] \quad (\text{A.5})$$

$$= |B_1^+| e^{i\phi^+} \left[ i \frac{\partial \phi^+}{\partial x} + \frac{\partial \phi^+}{\partial y} + \frac{\partial \ln |B_1^+|}{\partial x} - i \frac{\partial \ln |B_1^+|}{\partial y} \right] \quad (\text{A.6})$$

Similarly, for  $\beta_y$ :

$$\beta_y^+ = i \frac{\partial B_1^+}{\partial x} + \frac{\partial B_1^+}{\partial y} + i \frac{1}{2} \frac{\partial B_1^+}{\partial z} \quad (\text{A.7})$$

$$= i \frac{\partial |B_1^+|}{\partial x} e^{i\phi^+} - |B_1^+| \frac{\partial \phi^+}{\partial x} e^{i\phi^+} + \frac{\partial |B_1^+|}{\partial y} e^{i\phi^+} + i |B_1^+| \frac{\partial \phi^+}{\partial y} e^{i\phi^+} \quad (\text{A.8})$$

$$= |B_1^+| e^{i\phi^+} \left[ \frac{i}{|B_1^+|} \frac{\partial |B_1^+|}{\partial x} - \frac{\partial \phi^+}{\partial x} + \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial y} + i \frac{\partial \phi^+}{\partial y} \right] \quad (\text{A.9})$$

$$= |B_1^+| e^{i\phi^+} \left[ -\frac{\partial \phi^+}{\partial x} + i \frac{\partial \phi^+}{\partial y} + i \frac{\partial \ln |B_1^+|}{\partial x} + \frac{\partial \ln |B_1^+|}{\partial y} \right] \quad (\text{A.10})$$

For  $\beta_z$ , also assuming  $B_z$  is constant:

$$\beta_z^+ = -\frac{1}{2} \frac{\partial B_z}{\partial x} - i \frac{1}{2} \frac{\partial B_z}{\partial y} + \frac{\partial B_1^+}{\partial z} \quad (\text{A.11})$$

$$= -\frac{1}{2} \left( \frac{\partial B_z}{\partial x} + i \frac{\partial B_z}{\partial y} \right) + \frac{|B_1^+| e^{i\phi^+}}{\partial z} \quad (\text{A.12})$$

$$= |B_1^+| e^{i\phi^+} \left[ \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial z} + i \frac{\partial \phi^+}{\partial z} \right] \quad (\text{A.13})$$

Second term in Eq. A.1 can be written as:

$$\nabla^2 B_1^+ = \frac{\partial^2 B_1^+}{\partial x^2} + \frac{\partial^2 B_1^+}{\partial y^2} + \frac{\partial^2 B_1^+}{\partial z^2} \quad (\text{A.14})$$

Again, using  $B_1^+ = |B_1^+|e^{i\phi^+}$ , we get:

$$\frac{\partial^2 B_1^+}{\partial x^2} = \frac{\partial}{\partial x} \left[ \frac{\partial |B_1^+|}{\partial x} e^{i\phi^+} + i|B_1^+| \frac{\partial \phi^+}{\partial x} e^{i\phi^+} \right] \quad (\text{A.15})$$

$$= \frac{\partial^2 |B_1^+|}{\partial x^2} e^{i\phi^+} + i2 \frac{\partial |B_1^+|}{\partial x} \frac{\partial \phi^+}{\partial x} e^{i\phi^+} + i|B_1^+| \frac{\partial^2 \phi^+}{\partial x^2} e^{i\phi^+} - |B_1^+| \left( \frac{\partial \phi^+}{\partial x} \right)^2 e^{i\phi^+} \quad (\text{A.16})$$

$$= |B_1^+| e^{i\phi^+} \left[ \frac{1}{|B_1^+|} \frac{\partial^2 |B_1^+|}{\partial x^2} + i2 \frac{\partial \ln |B_1^+|}{\partial x} \frac{\partial \phi^+}{\partial x} + i \frac{\partial^2 \phi^+}{\partial x^2} - \left( \frac{\partial \phi^+}{\partial x} \right)^2 \right] \quad (\text{A.17})$$

$$= |B_1^+| e^{i\phi^+} \left[ - \left( \frac{\partial \phi^+}{\partial x} \right)^2 + \frac{1}{|B_1^+|} \frac{\partial^2 |B_1^+|}{\partial x^2} + i2 \frac{\partial \ln |B_1^+|}{\partial x} \frac{\partial \phi^+}{\partial x} + i \frac{\partial^2 \phi^+}{\partial x^2} \right] \quad (\text{A.18})$$

Following same steps for  $\frac{\partial^2 B_1^+}{\partial y^2}$  and  $\frac{\partial^2 B_1^+}{\partial z^2}$  gives:

$$\frac{\partial^2 B_1^+}{\partial y^2} = |B_1^+| e^{i\phi^+} \left[ - \left( \frac{\partial \phi^+}{\partial y} \right)^2 + \frac{1}{|B_1^+|} \frac{\partial^2 |B_1^+|}{\partial y^2} + i2 \frac{\partial \ln |B_1^+|}{\partial y} \frac{\partial \phi^+}{\partial y} + i \frac{\partial^2 \phi^+}{\partial y^2} \right] \quad (\text{A.19})$$

and;

$$\frac{\partial^2 B_1^+}{\partial z^2} = |B_1^+| e^{i\phi^+} \left[ - \left( \frac{\partial \phi^+}{\partial z} \right)^2 + \frac{1}{|B_1^+|} \frac{\partial^2 |B_1^+|}{\partial z^2} + i2 \frac{\partial \ln |B_1^+|}{\partial z} \frac{\partial \phi^+}{\partial z} + i \frac{\partial^2 \phi^+}{\partial z^2} \right] \quad (\text{A.20})$$

Rewriting Eq.A.14 using Eq.s A.15-A.20:

$$\begin{aligned} \nabla^2 B_1^+ = & |B_1^+| e^{i\phi^+} - \left[ \left( \left( \frac{\partial \phi^+}{\partial x} \right)^2 + \left( \frac{\partial \phi^+}{\partial y} \right)^2 + \left( \frac{\partial \phi^+}{\partial z} \right)^2 \right) + i \nabla^2 \phi^+ \right. \\ & \left. + \frac{1}{|B_1^+|} \nabla^2 |B_1^+| + i 2 \nabla \ln |B_1^+| \cdot \nabla \phi^+ \right] \end{aligned} \quad (\text{A.21})$$

Defining  $\Omega$  as:

$$\Omega = \begin{bmatrix} i \frac{\partial \phi^+}{\partial x} + \frac{\partial \phi^+}{\partial y} + \frac{\partial \ln |B_1^+|}{\partial x} - i \frac{\partial \ln |B_1^+|}{\partial y} \\ -\frac{\partial \phi^+}{\partial x} + i \frac{\partial \phi^+}{\partial y} + i \frac{\partial \ln |B_1^+|}{\partial x} + \frac{\partial \ln |B_1^+|}{\partial y} \\ \frac{1}{|B_1^+|} \frac{\partial |B_1^+|}{\partial z} + i \frac{\partial \phi^+}{\partial z} \end{bmatrix} \quad (\text{A.22})$$

Combining all results and rewriting Eq. A.1 gives:

$$\begin{aligned} \Omega \cdot \nabla \ln \gamma + & \left[ \left( \frac{\partial \phi^+}{\partial x} \right)^2 + \left( \frac{\partial \phi^+}{\partial y} \right)^2 + \left( \frac{\partial \phi^+}{\partial z} \right)^2 \right] - i \nabla^2 \phi^+ \\ & - \frac{1}{|B_1^+|} \nabla^2 |B_1^+| - i 2 \nabla \ln |B_1^+| \cdot \nabla \phi^+ + i \omega \mu_0 \gamma = 0 \end{aligned} \quad (\text{A.23})$$

Making the assumptions that  $\sigma \gg i\omega\epsilon$ ,  $Re\left\{\frac{\nabla\gamma}{\gamma}\right\} \approx \frac{\nabla\sigma}{\sigma} = -\frac{\nabla\rho}{\rho}$  where  $\sigma = \frac{1}{\rho}$ , we can neglect the real part of the equation and write only the imaginary parts:

$$\begin{bmatrix} -\frac{\partial \phi^+}{x} + \frac{1}{|B_1^+| \frac{\partial |B_1^+|}{\partial y}} \\ -\frac{\partial \phi^+}{y} - \frac{1}{|B_1^+| \frac{\partial |B_1^+|}{\partial x}} \\ -\frac{\partial \phi^+}{\partial z} \end{bmatrix}^T \begin{bmatrix} \frac{1}{\rho} \frac{\partial \rho}{\partial x} \\ \frac{1}{\rho} \frac{\partial \rho}{\partial y} \\ \frac{1}{\rho} \frac{\partial \rho}{\partial z} \end{bmatrix} - \nabla^2 \phi^+ - \frac{2}{|B_1^+|} \nabla |B_1^+| \cdot \nabla \phi^2 = -\omega \mu_0 \sigma \quad (\text{A.24})$$

Multiplying by  $\rho$ :

$$\begin{bmatrix} \frac{\partial \phi^+}{x} + \frac{1}{|B_1^+| \frac{\partial |B_1^+|}{\partial y}} \\ \frac{\partial \phi^+}{y} - \frac{1}{|B_1^+| \frac{\partial |B_1^+|}{\partial x}} \\ \frac{\partial \phi^+}{\partial z} \end{bmatrix}^T \begin{bmatrix} \frac{\partial \rho}{\partial x} \\ \frac{\partial \rho}{\partial y} \\ \frac{\partial \rho}{\partial z} \end{bmatrix} + \left[ \nabla^2 \phi^+ + \frac{2}{|B_1^+|} \nabla |B_1^+| \cdot \nabla \phi^+ \right] \rho = \omega \mu_0 \quad (\text{A.25})$$

Applying same steps to  $|B_1^-|$ , we get:

$$\begin{bmatrix} \frac{\partial \phi^-}{x} - \frac{1}{|B_1^-| \frac{\partial |B_1^-|}{\partial y}} \\ \frac{\partial \phi^-}{y} + \frac{1}{|B_1^-| \frac{\partial |B_1^-|}{\partial x}} \\ \frac{\partial \phi^-}{\partial z} \end{bmatrix}^T \begin{bmatrix} \frac{\partial \rho}{\partial x} \\ \frac{\partial \rho}{\partial y} \\ \frac{\partial \rho}{\partial z} \end{bmatrix} + \left[ \nabla^2 \phi^- + \frac{2}{|B_1^-|} \nabla |B_1^-| \cdot \nabla \phi^- \right] \rho = \omega \mu_0 \quad (\text{A.26})$$

Then, we make the assumption that;

$$\frac{1}{|B_1^+|} \nabla |B_1^+| \approx \frac{1}{|B_1^-|} \nabla |B_1^-|$$

meaning that transmit and receive sensitivities of the employed coils are similar. In the cases where the same birdcage coil is used for both transmit and receive, the assumption holds. Even if different coils or coil arrays are used for transmit and receive signals, it is plausible to assume that signals from each coil is combined in a way that coil sensitivities will be similar, and the assumption again holds.

Also defining transceive phase as  $\phi^{tr} \triangleq \phi^+ + \phi^-$ , summing Eq.s A.25 and A.26, and adding an artificial diffusion term for regularization, we obtain the final form of bias-corrected phase-based cr-MREPT.

$$-c \nabla^2 \rho + \nabla \phi \cdot \nabla \rho + \left[ \nabla^2 \phi + \frac{2}{|B_1^+|} \nabla |B_1^+| \cdot \nabla \phi \right] \rho = 2\omega \mu_0 \quad (\text{A.27})$$

# Appendix B

## Matlab Code for cr-MREPT Library

```
%% Bias-corrected standart and cr-MREPT — 12.2025 — v5
% Works for 7 different simulation phantoms
% Select a phantom, select the desired options and run.
% 3D cylinder phantom is added.
% Scaling is fixed.
% Resolution phantom is added.
% Boundary condition is added.
clear all; close all;

%% Select phantom
% 1: Uniform
% 2: 2 Anomalies
% 3: 4 Anomalies
% 4: Brain simulation
% 5: 3D Cylinder
%     5.1: Bottom Slice
%     5.2: Middle Slice
%     5.3: Top Slice
% 6: 3D Brain
% 7: Resolution
```

```

opts.phantom = 2;

%% Other options
% Bias correction
% 0: No bias correction
% 1: Apply bias correction
opts.biasCorrection = 1;

% Plot options
% 0: None – No graphs are plotted
% 1: Reconstruction results only – Only conductivity results are plotted
% 2: Results only – Obtained results are plotted
% 3: All – Sub-results are plotted
% 4: Debug – Everything is plotted
opts.plots = 1;

% Noise
opts.add_noise_to_data = 0;
opts.noise_level = 0.01;

% Diffusion Coefficient
opts.diff_coef = -0.01;

% Mesh size
opts.meshSize = 0.0015;

% Boundary Condition
opts.boundaryCondition = 0;
opts.boundaryConditionValue = 0.5;

%% Definitions
constants.mu0 = 4e-7*pi;
constants.f0 = 127e6;
constants.w0 = 2*pi*constants.f0;
constants.eps0 = 8.854e-12;

```

```

constants.scl      = 1;

%% Load data and set-up
if(opts.phantom == 1)
    load('sigma_uniform.mat');
    load('B1p_complex_water_bc.mat');
    load('ROI_121_0.15_v2.mat');

elseif(opts.phantom == 2)
    load('sigma_2anomalies.mat');
    load('B1p_complex_birdcage_v3.mat');
    load('ROI_121_0.15_v2.mat');

elseif(opts.phantom == 3)
    load('sigma_4anomalies.mat');
    load('B1p_complex_birdcage_4anomalies_v1.mat');
    load('ROI_121_0.15_v2.mat');

elseif(opts.phantom == 4)
    load('sigma_head_transposed.mat');
    load('head4_sim_b1p.mat');
    load('ROI_161_0.15_v2.mat');
    data.mesh.complex.ch1 = (data.mesh.complex.ch1);
    constants.scl = 0.95;

elseif(opts.phantom == 5.1)
    load('cyl3D_sliceBot_v1.mat');
    load('cyl3D_sigma_slice_V1.mat');
    load('ROI_2D_51x51x51_1mm.mat');

elseif(opts.phantom == 5.2)
    load('cyl3D_slice_v1.mat');
    load('cyl3D_sigma_slice_V1.mat');
    load('ROI_2D_51x51x51_1mm.mat');

```

```

elseif(opts.phantom == 5.3)
    load('cyl3D_sliceUp_v1.mat');
    load('cyl3D_sigma_slice_V1.mat');
    load('ROI_2D_51x51x51_1mm.mat');

elseif(opts.phantom == 6)
    load('data_slice.mat');
    load('sigma_slice.mat');
    load('ROI_xy.mat');
    sigma_true = (slice.xy);
    data.mesh.complex.ch1 = transpose(data_slice.xy);
    constants.scl = 0.95;

elseif(opts.phantom == 7)
    load('resolution_Sim_v1.mat');
    load('sigma_resolutionSim.mat');
    load('ROI_131_0.1_v1.mat');
    % data.mesh.complex.ch1 = transpose(data.mesh.complex.ch1);
    % sigma_true = (slice.xz);
    % data.mesh.complex.ch1 = transpose(data_slice.xz);
    % ROI.yLin = ROI.zLin;
    % ROI.yMesh = ROI.zMesh;
end

if(opts.plots)
    figure
    imagesc(flip(sigma_true))
    title('True Sigma Distribution')
    colormap jet; clim([0 1]);
end

%% EM Simulation for B1+ magnitude
% Find outer boundary
boundary.B = bwboundaries(sigma_true);
boundary.ind = cell2mat(boundary.B(1,:));

```

```

boundary.boundary = zeros(size(sigma_true));
for i = 1:length(boundary.ind)
    boundary.boundary(boundary.ind(i,1), boundary.ind(i,2)) = 1;
end
if(opts.plots > 1)
    figure
    imagesc(boundary.boundary)
    title('Outer Object Boundary')
end

% Set-up EM simulation
EMmodel.model = createpde("electromagnetic","harmonic");
EMmodel.model.FieldType = "magnetic";
EMmodel.SQ = [3,4,-1,-1,1,1,-1,1,1,-1]';
boundary.indHold = boundary.ind; boundary.ind(end,:) = [];
boundary.aa = boundary.ind*ROI.dx - max(ROI.xLin)-ROI.dx;

EMmodel.P1 = [2,length(boundary.ind),boundary.aa(:)']';
EMmodel.mask = [2,length(boundary.ind),0.9*boundary.aa(:)']';
EMmodel.SQ = [EMmodel.SQ;zeros(length(EMmodel.P1) ...
    - length(EMmodel.SQ),1)];

EMmodel.gm = [EMmodel.SQ,EMmodel.P1];
EMmodel.g = decsg(EMmodel.gm);
EMmodel.gg = geometryFromEdges(EMmodel.model,EMmodel.g);

EMmodel.EdgeID_all = faceEdges(EMmodel.gg,1);
EMmodel.EdgeID_object = faceEdges(EMmodel.gg,2);
EMmodel.outer_edge = setdiff(EMmodel.EdgeID_all,...
    EMmodel.EdgeID_object);

if(opts.plots > 2)
    figure
    pdegplot(EMmodel.model,"FaceLabels","on")
end

```

```

EMmodel.model.VacuumPermittivity = constants.mu0;
EMmodel.model.VacuumPermeability = constants.eps0;

electromagneticProperties(EMmodel.model,"Face",1, ...
    "RelativePermittivity",1, ...
    "RelativePermeability",1, ...
    "Conductivity",0);
electromagneticProperties(EMmodel.model,"Face",2, ...
    "RelativePermittivity",60, ...
    "RelativePermeability",1, ...
    "Conductivity",0.5);

EMmodel.H = @(location , state) [-1;-1i]*1;
EMmodel.BC = electromagneticBC(EMmodel.model,"Edge", ...
    EMmodel.outer_edge,"MagneticField",EMmodel.H);
EMmodel.mesh = generateMesh(EMmodel.model,"Hmax",0.005);
EMmodel.result = solve(EMmodel.model,"Frequency",constants.w0);

EMmodel.Hp = (EMmodel.result.MagneticField.Hx ...
    + 1i*EMmodel.result.MagneticField.Hy)/2;
EMmodel.Hm = conj(EMmodel.result.MagneticField.Hx ...
    - 1i*EMmodel.result.MagneticField.Hy)/2;

EMmodel.ROI_sim.ind = ...
    abs(EMmodel.model.Mesh.Nodes(1,:)) < 1.1*max(ROI.xLin) ...
    & abs(EMmodel.model.Mesh.Nodes(2,:)) < 1.1*max(ROI.yLin);
EMmodel.ROI_sim.x = EMmodel.model.Mesh.Nodes(1,EMmodel.ROI_sim.ind);
EMmodel.ROI_sim.y = EMmodel.model.Mesh.Nodes(2,EMmodel.ROI_sim.ind);
EMmodel.Hp_cut = EMmodel.Hp(EMmodel.ROI_sim.ind);
EMmodel.Hm_cut = EMmodel.Hm(EMmodel.ROI_sim.ind);

results.Hp_cart = reshape(griddata(EMmodel.ROI_sim.x,...
    EMmodel.ROI_sim.y,EMmodel.Hp_cut,ROI.xLin,ROI.yLin),...,
    size(sigma_true,1),size(sigma_true,2));

```

```

results.Hm_cart = reshape( griddata(EMmodel.ROI_sim.x,...
    EMmodel.ROI_sim.y,EMmodel.Hm_cut,ROI.xLin,ROI.yLin)...
    ,size(sigma_true,1),size(sigma_true,2));

if(opts.plots == 4)
    figure
    pdegplot(EMmodel.model,"FaceLabels","on");
    hold on;
    pdeplot(EMmodel.model,"XYData",abs(EMmodel.Hp));
    title('B1+ Magnitude - all ')
end

if(opts.plots > 1)
    figure
    imagesc(abs(results.Hp_cart))
    title('B1+ Magnitude - center ')
end

%% Create masked ROI and mesh
% Uses outer object boundary automatically

[ROI.masked.ps, ROI.masked.es, ROI.masked.ts] = ...
    initmesh( decsg(EMmodel.mask), 'hmax', opts.meshSize );
ROI.masked.x = ROI.masked.ps(1,:)*constants.scl;
ROI.masked.y = ROI.masked.ps(2,:)*constants.scl;
ROI.masked.z = zeros(size(ROI.masked.x));
ROI.masked.faces = ROI.masked.ts(1:3,:);

ROI.masked.pp = [ROI.masked.x; ROI.masked.y];

ROI.masked.edgeNodes = unique(ROI.masked.es(1:2,:))';
ROI.masked.innerNodes = ones(size(ROI.masked.x));
ROI.masked.innerNodes(ROI.masked.edgeNodes) = 0;
ROI.masked.innerNodes = find(ROI.masked.innerNodes);
ROI.masked.pp = [ROI.masked.x; ROI.masked.y];
ROI.masked.tt = [ROI.masked.faces; ones(1,size(ROI.masked.faces,2))];

```

```

%% Create masked ROI and mesh
% Define ROI manually

%% rcn=12;rows3=zeros(1,rcn)';cols3=rows3;
%% radius=0.055;
%% for i=1:rcn
%%     rows3(i)=radius*cos(pi/6*i);
%%     cols3(i)=radius*sin(pi/6*i);
%% end
%% mask = poly2mask((cols3+0.09)/0.0015+1,...
%% (rows3+0.09)/0.0015+1,121,121);
%% p1 = [2; length(rows3); rows3; cols3];
%
% cols3 = transpose([0 -0.0337 -0.0604 -0.0698 -0.0442 -0.0153
...
0 0.0153 0.0442 0.0698 0.0604 0.0337]);
% rows3 =-1* transpose([0.0760 0.0760 0.0465 0.0113 -0.0739 ...
-0.0887 -0.0866 -0.0887 -0.0739 0.0113 0.0465 0.0760]);
% mesh_size=0.0015;
% p1 = [2; length(rows3); cols3; rows3]; %%% This line here
%
% [ROI.ps, ROI.es, ROI.ts]=initmesh(decsg(p1),'hmax',opts.meshSize);
%
% ROI.masked.x = ROI.ps(1,:);
% ROI.masked.y = ROI.ps(2,:);
% ROI.masked.z = zeros(size(ROI.masked.x));
% ROI.masked.faces = ROI.ts(1:3,:);
%
% ROI.pp = [ROI.masked.x; ROI.masked.y];
%
% ROI.masked.edgeNodes = unique(ROI.es(1:2,:))';
% ROI.innerNodes = ones(size(ROI.masked.x));
% ROI.innerNodes(ROI.masked.edgeNodes) = 0;
% ROI.masked.innerNodes = find(ROI.innerNodes);

```

```

% ROI.masked.pp = [ROI.masked.x; ROI.masked.y];
% ROI.masked.tt = [ROI.masked.faces; ones(1, size(ROI.masked.faces, 2))];

%% Start Reconstruction
tic
recon.ang = (angle(data.mesh.complex.ch1));
recon.abs = (abs(results.Hp_cart));
% load('cube2D_v3.mat')
% recon.abs = (abs(data.mesh.complex.ch1));

if(opts.plots == 4)
    figure
    imagesc(recon.ang)
    title('Phase data')
end

% Add noise
if opts.add_noise_to_data==1
    recon.stdnoise = opts.noise_level;
    recon.HpCnoise = recon.stdnoise * (rand(size(recon.ang)) - 0.5);
    recon.ang = recon.ang + recon.HpCnoise;
end

% Gaussian filter % How to pick this automatically?
% recon.h2 = fspecial('gaussian', 3, 0.5);
recon.h2 = fspecial('gaussian', 5, 2);
% recon.h2 = fspecial('gaussian', [7 7], 5);

recon.ang_filtered = filter2(recon.h2, recon.ang);
recon.abs_filtered = filter2(recon.h2, recon.abs);
recon.abs_log      = log(recon.abs_filtered);

if(opts.plots == 4)
    figure
    imagesc(recon.ang_filtered)

```

```

        title('Filtered phase data')
    end

    [recon.dx, recon.dy] = gradient(recon.ang_filtered,ROI.dx,ROI.dy);
    recon.lap = 4*del2(recon.ang_filtered,ROI.dx,ROI.dy);

    if(opts.plots == 4)
        figure
        imagesc(recon.lap)
        title('Laplacian of phase data')
    end

    recon.trimesh.phase.lap = griddata(ROI.xLin,ROI.yLin,recon.lap(:),...
        ROI.masked.x,ROI.masked.y,'linear');
    recon.trimesh.PhaseLapFace = ...
        mean(recon.trimesh.phase.lap(ROI.masked.faces),1);

    recon.trimesh.phase.phase = griddata(ROI.xLin,ROI.yLin,...
        recon.ang(:),ROI.masked.x,ROI.masked.y,'linear');
    recon.trimesh.phase.dx = griddata(ROI.xLin,ROI.yLin,...
        recon.dx(:),ROI.masked.x,ROI.masked.y,'linear');
    recon.trimesh.phase.dy = griddata(ROI.xLin,ROI.yLin,...
        recon.dy(:),ROI.masked.x,ROI.masked.y,'linear');
    recon.trimesh.PhasedxFace = ...
        mean(recon.trimesh.phase.dx(ROI.masked.faces),1);
    recon.trimesh.PhasedyFace = ...
        mean(recon.trimesh.phase.dy(ROI.masked.faces),1);

    if(opts.plots == 4)
        figure
        pdesurf(ROI.masked.pp,ROI.masked.tt,recon.trimesh.phase.phase');
        colormap jet;
        title('Phase data in triangular mesh')
    end

```

```

figure
pdesurf(ROI.masked.pp,ROI.masked.tt,recon.trimesh.phase.dx');
colormap jet;
title('x-derivative of phase data in triangular mesh')

figure
pdesurf(ROI.masked.pp,ROI.masked.tt,recon.trimesh.phase.dy');
colormap jet;
title('y-derivative of phase data in triangular mesh')

figure
pdesurf(ROI.masked.pp,ROI.masked.tt,recon.trimesh.phase.lap');
colormap jet;
title('Laplacian of phase data in triangular mesh')
end

[recon.complexMagnitude.dx, recon.complexMagnitude.dy] = ...
    gradient(recon.abs_log,ROI.dx,ROI.dy);
recon.trimesh.Magnitude.dx = griddata(ROI.xLin,ROI.yLin,...
    recon.complexMagnitude.dx(:),ROI.masked.x,ROI.masked.y,'linear');
recon.trimesh.Magnitude.dy = griddata(ROI.xLin,ROI.yLin,...
    recon.complexMagnitude.dy(:),ROI.masked.x,ROI.masked.y,'linear');
recon.trimesh.MagnitudedxFace = ...
    mean(recon.trimesh.Magnitude.dx(ROI.masked.faces),1);
recon.trimesh.MagnitudedyFace = ...
    mean(recon.trimesh.Magnitude.dy(ROI.masked.faces),1);

recon.absFace = mean(recon.abs_filtered(ROI.masked.faces),1);

recon.mag_term = 2 * (recon.trimesh.MagnitudedxFace ...
    .* recon.trimesh.PhasedxFace + recon.trimesh.MagnitudedyFace ...
    .* recon.trimesh.PhasedyFace);
recon.mag_term_nodes = 2 * (recon.trimesh.Magnitude.dx ...
    .* recon.trimesh.phase.dx + recon.trimesh.Magnitude.dy ...
    .* recon.trimesh.phase.dy);

```

```

if(opts.plots == 4)
    figure
    imagesc(recon.abs_log);
    colormap jet;
    title('Magnitude data in cartesian mesh')

    figure
    pdesurf(ROI.masked.pp,ROI.masked.tt,recon.trimesh.Magnitude.dx');
    colormap jet;
    title('x-derivative of magnitude data in triangular mesh')

    figure
    pdesurf(ROI.masked.pp,ROI.masked.tt,recon.trimesh.Magnitude.dy');
    colormap jet;
    title('y-derivative of magnitude data in triangular mesh')
end

if(opts.plots > 2)
    figure
    pdesurf(ROI.masked.pp,ROI.masked.tt,recon.mag_term); colormap jet;
    title('Magnitude term for bias correction')
end

% Standart
if opts.biasCorrection
    recon.cond.std = ...
        (recon.trimesh.phase.lap + recon.mag_term_nodes)...
        /constants.w0/constants.mu0;
else
    recon.cond.std = recon.trimesh.phase.lap...
        /constants.w0/constants.mu0;
end

% crMREPT

```

```

if opts.biasCorrection
[recon.A,recon.Dt2n] = ...
    form_full_matrix_trimesh_with_new_diffusion_matrix ...
    (ROI.masked.pp,ROI.masked.tt ,recon.trimesh.phase.phase ,...
    (recon.trimesh.PhasedxFace),(recon.trimesh.PhasedyFace) ,...
    recon.trimesh.PhaseLapFace + recon.mag_term,opts.diff_coef,1);
else
[recon.A,recon.Dt2n] = ...
    form_full_matrix_trimesh_with_new_diffusion_matrix ...
    (ROI.masked.pp,ROI.masked.tt ,recon.trimesh.phase.phase ,...
    (recon.trimesh.PhasedxFace),(recon.trimesh.PhasedyFace) ,...
    recon.trimesh.PhaseLapFace,opts.diff_coef,1);
end

recon.b          = constants.w0 * constants.mu0 ...
    * ones(1,length(ROI.masked.faces));
recon.b          = recon.b.';
recon.sol        = recon.A\recon.b;
recon.cond.cr    = 1./ recon.sol;

% BC
if(opts.boundaryCondition)
local.b          = constants.w0 * constants.mu0 ...
    * ones(1,length(ROI.masked.faces));
local.b          = local.b.';
% nnn=1:length(ROI.local.ind.all); nnn(ROI.local.outernodes)=-1;
% midnodes = nnn(nnn>0);
Apn1 = recon.A(:,ROI.masked.innerNodes);

bc_out = 1/opts.boundaryConditionValue;
bpn1 = local.b - recon.A(:,ROI.masked.edgeNodes)*bc_out ...
    *ones(length(ROI.masked.edgeNodes),1);
rrr=Apn1\bpn1;
sol=zeros(length(ROI.masked.x),1);
sol(ROI.masked.edgeNodes) = bc_out;

```

```

sol(ROI.masked.innerNodes) = rrr;

local.cond.crBC = 1./sol;
end
toc
%%
if(opts.plots)
    figure
    pdesurfk(ROI.masked.pp,ROI.masked.tt,recon.cond.std');
    colormap jet; clim([0 1]);
    % zlim([0 1]);
    % ylim([min(ROI.masked.y) max(ROI.masked.y)]);
    % xlim([min(ROI.masked.x) max(ROI.masked.x)]);
    title('Standart MREPT')

    figure
    pdesurfk([ROI.masked.x; ROI.masked.y],ROI.masked.tt,...
        recon.cond.cr);
    colormap jet; clim([0 1]);
    % zlim([0 1]);
    % ylim([min(ROI.masked.y) max(ROI.masked.y)]);
    % xlim([min(ROI.masked.x) max(ROI.masked.x)]);
    title('cr-MREPT')

    if(opts.boundaryCondition)
        figure
        pdesurfk([ROI.masked.x; ROI.masked.y],ROI.masked.tt,...
            local.cond.crBC);
        colormap jet; clim([0 1]);
        % zlim([0 1]);
        % ylim([min(ROI.masked.y) max(ROI.masked.y)]);
        % xlim([min(ROI.masked.x) max(ROI.masked.x)]);
        title('cr-MREPT - with BC')
    end
end
end

```