

LOW-FREQUENCY CONDUCTIVITY IMAGING USING MRI GRADIENT INDUCED CURRENTS

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By
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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

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Due to the switching of Magnetic Resonance Imaging (MRI) gradient fields, electric fields are induced in imaged subjects which give rise to ‘subject eddy currents’. The feasibility of low-frequency conductivity imaging based on measuring the magnetic field (subject eddy field) due to subject eddy currents is investigated within the frame of two main goals. First goal is to understand whether conductivity reconstruction is possible provided that subject eddy fields are accurately measured. Regarding this goal, the inverse problem of obtaining conductivity distribution from subject eddy fields is formulated as a convection-reaction equation and a conductivity reconstruction algorithm is developed. In the simulations, successful conductivity reconstructions are obtained pointing the feasibility of the proposed algorithm. The second goal is to understand the fidelity by which subject eddy fields must be measured for accurately reconstructing conductivity. For measuring subject eddy fields, a pulse sequence is developed by which the contribution of subject eddy fields to MR phase images is determined. It is found that this contribution cannot be measured with an uncertainty sufficiently low for accurate conductivity reconstruction. Furthermore, some artifacts other than random noise are observed in the measured phases which are modeled by considering the effects of magnetic fields due to MRI system imperfections during readout. For feasible subject eddy current based conductivity imaging, it is required that the span of the phase accumulated by subject eddy fields is increased, and the mentioned artifacts are eliminated from the phase measurements. For the first requirement, the state-of-the-art gradient systems are evaluated and also a multi-spin-echo pulse sequence is developed. This pulse sequence is analyzed by using the extended phase graph framework. For the second requirement, the possibility of using geometric distortion correction methods are evaluated. It is

found that, if the multi-spin-echo pulse sequence is used in small-sized preclinical MRI scanners which have extremely high gradient fields, the span of accumulated phase can be sufficiently increased for the feasibility. On the other hand, it is found that the geometric distortions cannot be corrected to the degree that the level of artifacts becomes sufficiently low for the feasibility.



Keywords: eddy current, induced current, gradient field, low-frequency conductivity imaging, geometric distortion, extended phase graph, magnetic resonance imaging.

ÖZET

MRG GRADYANLARININ ENDÜKLEDİĞİ AKIM KULLANILARAK DÜŞÜK FREKANS İLETKENLİK GÖRÜNTÜLEME

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Manyetik Rezonans Görüntüleme (MRG) kullanılan gradyan alanların anahatarlanması, görüntülenen cisim ya da canlı içerisinde elektrik alanların endüklenmesine neden olur ve bu yolla ‘cisim girdap akımları’ oluşur. Cisim girdap akımlarından kaynaklanan manyetik alanların (cisim girdap alanı) ölçülmesine dayanan düşük-frekans iletkenlik görüntülemesinin fizibilitesi (yapılabilirliği) iki amaç çerçevesinde incelenmiştir. Birinci amaç, cisim girdap alanlarının hatasız olarak ölçüldüğü varsayıldığında iletkenliğin geriçatılmasının mümkün olup olmadığının anlaşılmasıdır. Bu amaçla, iletkenlik dağılımının cisim girdap alanlarından elde edilmesi olarak tanımlanan ters problem, bir taşınım-reaksiyon denklemi olarak formüle edilmiş ve bir iletkenlik geriçatım algoritması geliştirilmiştir. Yapılan benzetimlerde, önerilen algoritmanın fizibilitesine işaret eden başarılı iletkenlik geriçatımları elde edilmiştir. İkinci amaç, iletkenliğin yüksek doğruluklu olarak geriçatılması için cisim girdap alanlarının aslına ne kadar uygun olarak ölçülmesi gerektiğinin anlaşılmasıdır. Cisim girdap alanlarının ölçülmesi için bu alanların MR fazına olan katkısının elde edildiği bir darbe dizini geliştirilmiştir. Bu katkının, yüksek doğruluklu bir iletkenlik geriçatımı için yeterli derecede belirsizlikle ölçülemeyeceği anlaşılmıştır. Ayrıca, ölçülen fazlarda rastgele gürültü dışında bazı artefaktlar da gözlenmiştir. MRG cihazının ideal olmaması nedeniyle oluşan manyetik alan etkileri gözetilerek bu artefaktlar modellenmiştir. Cisim girdap akımı temelli iletkenlik görüntülemenin yapılabilir olması için cisim girdap alanlarının biriktirdiği fazın arttırılması ve faz ölçümlerinin bahsedilen artefaktlardan arındırılması gerekmektedir. İlk gereksinim için en ileri gradyan sistemleri değerlendirilmiş ve ayrıca bir çoklu-spin-eko darbe dizini geliştirilmiştir. Bu darbe dizini, ‘genişletilmiş faz çizgesi’ çerçevesinde analiz

edilmiştir. İkinci gereksinim için geometrik bozulmaların düzeltilmesi amacıyla önerilen yöntemler değerlendirilmiştir. Çoklu-spin-eko sekansının, oldukça yüksek gradyan alanlara sahip küçük boyutlu prelinik MR cihazlarında kullanılması durumunda biriktirilen fazdaki artışın hassas bir iletkenlik geriçatımı için yeterli olduğu anlaşılmıştır. Diğer taraftan, geometrik bozulmaların, artefaktları kabul edilebilecek seviyeye indirebilecek derecede düzeltilemeyeceği anlaşılmıştır.



Anahtar sözcükler: girdap akımı, endüklenen akım, gradyan alan, düşük frekanslı iletkenlik görüntüleme, geometrik bozulmalar, genişletilmiş faz çizgesi, manyetik rezonans görüntüleme.

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Chapter 1

Introduction

1.1 Motivation

Imaging electrical conductivity of biological tissues has been an active research area for decades. Conductivity varies among different tissues and thus imaging its distribution provides anatomical information with a different contrast mechanism [1]-[3] (see Table 1.1). Conductivity of tissues also varies with the frequency of induced or injected currents [2]. At low frequencies, the lipid membrane of cells acts as an insulator and prevents currents from entering the cells, whereas at high frequencies, currents can pass through the capacitance of the cell membrane [4]. This implies that the lower and upper frequency spectra of conductivity convey different information about tissues and thus they have different potential application areas.

One of the most important application areas of high-frequency conductivity imaging is in the field of MR safety. Local assessment of specific absorption rate (SAR), which is defined as the power absorbed per unit mass of tissues, requires the knowledge of conductivity distribution [5]. Local SAR information

is especially important in high-field MRI in order to evaluate hot-spots where tissue heat is increased. On the other hand, low frequency conductivity maps can be used in applications such as monitoring thermal therapeutic procedures [6], electroencephalogram source localization [7, 8], and the planning of transcranial magnetic stimulation [9]-[11]. Furthermore, it is known that both high and low frequency conductivities depend on the pathological state of tissues. Therefore, one of the most promising application area for conductivity imaging seems detection, characterization, and follow-up of the prognosis of tumors [12]-[19].

Tissue	Frequency (kHz)	Conductivity (S/m)
Cerebrospinal fluid (human)	1	1.56
Blood (human)	DC	0.67
Plasma (human)	DC	1.42
Skeletal muscle (longitudinal fibers) (human)	DC	0.41
Skeletal muscle (transverse fibers) (human)	0.1	0.15
Fat (dog)	0.01	0.04
Bone (human)	0.1	0.00625

Table 1.1: Typical electrical conductivities of some biological tissues at low frequencies (reproduced from [3])

Several MRI-based techniques have been proposed for conductivity imaging at high and low frequencies. For high frequency conductivity imaging, Magnetic Resonance Electrical Properties Tomography (MREPT) techniques constitute the largest class. In these techniques, the distribution of radiofrequency (RF)-field (B_1), which is applied during an MRI session, is measured via special pulse sequences and techniques. Since B_1 field is perturbed by the underlying electrical properties of imaged subjects, electrical properties are reconstructed from the B_1 field distribution using reconstruction algorithms [5], [20]-[25].

For low frequency conductivity imaging, techniques classified as Magnetic Resonance Electrical Impedance Tomography (MREIT) are the most widely known

[26]-[30]. In these techniques, currents are injected into imaged subjects via surface electrodes. Distribution of magnetic fields due to internal currents is measured by exploiting the fact that these magnetic fields cause additional phase accumulation in MRI phase. This information is then used for solving the inverse problem which is defined as the reconstruction of conductivity from the measured magnetic field.

In MREIT, current injection causes problems such as pain sensation and geometric distortions, which are triggered by denser current density near electrodes [27]. To deal with these challenges, the Induced Current-MREIT technique has been proposed in which electrical currents are induced inside imaged subjects by means of external coils [31]. However the use of external coils inside an MRI scanner limits the practicality of this technique. As a remedy for this problem, it has been proposed to use readily available MRI gradient coils for inducing “subject eddy currents” inside subjects [32]-[41]. Subject eddy currents generate secondary magnetic fields which are referred to as “subject eddy fields”. Similar to MREIT, the ultimate purpose is to reconstruct conductivity from the measured subject eddy fields. However no experimental conductivity reconstruction has been presented yet [32]-[41].

1.2 Objective and Scope of the Thesis

This thesis investigates the feasibility of low-frequency conductivity imaging using subject eddy currents induced by the switching of the slice-selection gradient. The feasibility is investigated within the frame of two main goals. One goal is to understand whether conductivity reconstruction is possible provided that subject eddy fields are accurately measured. Regarding this goal, the inverse problem of obtaining the conductivity distribution from subject eddy fields is formulated as

a convection-reaction partial differential equation (PDE). Successful conductivity reconstructions are obtained by solving this equation using simulated data. The other goal is to understand the fidelity by which subject eddy fields must be measured for accurately reconstructing conductivity. For measuring subject eddy fields, a novel spin-echo pulse sequence is developed by which the contribution of subject eddy fields to MR phase images is determined. It is found that this contribution cannot be measured with an uncertainty sufficiently low for accurate conductivity reconstruction. In addition to random noise, some bias artifacts are observed in the phase measurements. These artifacts are modeled by considering the effects of undesired magnetic fields due to system imperfections during readout. In the final part of the thesis, we have evaluated the possibility of using geometric distortion correction methods for eliminating these artifacts. Furthermore, for increasing the span of the phase accumulated by subject eddy fields, a multi-spin-echo pulse sequence is proposed and different aspects of this pulse sequence are analyzed using the extended phase graph framework.

The text and figures presented in this thesis are mainly based on a journal publication by the author [41]. The content of Chapters 2, 3 and 4 was in part presented in the 21st and 23rd Annual Meetings of International Society for Magnetic Resonance in Medicine (ISMRM) [33, 38].

1.3 Organization of the Thesis

This thesis consists of six chapters. Chapter 2 describes system and subject eddy currents and discusses the measurement and calculation of subject eddy fields. The MRI pulse sequence proposed for measuring z-component of subject eddy fields is investigated. Chapters 3 and 4 investigate the two feasibility aspects of subject eddy current based conductivity imaging: Chapter 3 investigates the feasibility of the proposed conductivity reconstruction algorithm in the simulation

environment. Chapter 4 investigates the measurement of subject eddy fields with the aim of understanding if the noise in the measured subject eddy field is sufficiently low for an accurate conductivity reconstruction. Chapter 5 investigates the bias artifacts observed in the phase measurements by considering the effects of undesired magnetic fields due to system imperfections during readout. Chapter 6 suggests and analyzes possible solutions to make the subject eddy current based conductivity imaging feasible.



Chapter 2

Theory

2.1 System Eddy Currents and Fields

Due to the switching of gradient fields, electrical currents are induced on the metallic system components of an MRI scanner such as RF shields, RF and gradient coils, thermal shields of the magnet and the magnet itself [42]. Throughout this thesis, currents induced on these system components will be referred to as "system eddy currents". System eddy currents generate undesired secondary magnetic fields which oppose the applied gradient field. These fields will be referred to as "system eddy fields".

After switching gradient fields off, system eddy currents and fields decay exponentially with multiple time constants [43]. The number of time constants and the level of each time constant depend on the geometry, magnetic permeability (μ) and conductivity (σ) of the component on which eddy current is induced [44]. For the MRI system components, which are made of copper or aluminum, the magnetic permeability can be taken as μ_0 , whereas the conductivity differs

among the components mostly because of the fact that the conductivity is inversely proportional to the temperature [43]. For instance, components such as RF shields, RF and gradient coils are at the room temperature; heat radiation shields have temperature of about 50K; and the magnet has temperature of about 4K [43, 45]. Therefore time constants for eddy currents vary in the range from a few to hundreds of milliseconds [43, 42].

Spatial dependence of system eddy fields within the imaging volume is mainly described by zero-order system eddy fields, which are spatially constant, and first-order system eddy fields, which change linearly in x-, y-, or z-axes like imaging gradients [46]. Higher order spatial components are generally small and most often they are not measured nor corrected. Regardless of the axis in which gradient field is applied, first order eddy fields are generated in all axes. However they are most dominant in the axis in which the gradient field is applied [46].

Rise times of typical gradient fields indicate that gradient fields have dominantly low-frequency components. Therefore, displacement currents are negligible compared with conductive currents. In this case, the governing equations for the electric field ($\mathbf{E}$) and system eddy field ($\mathbf{B}_{sys}$) are given during the switching of gradient fields as

$$\nabla \times \mathbf{E}(t) = -\frac{\partial \mathbf{B}_p(t)}{\partial t} - \frac{\partial \mathbf{B}_{sys}(t)}{\partial t} \quad (2.1a)$$

$$\nabla \times \mathbf{B}_{sys} = \mu_0 \sigma_{sys} \mathbf{E}(t) = \mu_0 \mathbf{J}_{sys}(t) \quad (2.1b)$$

where $\mathbf{B}_p$ is the x-, y-, or z-gradient field which ramp up or down in time, $\mathbf{J}_{sys}$ is the system eddy current density defined on system components, σ_{sys} is the electrical conductivity distribution of system components, and magnetic permeability is taken as μ_0 for the system components.

System eddy fields distort the primary gradient field and create undesired effects in MRI such as ghosting and geometric distortions [42]. In modern clinical MRI scanners, actively shielded gradient coils and gradient waveform pre-emphasis are used as standard for eliminating eddy current effects [42]. Although

most of the system eddy field in the volume of interest is eliminated by these methods, a residual field remains which is reflected as accumulated phase in MRI images.

2.2 Subject Eddy Currents and Fields

Due to the switching of gradient fields, electric fields are induced also in imaged subjects which give rise to internal eddy currents. In this thesis, these eddy currents are referred to as “subject eddy currents”. Subject eddy currents generate additional magnetic fields which will be referred to as “subject eddy fields”. The governing equations for subject eddy currents (J_{sub}) and subject eddy fields $\mathbf{B}_{sub}$ are obtained using three assumptions: (i) The contribution of $\mathbf{B}_{sys}$ to electric fields is negligible inside imaged subjects since $\mathbf{B}_{sys}$ is 0.05% (or less) of $\mathbf{B}_p$ in the imaging volume via eddy current compensation techniques [47]. (ii) $\mathbf{B}_{sub}$ is significantly lower than $\mathbf{B}_p$, and thus its contribution to electrical field is also negligible (this assumption is validated by the levels of simulated $\mathbf{B}_{sub}$). (iii) Displacement currents are negligible compared to conductive currents because of the low-frequency nature of gradient fields. Therefore, the governing equations during the switching of gradient fields are obtained inside the imaged subject as

$$\nabla \times \mathbf{E}(t) = -\frac{\partial \mathbf{B}_p(t)}{\partial t} \quad (2.2a)$$

$$\nabla \times \mathbf{B}_{sub} = \mu_0 \sigma \mathbf{E}(t) = \mu_0 \mathbf{J}_{sub}(t) \quad (2.2b)$$

where σ is the conductivity distribution of the imaged subject, and the magnetic permeability of the imaged subject is taken as μ_0 . Because of the assumption that $\mathbf{B}_{sub} \ll \mathbf{B}_p$, Equation (2.2a) and Equation (2.2b) become uncoupled, and thus subject eddy currents can be assumed to be instantly vanishing after the gradient ramp, which is in contrast to slowly decaying system eddy currents. Note that, although the contribution of $\mathbf{B}_{sys}$ to electric field is negligible, $\mathbf{B}_{sys}$ itself can cause significant phase accumulation in the MRI phase images [42, 47]. In the

next section, we will discuss how this phase accumulation is eliminated when the phase due to $\mathbf{B}_{sub}$ is measured.

2.3 Measurement of Subject Eddy Fields due to Slice-Selection Gradients

Subject eddy fields due to switching of any of the x-, y-, or z-gradients cause additional phase accumulation in MRI images. In this thesis, the subject eddy field due to the switching of z-gradient is investigated. For measuring z-component of this field, we have developed a method that is based on a novel spin-echo pulse sequence. Timing diagram of the proposed pulse sequence is shown in Figure 2.1. Slice-selection direction is taken as the z-direction. Since the z-gradient is linearly ramped up or down with the same slew rate at all edges, the subject eddy field is constant and its magnitude is equal at all edges, as evident from Equations (2.2a) and (2.2b). Two separate measurements, one using G_z^+ and one using G_z^- , are performed using this pulse sequence. The waveforms of $B_{sub,z}$ and $\varphi_{sub,z}$ for the case of G_z^+ are shown at the sixth and seventh rows of Figure 2.1. For increasing $\varphi_{sub,z}$, the directions of excitation and refocusing z-gradient lobes are opposite to each other in contrast to a conventional spin-echo sequence. The first lobe of $B_{sub,z}$ does not contribute to $\varphi_{sub,z}$ since it is before the excitation and the contribution of third and fourth lobes cancel each other. On the other hand, the fifth and sixth lobes, which are opposite of each other, both contribute to $\varphi_{sub,z}$ because of the refocusing RF pulse applied in between. Consequently, only the second, fifth, and sixth lobes of $B_{sub,z}$ have a net contribution to $\varphi_{sub,z}$ which is determined as follows

$$\varphi_{sub,z} = \gamma B_{sub,z} (\tau_{exc} + 2\tau_{rfc}) \quad (2.3)$$

where γ is the gyromagnetic ratio, $B_{sub,z}$ is the z-component of the subject eddy field due to the switching of the z-gradient, and τ_{exc} and τ_{rfc} are the relevant

ramp times shown in Figure 2.1 ($B_{sub,z}$ will be hereafter shortly referred to as the “subject eddy field”). When G_z^+ and G_z^- are used in two separate measurements, the acquired MR phase images can be expressed as

$$\varphi^+(x, y) = \varphi_{sub,z}(x, y) + \varphi_{RF}(x, y) + \varphi_{sys,z}(x, y) + \varphi_{other}(x, y) \quad (2.4a)$$

$$\varphi^-(x, y) = -\varphi_{sub,z}(x, y) + \varphi_{RF}(x, y) - \varphi_{sys,z}(x, y) + \varphi_{other}(x, y) \quad (2.4b)$$

where φ_{RF} is the phase of the RF field (transceive phase of the B1-field), $\varphi_{sys,z}$ is the phase accumulated by the z-component of the system eddy field due to the switching of the z-gradient ($B_{sys,z}$), and φ_{other} is the phase accumulated by the sum of system and subject eddy fields due to the switching of other gradients (since a spin-echo pulse sequence is used, the main magnetic field (B0) inhomogeneity does not have a net contribution to the accumulated phase). If the measurements using G_z^+ and G_z^- are also performed for a nonconductive phantom in which $\varphi_{sub,z}$ is zero, $\varphi_{sub,z}$ can be obtained using

$$\left\{ \frac{\varphi^+(x, y) - \varphi^-(x, y)}{2} \right\}_{\sigma=\sigma_0} = \varphi_{sub,z} + \varphi_{sys,z} \quad (2.5a)$$

$$\left\{ \frac{\varphi^+(x, y) - \varphi^-(x, y)}{2} \right\}_{\sigma=0} = \varphi_{sys,z} \quad (2.5b)$$

$$\left\{ \frac{\varphi^+(x, y) - \varphi^-(x, y)}{2} \right\}_{\sigma=\sigma_0} - \left\{ \frac{\varphi^+(x, y) - \varphi^-(x, y)}{2} \right\}_{\sigma=0} = \varphi_{sub,z} \quad (2.5c)$$

where σ_0 denotes the conductivity distribution of the imaging phantom. Once $\varphi_{sub,z}$ is measured, one may use Equation (2.3) with known values of τ_{exc} , and τ_{rfc} for obtaining $B_{sub,z}$.

2.4 Forward Problem Definition

Given the geometry and conductivity distribution of the imaged subject, and the geometry and current of the gradient coils, the forward problem for the eddy current based conductivity imaging is defined as the calculation of gradient fields

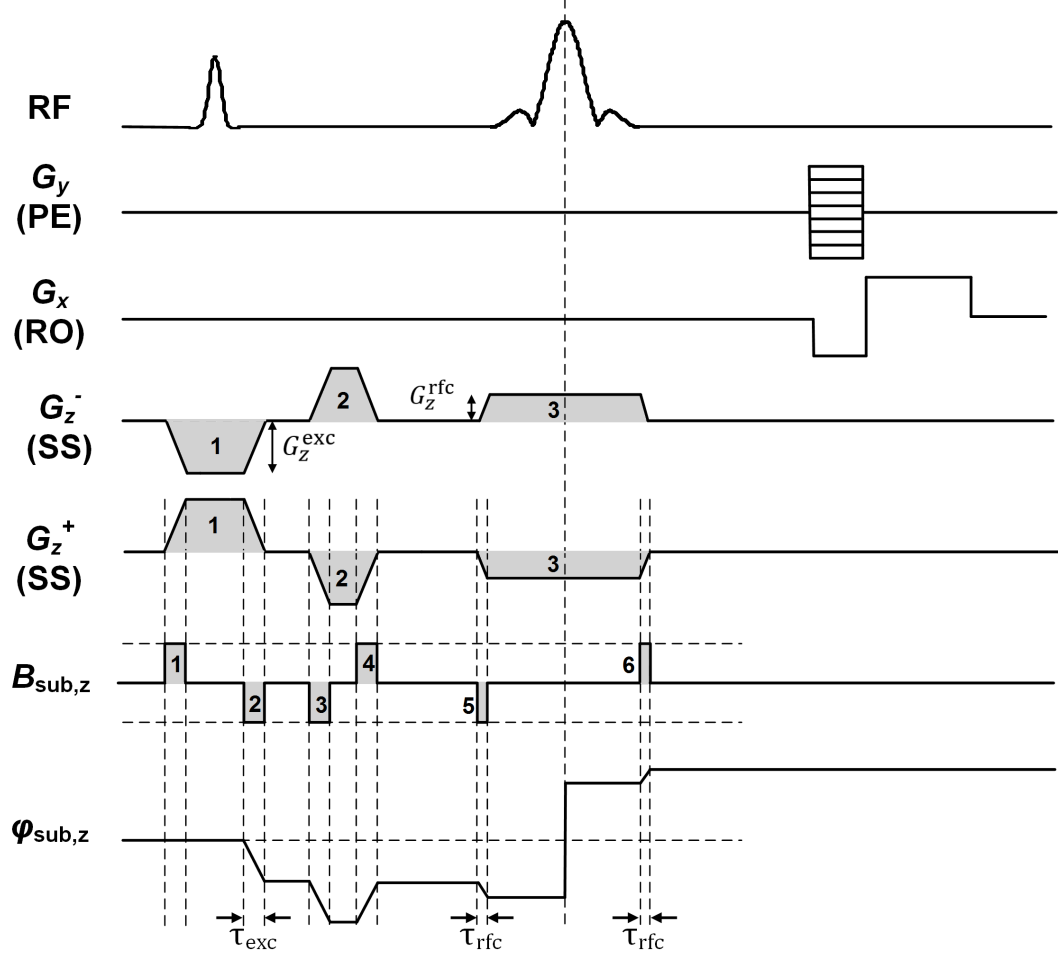


Figure 2.1: The timing diagram of the proposed spin-echo pulse sequence for measuring the phase accumulated by the z-component of the subject eddy field ($B_{sub,z}$) which is induced due to the switching of the z-gradient (RF: radiofrequency field, PE: Phase Encoding, RO: Readout, SS: slice selection). The ramping times of the z-gradient field are exaggerated for better visualization of $B_{sub,z}$. Two separate measurements, one using G_z^+ and one using G_z^- , are performed. The waveforms of $B_{sub,z}$ and $\varphi_{sub,z}$ for the case of G_z^+ are shown at the sixth and seventh rows. The values of G_z^{exc} , G_z^{rfc} , τ_{exc} , and τ_{rfc} will be later provided in Table 4.2.

($\mathbf{B}_p$), subject eddy currents ($\mathbf{J}_{sub}$) and subject eddy fields ($\mathbf{B}_{sub}$). Note that the spatial or temporal components of system eddy currents are purely related to the geometry and structure of an MRI scanner, i.e. they are not related to the conductivity of imaged subjects. Therefore, calculation of system eddy fields is not necessary for defining forward or inverse problems of eddy current based conductivity imaging.

In this thesis, $\mathbf{B}_p$, $\mathbf{B}_{sub}$, and $\mathbf{J}_{sub}$ are calculated simultaneously by solving a partial differential equation (PDE) for the vector magnetic potential. In the following, this PDE will be derived. In the solution domain, which contains the gradient coil and imaged subject, Maxwell's equations are written as

$$\nabla \times \mathbf{E}(t) = -\frac{\partial \mathbf{B}(t)}{\partial t} \quad (2.6)$$

$$\nabla \times \mathbf{B}(t) = \mu_0(\mathbf{J}_{sub}(t) + \mathbf{J}_{coil}(t)) \quad (2.7)$$

$$\nabla \cdot \mathbf{B}(t) = 0 \quad (2.8)$$

where $\mathbf{B}(t)$ is the total magnetic field, i.e. $\mathbf{B}(t) = \mathbf{B}_p(t) + \mathbf{B}_{sub}(t)$, $\mathbf{J}_{sub}(t)$ is the subject eddy current, and $\mathbf{J}_{coil}(t)$ is the current running on the gradient coil which is the source for $\mathbf{B}_p$. Note that displacement currents are assumed to be negligible compared to conductive currents because of the low-frequency nature of gradient fields [44], and it is assumed that the magnetic permeabilities of imaged subjects are μ_0 . In addition to these equations, the continuity equation is given as

$$\nabla \cdot (\mathbf{J}_{sub}(t) + \mathbf{J}_{coil}(t)) = 0 \quad (2.9)$$

Since $\mathbf{B}$ is divergence-free as stated in Equation (2.8), the vector magnetic potential ($\mathbf{A}(t)$) is introduced as follows:

$$\nabla \times \mathbf{A}(t) = \mathbf{B}(t) \quad (2.10)$$

Using the time-derivative of Equation (2.10) in Equation (2.6), $\mathbf{E}(t) + \frac{\partial \mathbf{A}(t)}{\partial t}$ is obtained as a curl-free vector and thus this vector can be written as a gradient

of a scalar quantity. This scalar quantity is defined as the scalar potential and denoted with ϕ . Therefore, $\mathbf{E}(t)$ becomes

$$\mathbf{E}(t) = -\frac{\partial \mathbf{A}(t)}{\partial t} - \nabla \phi \quad (2.11)$$

Scalar and vector magnetic potentials are auxiliary functions which are used for the calculation of the electromagnetic fields. Equation (2.10) specifies only the curl of vector magnetic potential $\mathbf{A}(t)$. In order to specify $\mathbf{A}(t)$ uniquely, its divergence should also be specified, i.e. a gauge should be fixed to $\mathbf{A}(t)$. One possibility is to define a new vector potential ($\mathbf{A}^*(t)$) such that

$$\frac{\partial \mathbf{A}^*(t)}{\partial t} = \frac{\partial \mathbf{A}(t)}{\partial t} + \nabla \phi \quad (2.12)$$

in which case Equation (2.11) becomes $\mathbf{E}(t) = -\frac{\partial \mathbf{A}^*(t)}{\partial t}$ [44]. Using Equation (2.10) in Equation (2.7) and noting that $\mathbf{J}_{sub} = \sigma(\mathbf{r})\mathbf{E}(t)$ where $\sigma(\mathbf{r})$ is the conductivity distribution of the imaged subject, the aforementioned PDE for the vector magnetic potential is obtained as

$$\nabla \times \nabla \times \mathbf{A}^*(t) = -\sigma(\mathbf{r})\frac{\partial \mathbf{A}^*(t)}{\partial t} + \mathbf{J}_{coil}(t) \quad (2.13)$$

It has been shown that Equation (2.13) has an implied gauge of $\nabla \cdot (\sigma(\mathbf{r})\mathbf{A}^*(t)) = \nabla \cdot \mathbf{J}_{sub} = 0$ which does not have to be imposed [48]. Therefore, the continuity equation given by (2.9) holds. Equation (2.13) has a unique solution provided that $\mathbf{A}^*(t)$ or $\nabla \times \mathbf{A}^*(t)$ is specified on the boundary of the solution domain [48]. The numerical methods for solving this equation will be discussed in Section 3.2.1.

Chapter 3

Feasibility of Conductivity Reconstruction from Subject Eddy Fields

In this thesis, the feasibility of the eddy current based conductivity imaging is investigated within the frame of two main goals as discussed in Chapter 1. The current chapter is about the first goal which is to understand whether conductivity reconstruction is possible provided that subject eddy fields are accurately measured. Regarding this goal, a novel conductivity reconstruction algorithm is developed in this chapter and its feasibility and performance are evaluated.

3.1 Convection-Reaction Equation based Algorithm

Taking curl of both sides in Equation (2.2b) we obtain

$$\nabla \times \nabla \times \mathbf{B}_{sub} = \mu_0 (\nabla \times \mathbf{J}_{sub}(t)) \quad (3.1)$$

Using the identity $\nabla \times \nabla \times \mathbf{B}_{sub} = \nabla (\nabla \cdot \mathbf{B}_{sub}) - \nabla^2 \mathbf{B}_{sub}$ and the fact that $\nabla \cdot \mathbf{B}_{sub} = 0$, we obtain the following equation

$$-\nabla^2 \mathbf{B}_{sub} = \mu_0 (\nabla \times \mathbf{J}_{sub}) \quad (3.2)$$

Noting that $\mathbf{J}_{sub} = \sigma(\mathbf{r})\mathbf{E}$, Equation (3.2) becomes

$$-\nabla^2 \mathbf{B}_{sub} = \mu_0 (\nabla \sigma \times \mathbf{E} + \sigma \nabla \times \mathbf{E}) \quad (3.3)$$

Considering the relation that $\mathbf{E} = \mathbf{J}_{sub}/\sigma(\mathbf{r})$, the z-component of Equation (3.3) becomes

$$\nabla^2 B_{sub,z} = \frac{\mu_0}{\sigma} \left(\frac{\partial \sigma}{\partial y} J_{sub,x} - \frac{\partial \sigma}{\partial x} J_{sub,y} \right) + \mu_0 \sigma \frac{\partial B_{p,z}(t)}{\partial t} \quad (3.4)$$

Substituting ρ^{-1} for σ , the following equation is obtained

$$\tilde{\nabla} \rho \cdot (-J_{sub,y}, J_{sub,x}) + \rho \frac{\nabla^2 B_{sub,z}}{\mu_0} = \frac{\partial B_{p,z}(t)}{\partial t} \quad (3.5)$$

where $\tilde{\nabla}$ is the two-dimensional gradient operator defined as $\tilde{\nabla} = \left(\frac{\partial}{\partial x}, \frac{\partial}{\partial y} \right)$, ρ is the resistivity ($\rho = \sigma^{-1}$), $J_{sub,x}$ and $J_{sub,y}$ are the x- and y-components of the subject eddy current, $B_{sub,z}$ and $B_{p,z}$ are the z-components of the subject eddy field and the gradient field respectively. Equation (3.5) can be recognized to be in the form of a convection-reaction equation where $\tilde{\nabla} \rho \cdot (-J_{sub,y}, J_{sub,x})$ is the convection term, $\rho \frac{\nabla^2 B_{sub,z}}{\mu_0}$ is the reaction term and $\frac{\partial B_{p,z}(t)}{\partial t}$ is the source term. This equation is the central equation for the inverse problem of obtaining conductivity from subject eddy field. Note that $J_{sub,x}$ and $J_{sub,y}$ are also unknowns and should be reconstructed beforehand. The relation between $(J_{sub,x}, J_{sub,y})$ and $B_{sub,z}$ is obtained by taking the z-component of Equation (3.2).

$$\frac{\nabla^2 B_{sub,z}}{\mu_0} = \frac{\partial J_{sub,x}}{\partial y} - \frac{\partial J_{sub,y}}{\partial x} \quad (3.6)$$

Equation (3.6) is the same as the fundamental relation used in the Magnetic Resonance Current Density Imaging (MRCDI) [49] and thus any MRCDI algorithm may be used for solving this equation. In this thesis, the MRCDI algorithm proposed by Park et al. is used [50] in which the following PDE is solved for β

$$\begin{aligned}\tilde{\nabla}^2 \beta &= \frac{\nabla^2 B_{sub,z}}{\mu_0} \text{ in } \Omega \\ \beta &= 0 \quad \text{on } \partial\Omega\end{aligned}\tag{3.7}$$

where Ω denotes the region that stays inside the imaging subject at the imaging slice and it is also defined as the region-of-interest (ROI), $\partial\Omega$ denotes the boundary of ROI, and $\tilde{\nabla}^2$ is the two-dimensional Laplace operator defined as $\tilde{\nabla}^2 = \left(\frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}\right)$. The x- and y-components of the reconstructed subject eddy current ($J_{sub,x}^*$ and $J_{sub,y}^*$) are obtained from $(J_{sub,x}^*, J_{sub,y}^*) = \left(\frac{\partial\beta}{\partial y}, -\frac{\partial\beta}{\partial x}\right)$. Note that $J_{sub,z}$ and some components of $J_{sub,x}$ and $J_{sub,y}$ do not generate $B_{sub,z}$, and thus they are undetectable. Therefore $\mathbf{J}^* = (J_{sub,x}^*, J_{sub,y}^*, 0)$ is only an estimate to true $\mathbf{J}_{sub}$. It has been shown that the overall error in the reconstructed subject eddy current is proportional to $\|J_{sub,z}\|$ and $\left\|\frac{\partial J_{sub,z}}{\partial z}\right\|$ at the imaging slice [50].

In regions where conductivity slowly varies, $\nabla\rho$ in Equation (3.5) can be neglected as done in the Wen's MREPT formula [51], and conductivity can be directly reconstructed using the following pointwise formula

$$\sigma \cong \frac{\nabla^2 B_{sub,z}}{\mu_0 \partial B_{p,z}(t) / \partial t}\tag{3.8}$$

3.2 Methods

3.2.1 Solution of the Forward Problem

As discussed in Section 2.4, the forward problem is defined by the following equation

$$\nabla \times \nabla \times \mathbf{A}^*(t) = -\sigma(\mathbf{r}) \frac{\partial \mathbf{A}^*(t)}{\partial t} + \mathbf{J}_{coil}(t) \quad (3.9)$$

where $\mathbf{J}_{coil}(t)$ is the current running on the gradient coil which is the source for $\mathbf{B}_p$, $\nabla \times \mathbf{A}^*(t) = \mathbf{B}(t)$ and $\mathbf{B}(t)$ is the total magnetic field, i.e. $\mathbf{B}(t) = \mathbf{B}_p(t) + \mathbf{B}_{sub}(t)$. Equation (3.9) is solved using the ‘Magnetic Fields’ module of the Finite Element Method (FEM) package Comsol Multiphysics 4.2a (Comsol AB, Stockholm, Sweden). Since Equation (3.9) is a time-dependent PDE, it is solved using the “time-dependent solver” of the Comsol Multiphysics software. By solving this equation, the subject eddy current is obtained from $\mathbf{J}_{sub}(t) = -\sigma(\mathbf{r}) \frac{\partial \mathbf{A}^*(t)}{\partial t}$. In order to obtain $\mathbf{B}_{sub}(t)$, Equation (3.9) is solved again by assigning conductivity of the imaged object to zero and $\mathbf{B}_p$ is found by $\mathbf{B}_p = \nabla \times \mathbf{A}^*(t)$ since $\mathbf{B}_{sub}(t) = 0$ for an object of zero conductivity. This $\mathbf{B}_p$ field is then subtracted from the previously calculated $\nabla \times \mathbf{A}^*(t)$ which equals $\mathbf{B}_p(t) + \mathbf{B}_{sub}(t)$.

The illustration of the Comsol Multiphysics model that is used for the solution of Equation (3.9) is shown in Figure 3.1. The outermost cylinder, which has radius of 60 cm and height of 300 cm, is the solution domain on which the tangential component of the vector magnetic potential ($\mathbf{A}^*(t)$) is taken zero. The z-gradient coil is modeled as a Maxwell pair and the radii of circular coils are 30 cm which are separated by $30\sqrt{3}$ cm [52]. The waveform of $\mathbf{J}_{coil}$ is assigned such that the z-gradient field linearly ramps up with a slew rate of 160 T/m/s. In the simulations performed using a time-step size of 1 ns, it is observed that $\mathbf{J}_{sub}(t)$ and $\mathbf{B}_{sub}(t)$ ramp up or down in 10 ns [40], and they stay constant between the ramp-up and ramp-down because of the constant $-\frac{\partial \mathbf{B}_p(t)}{\partial t}$. Therefore it can be safely assumed that $\mathbf{J}_{sub}(t)$ and $\mathbf{B}_{sub}(t)$ ramp up or down almost instantly once gradient fields are

switched on or off (This observation also verifies the waveform of $\mathbf{B}_{sub}(t)$ shown in Figure 2.1). Since we are interested in $\mathbf{B}_{sub}(t)$ during its plateau, a larger time-step size of $0.1 \mu s$ is used in other simulations and a few time-steps were sufficient for reaching the plateau.

3.2.2 Simulation Phantom

The cylindrical simulation phantom used in the simulations is shown in Figure 3.2. The phantom has radius of 7 cm and height of 19 cm. It is placed along the z-direction and its base is located at $z=-0.02$ m plane. The imaging slice is chosen as the $z = 0.13$ m plane (shown with the red line on the left), where the maximum subject eddy field occurs among other transversal slices. The background conductivity of the phantom is taken as 0.5 S/m and three cylindrical regions of conductivity anomaly are assumed along the phantom. The geometry and the assigned conductivity values of the anomalies are shown on the right-hand side of Figure 3.2.

3.2.3 Conductivity Reconstruction

For reconstructing conductivity, Equations (3.7) and (3.5) are solved consecutively at the imaging slice using the finite difference method [20]. For this purpose, the computed z-component of the subject eddy field ($B_{sub,z}$) is exported to MATLAB (The Mathworks, Natick, USA) from Comsol Multiphysics on a regular Cartesian grid which has spacing of 1 mm in x and y-directions. Since the Laplacian of $B_{sub,z}$ is calculated using a three-dimensional (5x5x3) Savitzky-Golay Laplacian kernel [53], $B_{sub,z}$ is exported to MATLAB also in slices 1 mm above and below the imaging slice. The finite-difference formulation of Equation

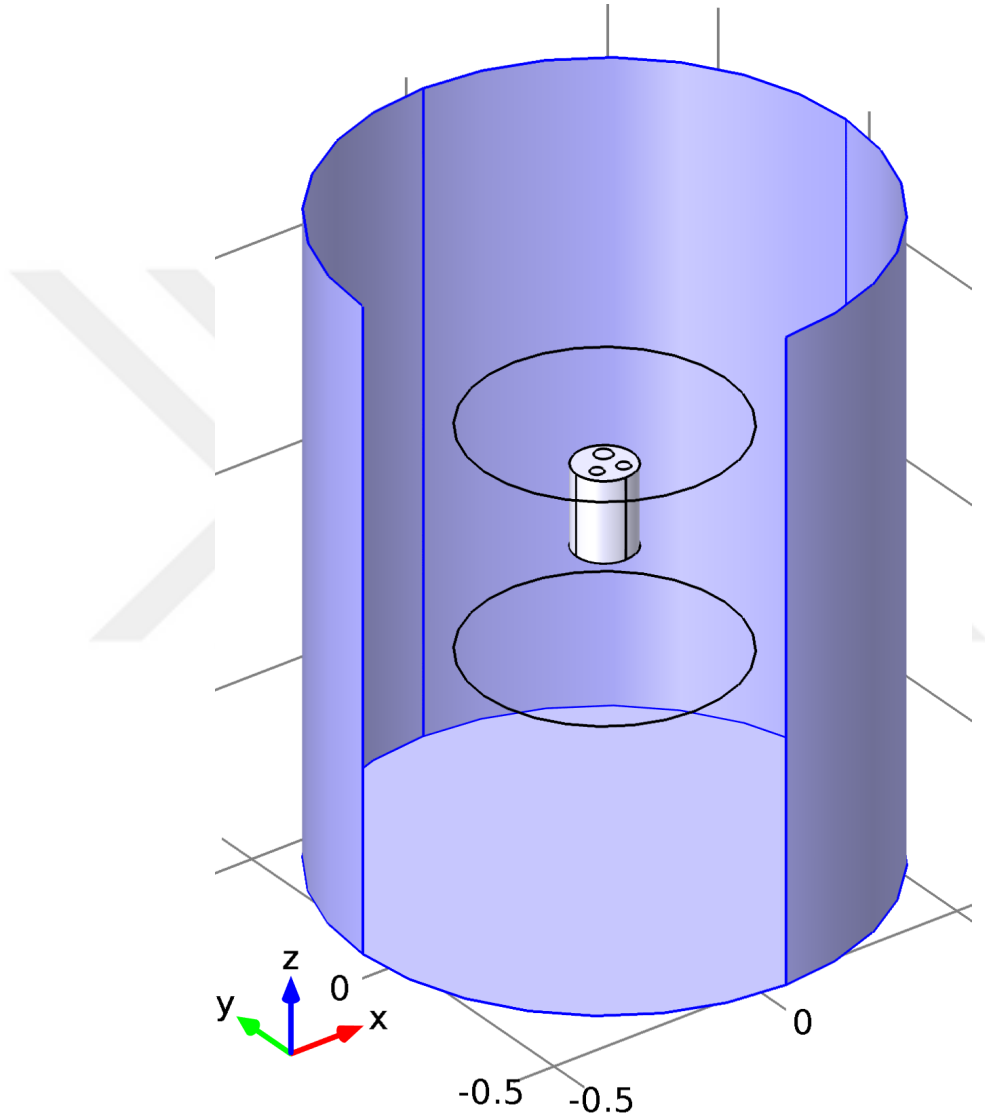


Figure 3.1: The illustration of the Comsol Multiphysics model which is used for the solution of the forward problem. The outermost cylinder is the solution domain on which the tangential component of the vector magnetic potential $\mathbf{A}^*(t)$ is taken zero. The z-gradient coil is obtained with the wire model of a Maxwell pair.

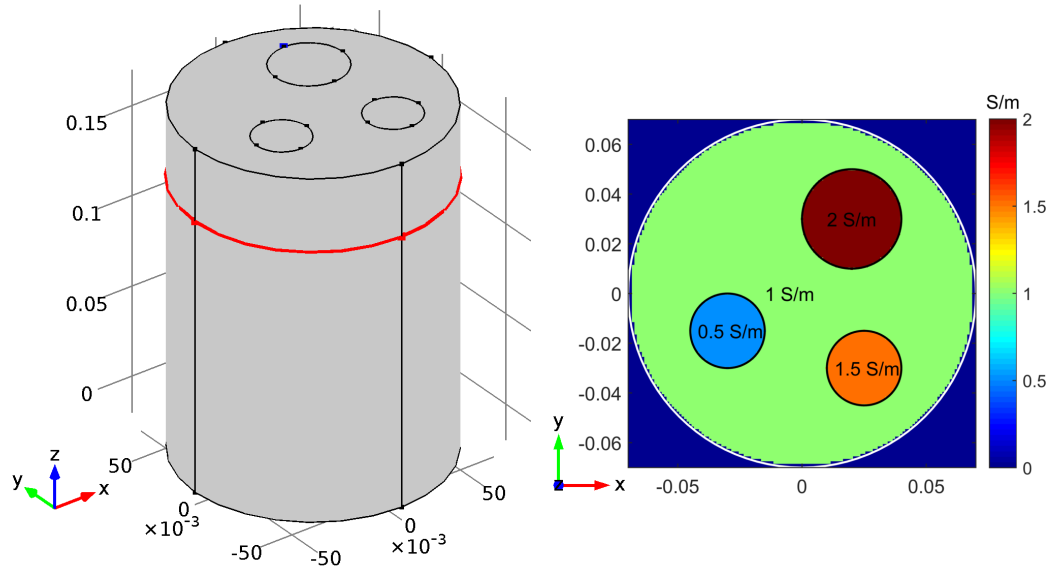


Figure 3.2: The illustration of the simulation phantom. The imaging slice is chosen as the $z = 0.13$ m plane as shown with the red line on the left. The background conductivity of the phantom is taken as 0.5 S/m and three cylindrical regions of conductivity anomaly are assumed along the phantom. The geometry and the assigned conductivity values are shown at the imaging slice on the right

(3.7) is obtained at a grid point (x^i, y^j) that is located inside the ROI (Ω) as

$$\frac{\beta^{i+1,j} + \beta^{i-1,j} + \beta^{i,j+1} + \beta^{i,j-1} - 4\beta^{i,j}}{\Delta^2} = \frac{(\nabla^2 B_{sub,z})^{i,j}}{\mu_0} \quad (3.10)$$

where $\beta^{i,j}$ denotes the β value at (x^i, y^j) , $i = 1, 2, \dots, N$ and $j = 1, 2, \dots, N$ where N denotes number of grid points inside the ROI, and Δ is the spacing of the grid. Equation (3.10) is converted into a matrix form as $\mathbf{A}_{N \times N} \mathbf{x}_{N \times 1} = \mathbf{b}_{N \times 1}$ where $\mathbf{x}_{N \times 1}$ consists of the unknown ρ values at grid points and $\mathbf{b}_{N \times 1}$ consists of $\frac{(\nabla^2 B_{sub,z})^{i,j}}{\mu_0}$ values at grid points. The Dirichlet boundary condition ($\beta = 0$ at $\partial\Omega$) is imposed by assigning β values at the boundary to zero, which decreases the number of equations and unknowns. $\mathbf{A}_{N \times N} \mathbf{x}_{N \times 1} = \mathbf{b}_{N \times 1}$ equation becomes $\mathbf{A}_{(N-B) \times (N-B)} \mathbf{x}_{(N-B) \times 1} = \mathbf{b}_{(N-B) \times 1}$ where B is the number of grid points at the boundary. This matrix equation is solved using MATLAB and the x- and y-components of the reconstructed subject eddy current are obtained at the grids from $\left(J_{sub,x}^{*(i,j)}, J_{sub,y}^{*(i,j)} \right) = \left(\frac{\partial \beta}{\partial y}, -\frac{\partial \beta}{\partial x} \right) = \left(\frac{\beta^{i,j+1} - \beta^{i,j-1}}{2\Delta}, -\frac{\beta^{i+1,j} - \beta^{i-1,j}}{2\Delta} \right)$.

For reconstructing conductivity, the finite-difference formulation of Equation (3.5) is obtained at a grid point (x^i, y^j) that is located inside the ROI (Ω) as

$$-\frac{\rho^{i+1,j} - \rho^{i-1,j}}{2\Delta} J_{sub,y}^{*(i,j)} + \frac{\rho^{i,j+1} - \rho^{i,j-1}}{2\Delta} J_{sub,x}^{*(i,j)} + \rho^{i,j} \frac{(\nabla^2 B_{sub,z})^{i,j}}{\mu_0} = K z_0 \quad (3.11)$$

where it is assumed that the z-gradient field is $\mathbf{B}_p(t) = K z t$ and $\frac{\partial \mathbf{B}_p(t)}{\partial t} = K z_0$ at the imaging slice where $z = z_0$ (K is the slew-rate). Equation (3.11) is converted into a matrix equation similar to the case of Equation (3.10). Dirichlet boundary condition is also imposed similarly and the ρ values at the boundary are assigned known resistivity of the background. Since there is no diffusion term in Equation (3.5), its numerical solution suffers from unwanted oscillations near interior and boundary layers [54]. As a remedy for this problem, an artificial diffusion term ($-c \nabla^2 \rho$) is added to Equation (3.5) which is a well-known stabilization technique [54]. Equation (3.11) is also updated to include the diffusion term. The c coefficient of 5×10^{-5} is chosen such that the oscillations vanish but yet no significant smoothing is introduced in the reconstructed conductivity [28, 20].

3.3 Results and Discussion

Figure 3.3 shows the results of the forward problem solution for the phantom described in Section 3.2.2. The forward problem is solved with respect to time and Figure 3.3 shows the quantities after they reach their plateau (refer to Section 3.2.1). Figures are obtained for the imaging slice ($z=0.13\text{m}$ plane) and the slew rate of the gradient field is 160 T/m/s . Figure 3.3a shows the magnitude distribution and vector plot of the subject eddy current ($\mathbf{J}_{sub}$). Since the gradient (primary) field is in the z -direction (into the page), it induces a rotating subject eddy current in the x - y plane such that the subject eddy field opposes the gradient (primary) field. Figure 3.3b shows the distribution of the subject eddy field ($B_{sub,z}$). The magnitude of $B_{sub,z}$ has maximum value of about 30 nT which occurs towards the center of the phantom. In Chapter 4, we will calculate how much this field contributes to the MRI phase and we will find out if one can measure this contribution. Figure 3.3c shows the Laplacian of the subject eddy field. Since $\mathbf{B}_p(t) = Kzt$ (the gradient field linearly increases with the slew rate of K), $\frac{\partial \mathbf{B}_p(t)}{\partial t}$ has constant value of Kz_0 at the imaging slice where $z_0 = 0.13\text{ m}$. Therefore, as evident from Equation (3.5), $\nabla^2 B_{sub,z}$ attains high magnitudes at the anomaly boundaries where $\nabla \rho$ is high. Since a $5 \times 5 \times 3$ Savitzky-Golay kernel is used in the calculation of $\nabla^2 B_{sub,z}$, the high-magnitude $\nabla^2 B_{sub,z}$ regions at the boundaries are 5 pixels wide.

Figures 3.4a and b show the distribution of the reconstructed subject eddy current magnitude ($|\mathbf{J}_{sub}|$) and the reconstructed conductivity which are obtained by solving Equations (3.7) and (3.5) consecutively. The relative L^2 -errors in the reconstructed $|\mathbf{J}_{sub}|$ and in the reconstructed conductivity are 3.1% and 6.1% respectively. The reconstruction errors are most pronounced in the regions near the anomaly boundaries. This is due to the fact that the actual conductivities jump at these boundaries, while the reconstructed ones change more smoothly. The smoothing is caused by the Savitzky-Golay kernel and by the artificial diffusion term introduced to Equation (3.5) both of which have low-pass filter effects

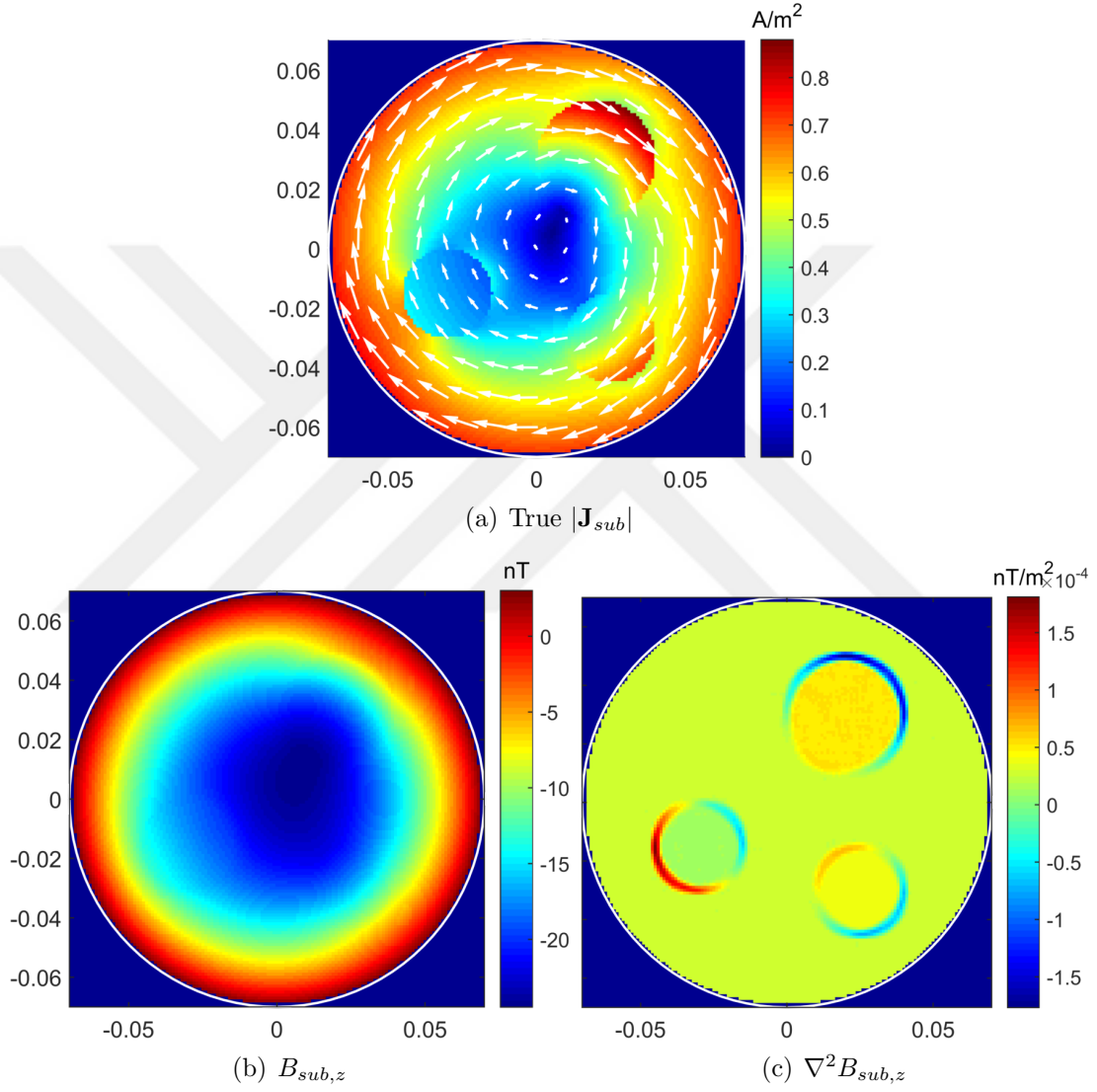


Figure 3.3: Results of the forward problem solution the at the imaging slice ($z=0.13$ m plane) of the cylindrical phantom which has three conductivity anomaly regions: (a) The magnitude distribution and vector plot of the actual subject eddy current ($\mathbf{J}_{sub}$); (b) the distribution of the z-component of the subject eddy field ($B_{sub,z}$); (c) the distribution of the Laplacian of $B_{sub,z}$

[28]. The relative L^2 -errors in the reconstructed conductivity and $|\mathbf{J}_{sub}|$ are less than 1% if the errors are calculated in a region where the actual conductivity is constant. Figure 3.4c shows the reconstructed conductivity when the point-wise formula given as Equation (3.8) is used in which the spatial variation of the conductivity is neglected. As expected, artifacts are observed at the boundaries of the anomalies. This shows that the contribution of the convective term in Equation (3.5) is significant especially at the internal boundaries.

The goal of this chapter was to investigate whether conductivity reconstruction is possible provided that subject eddy fields ($B_{sub,z}$) are accurately measured. It is observed that the proposed conductivity reconstruction algorithm performs well both in regions of homogeneous conductivity and in regions of high conductivity gradients. These loyal reconstruction results and the relative L^2 -errors indicate that the proposed algorithm is feasible.

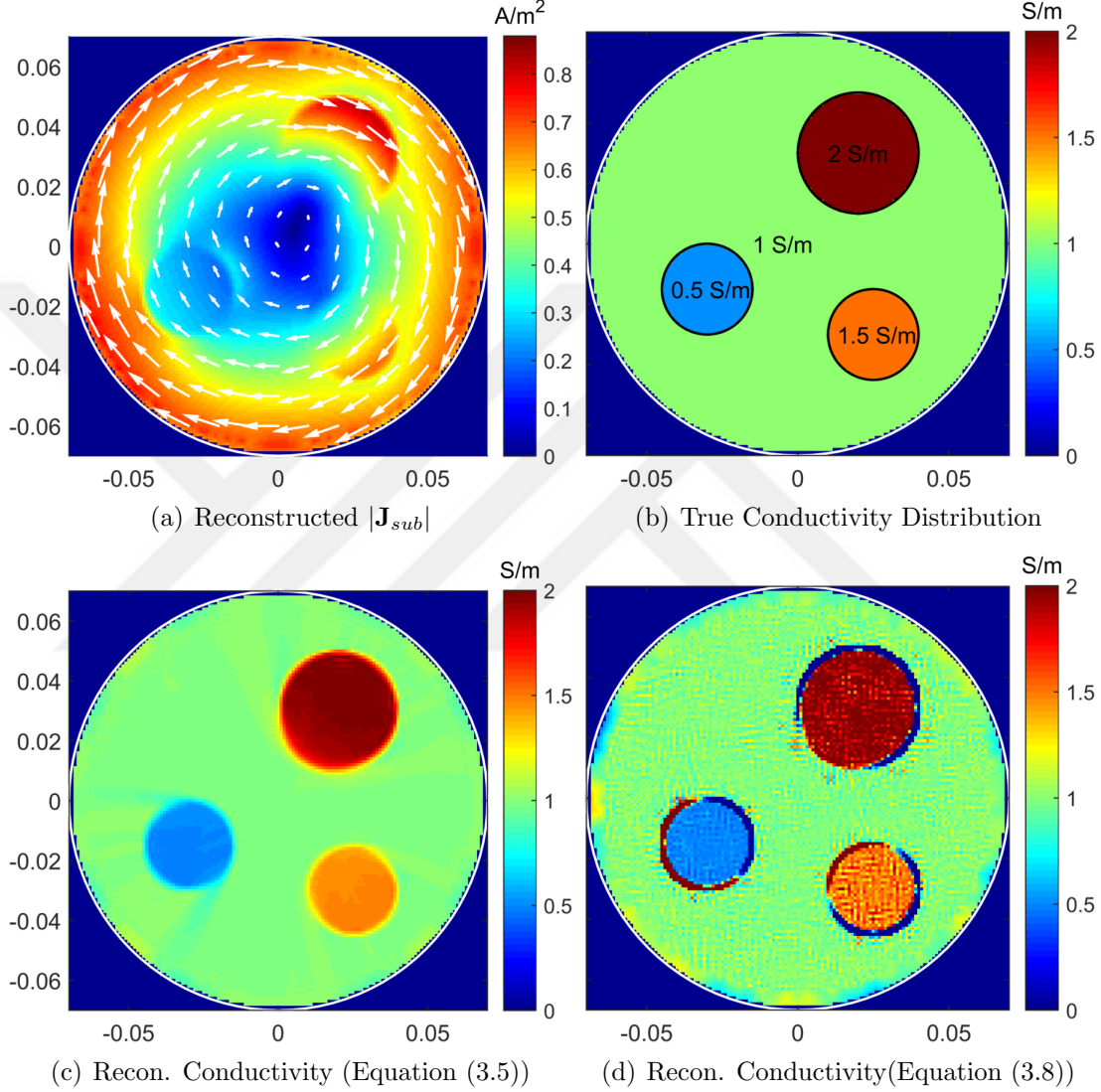


Figure 3.4: Reconstruction results at the imaging slice ($z=0.13$ m plane) of the cylindrical phantom which has three conductivity anomaly regions: (a) The magnitude distribution and vector plot of the subject eddy current which is reconstructed by solving Equation (3.7); (b) true conductivity distribution; (c) the distribution of the conductivity which is reconstructed by solving the convection-reaction equation (Equation (3.5)); (d) the distribution of the conductivity distribution which is reconstructed by the pointwise formula (Equation (3.8))

Chapter 4

Feasibility of Subject Eddy Field Measurements

In this thesis, the feasibility of the eddy current based conductivity imaging is investigated within the frame of two main goals as discussed in Chapter 1. The current chapter is about the second goal which is to understand the fidelity by which subject eddy fields must be measured for accurately reconstructing conductivity.

4.1 Analysis of Uncertainty in the Conductivity Reconstruction

We define uncertainty in a quantity as the standard deviation of noise in that quantity. In this section, we aim to investigate how the noise in input data (subject eddy field) is reflected to reconstructed conductivity. In other words, our task is to find a relation between the uncertainties of reconstructed conductivity

(σ) and subject eddy field $B_{sub,z}$. For the sake of simplicity, it is assumed that conductivity is slowly varying within a region of interest, and Equation (3.8) is used in the analysis. Note that, when the z-gradient is linearly ramped up or down with the same slew rate of K at all edges, $\frac{\partial B_{p,z}(t)}{\partial t}$ can be expressed at the imaging slice as Kz_0 where z_0 is the z-coordinate of the imaging slice. In this case, using Equation (2.3) in Equation (3.8) we get

$$\sigma \cong \frac{\nabla^2 \varphi_{sub,z}}{\mu_0 \gamma (\tau_{exc} + 2\tau_{rfc}) K z_0} \quad (4.1)$$

The $(\tau_{exc} + 2\tau_{rfc}) K$ term in Equation (4.1) can be recognized as $G_z^{exc} + 2G_z^{rfc}$ where G_z^{exc} and G_z^{rfc} are the magnitudes of the z-gradient during excitation and re-focusing respectively (see Table 4.2). Substituting $G_z^{exc} + 2G_z^{rfc}$ for $(\tau_{exc} + 2\tau_{rfc}) K$ in Equation (4.1), we obtain

$$\sigma \cong \frac{\nabla^2 \varphi_{sub,z}}{\gamma \mu_0 z_0 (G_z^{exc} + 2G_z^{rfc})} \quad (4.2)$$

Equation (4.2) involves $\nabla^2 \varphi_{sub,z}$. Given that $\varphi_{sub,z}$ is known on a Cartesian grid, the most basic way to calculate $\nabla^2 \varphi_{sub,z}$ is to use the finite difference formula given by

$$\begin{aligned} \nabla^2 \varphi_{sub,z}^{i,j,k} = & \frac{\varphi_{sub,z}^{i+1,j,k} - 2\varphi_{sub,z}^{i,j,k} + \varphi_{sub,z}^{i-1,j,k}}{\Delta x^2} + \\ & \frac{\varphi_{sub,z}^{i,j+1,k} - 2\varphi_{sub,z}^{i,j,k} + \varphi_{sub,z}^{i,j-1,k}}{\Delta y^2} + \\ & \frac{\varphi_{sub,z}^{i,j,k+1} - 2\varphi_{sub,z}^{i,j,k} + \varphi_{sub,z}^{i,j,k-1}}{\Delta z^2} \end{aligned} \quad (4.3)$$

where the superscript i, j, k denotes the indices of $\varphi_{sub,z}$ at the Cartesian grid.

Equation (4.3) can be stated in the form a kernel as

$$\begin{aligned}
K_{fd}(:, :, 1) &= \begin{bmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{\Delta z^2} & 0 \\ 0 & 0 & 0 \end{bmatrix} \\
K_{fd}(:, :, 2) &= \begin{bmatrix} 0 & \frac{1}{\Delta y^2} & 0 \\ \frac{1}{\Delta x^2} & -2 \left(\frac{1}{\Delta x^2} + \frac{1}{\Delta y^2} + \frac{1}{\Delta z^2} \right) & \frac{1}{\Delta x^2} \\ 0 & \frac{1}{\Delta y^2} & 0 \end{bmatrix} \\
K_{fd}(:, :, 3) &= \begin{bmatrix} 0 & 0 & 0 \\ 0 & \frac{1}{\Delta z^2} & 0 \\ 0 & 0 & 0 \end{bmatrix}
\end{aligned} \tag{4.4}$$

where K_{fd} denotes the three-dimensional finite-difference kernel. Three-dimensional convolution of $\varphi_{sub,z}$ matrix with K_{fd} gives $\nabla^2 \varphi_{sub,z}$.

Another possibility for calculating $\nabla^2 \varphi_{sub,z}$ is to locally fit a polynomial to $\varphi_{sub,z}$ data so that the differentiation can simply be calculated from the coefficients of the polynomial. This method is known as the Savitzky-Golay differentiation [53]. As shown in the Appendix of this Chapter, Savitzky-Golay differentiation can also be stated in the form of a kernel for which the elements can be calculated analytically. If second-order polynomials are used, the three-dimensional 5x5x3

Savitzky-Golay kernel (K_{sg}) is obtained as

$$\begin{aligned}
K_{sg}(:, :, 1) &= \begin{bmatrix} 4a+c & a+c & c & a+c & 4a+c \\ a+c & -2a+c & -b+c & -2a+c & a+c \\ c & -b+c & -4a+c & -b+c & c \\ a+c & -2a+c & -b+c & -2a+c & a+c \\ 4a+c & a+c & c & a+c & 4a+c \end{bmatrix} \\
K_{sg}(:, :, 2) &= \begin{bmatrix} 4a-2c & a-2c & -2c & a-2c & 4a-2c \\ a-2c & -2a-2c & -b-2c & -2a-2c & a-2c \\ -2c & -b-2c & -4a-2c & -b-2c & -2c \\ a-2c & -2a-2c & -b-2c & -2a-2c & a-2c \\ 4a-2c & a-2c & -2c & a-2c & 4a-2c \end{bmatrix} \\
K_{sg}(:, :, 3) &= \begin{bmatrix} 4a+c & a+c & c & a+c & 4a+c \\ a+c & -2a+c & -b+c & -2a+c & a+c \\ c & -b+c & -4a+c & -b+c & c \\ a+c & -2a+c & -b+c & -2a+c & a+c \\ 4a+c & a+c & c & a+c & 4a+c \end{bmatrix}
\end{aligned} \tag{4.5}$$

$$a = \frac{1}{105\Delta x^2} \quad b = \frac{1}{35\Delta x^2} \quad c = \frac{1}{25\Delta z^2}$$

where it is assumed that $\Delta y = \Delta x$. Note that the elements of K_{sg} does not depend on the values of the function for which Laplacian will be calculated. Whether K_{fd} or K_{sg} is used, Equations 4.4 and 4.5 indicate that the $\nabla^2 \varphi_{sub,z}$ value in one pixel can be obtained as the linear combination of the $\varphi_{sub,z}$ values within the neighborhood of that pixel which is defined by the size of the kernel. This fact can be stated in the equation form for the 5x5x3 Savitzky-Golay kernel as

$$\nabla^2 \varphi_{sub,z}^{i,j,k} = \sum_{u=-2}^{u=2} \sum_{v=-2}^{v=2} \sum_{p=-1}^{p=1} c^{u,v,p} \varphi_{sub,z}^{i+u,j+v,k+p} \tag{4.6}$$

where $c^{u,v,p}$ denotes the value of the K_{sg} element at the index (u, v, p) . It is known that the noise distributions for each pixel of $\varphi_{sub,z}$ are independent and identically distributed [55]. Therefore, using Equation (4.6) and the law of error propagation [56], the uncertainty of $\nabla^2 \varphi_{sub,z}$ can be stated as a function of uncertainty of $\varphi_{sub,z}$ as

$$u(\nabla^2 \varphi_{sub,z}) = u(\varphi_{sub,z}) \left[\sum_{u=-2}^{u=2} \sum_{v=-2}^{v=2} \sum_{p=-1}^{p=1} (c^{u,v,p})^2 \right]^{1/2} \quad (4.7)$$

The $\left[\sum_{u=-2}^{u=2} \sum_{v=-2}^{v=2} \sum_{p=-1}^{p=1} (c^{u,v,p})^2 \right]^{1/2}$ term in this equation will be referred to as the root sum-of-squares (RSS) for a kernel and will be denoted with $rss(\cdot)$, e.g. $rss(K_{sg})$ denotes the RSS for K_{sg} kernel. RSS is an important parameter for an kernel in the sense that it determines how the kernel effects the uncertainty [56]. Assuming $\Delta x = \Delta y = \Delta z = 1$, $rss(K_{fd}) = 6.48$ while $rss(K_{sg}) = 0.53$ which means that the 5x5x3 Savitzky-Golay kernel is more robust to noise compared with finite-difference formulation. Indeed, it has been shown that, when Savitzky-Golay Laplacian kernel is used, RSS becomes minimum compared with any other Laplacian kernel of the same size [56]. Therefore, in this analysis, it is assumed that $\nabla^2 \varphi_{sub,z}$ is calculated using Savitzky-Golay differentiation. Using Equations (4.7), (4.5) and (4.2), uncertainty of conductivity is obtained as

$$u(\sigma) = \frac{u(\varphi_{sub,z})}{\gamma \mu_0 z_0 (G_z^{exc} + 2G_z^{rfc})} \left[\frac{4}{105\Delta x^4} + \frac{6}{25\Delta z^4} \right]^{1/2} \quad (4.8)$$

where $\left[\frac{4}{105\Delta x^4} + \frac{6}{25\Delta z^4} \right]^{1/2}$ equals $rss(K_{sg})$ and $\Delta y = \Delta x$.

Since Laplacian operator amplifies high spatial frequency components of $\varphi_{sub,z}$, the noise inherent in $\varphi_{sub,z}$ measurements is also amplified. A common solution to this problem is the low-pass filtering of $\varphi_{sub,z}$ before using it in the reconstruction algorithms. Therefore, the effects of low-pass filters to reconstructed conductivity should also be analyzed. A low-pass filter can be applied to $\varphi_{sub,z}$ in spatial domain by the convolution of $\varphi_{sub,z}$ with the filter kernel as in the case of Savitzky-Golay kernel (refer to Equation (4.6)). The uncertainty of the filtered data can

be obtained similar to Equation (4.7) as

$$u(\varphi_{sub,z}^{filt}) = u(\varphi_{sub,z}) \left[\sum_{u=-2}^{u=2} \sum_{v=-2}^{v=2} \sum_{p=-2}^{p=2} (h^{u,v,p})^2 \right]^{1/2} \quad (4.9)$$

where $\varphi_{sub,z}^{filt}$ is the filtered $\varphi_{sub,z}$ and $h^{u,v,p}$ denotes the elements of low-pass filter kernel. In the end, conductivity reconstruction process can be summarized as the convolution of $\varphi_{sub,z}$ with two kernels, one for filtering and one for Laplacian operation, and using Equation (4.2) to obtain conductivity. Each of these kernels effect the uncertainty of the final reconstructed conductivity as given by Equations (4.7) and (4.9). Since the application of these kernels is a linear operation, it is possible to convolve two kernels before, and then convolve $\varphi_{sub,z}$ with the resulting equivalent kernel (K_{eq}) which is obtained as

$$K_{eq} = K_{filt} * K_{sg} \quad (4.10)$$

where $*$ denotes the convolution operator, and K_{filt} is the low-pass filter kernel. Figure 4.1 shows two-dimensional kernels for K_{filt} , K_{sg} and K_{eq} when 5x5 Gaussian low-pass filter (standard deviation is 0.5) and 5x5 Savitzky-Golay differentiation filter is assumed. For a better visualization, two-dimensional kernels are chosen. As expected, K_{sg} is smoothed by the application of Gaussian filter (compare Figure 4.1c with 4.1b).

The equivalent kernel concept is particularly useful for analyzing the uncertainty of the reconstructed conductivity in the case when low-pass filters are used. The RSS of the equivalent kernel can be used for directly determining the relation between the uncertainties of reconstructed conductivity and $\varphi_{sub,z}$. Similar to Equation (4.8), we obtain

$$u(\sigma) = u(\varphi_{sub,z}) \frac{rss(K_{eq})}{\gamma \mu_0 z_0 (G_z^{exc} + 2G_z^{rfc})} \quad (4.11)$$

For comparison, Table 4.1 provides RSS values for kernels of different sizes ($\Delta x = \Delta y = \Delta z = 1$). For a desired uncertainty in the reconstructed conductivity,

Kernel	Kernel Size	RSS
Finite Difference	3x3x3	6.48
3x3x3 Savitzky-Golay	5x5x3	1.41
5x5x3 Savitzky-Golay	5x5x3	0.53
5x5x5 Savitzky-Golay	5x5x5	0.19
3x3x3 Gaussian	3x3x3	0.32
5x5x5 Gaussian	5x5x5	0.14
Finite Difference * 3x3x3 Gaussian	5x5x5	1.12
Finite Difference * 5x5x5 Gaussian	7x7x7	0.21
3x3x3 Gaussian * 3x3x3 Savitzky-Golay	5x5x5	0.49
3x3x3 Gaussian * 5x5x3 Savitzky-Golay	7x7x5	0.21
3x3x3 Gaussian * 5x5x5 Savitzky-Golay	7x7x7	0.11
5x5x5 Gaussian * 3x3x3 Savitzky-Golay	7x7x7	0.15
5x5x5 Gaussian * 5x5x3 Savitzky-Golay	9x9x7	0.085
5x5x5 Gaussian * 5x5x5 Savitzky-Golay	9x9x9	0.062

Table 4.1: Root sum-of-squares (RSS) values for different kernels ($\Delta x = \Delta y = \Delta z = 1$). * denotes the convolution operator. The standard deviation for Gaussian kernel is 0.5

which is denoted by $u(\sigma)_{des}$, the maximum uncertainty allowed in $\varphi_{sub,z}$, which is denoted by $u(\varphi_{sub,z})_{max}$, can be obtained by rearranging Equation (4.8) as

$$u(\varphi_{sub,z})_{max} = u(\sigma)_{des} \frac{\gamma \mu_0 z_0 (G_z^{exc} + 2G_z^{rfc})}{rss(K_{eq})} \quad (4.12)$$

In the next sections of this chapter, the feasibility of subject eddy field measurements will be analyzed using Equation (4.12). Our criteria for the feasibility is that $\varphi_{sub,z}$ is measured with an uncertainty lower than $u(\varphi_{sub,z})_{max}$.

In the analysis, it is assumed that a 3x3x3 Gaussian low-pass filter kernel (standard deviation=0.5) and a 5x5x3 Savitzky-Golay differentiation kernel are used together. Although larger kernels would increase $u(\varphi_{sub,z})_{max}$, we did not prefer to use them since this would make spatial resolution unacceptably high. Using the voxel size of 2x2x5 mm (see Table 4.2), $rss(K_{filt}) = 38364$, $rss(K_{sg}) = 52583$, and $rss(K_{eq}) = 28777$.

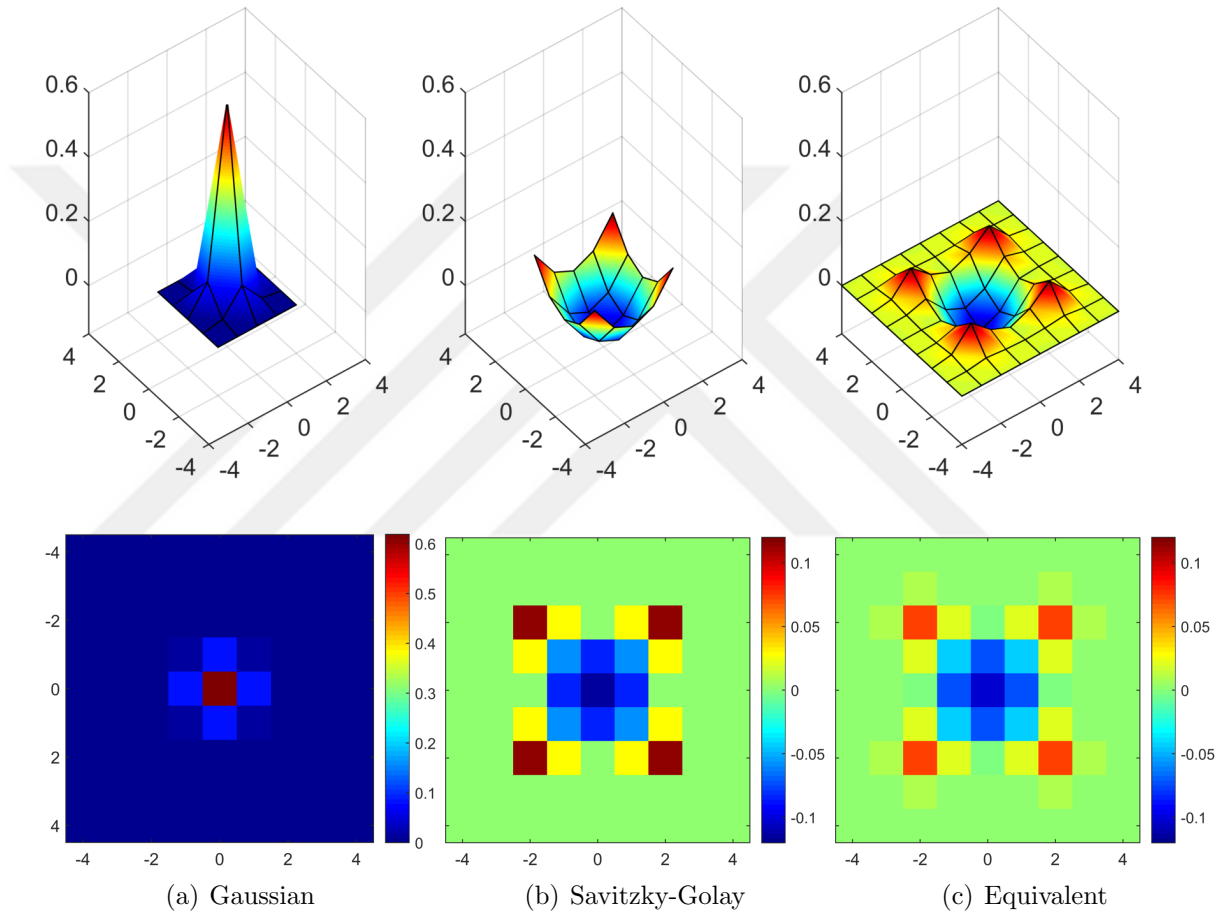


Figure 4.1: Illustration of different two-dimensional kernels (a): 5x5 Gaussian low-pass kernel with standard deviation 0.5, (b): 5x5 Savitzky-Golay differentiation kernel, (c): Convolution of 5x5 Gaussian kernel with 5x5 Savitzky-Golay differentiation kernel (Equivalent kernel). In order to visualize kernels with equal number of pixels, the kernels shown in (a) and (b) are zero-padded

4.2 Analysis of Uncertainty in the Phase due to Subject Eddy Field

In the previous section, we have analyzed the relation between $u(\sigma)$ and $u(\varphi_{sub,z})$. In this section, we will analyze $u(\varphi_{sub,z})$ by assuming that $\varphi_{sub,z}$ measured using the method described in Section 2.3 in which $\varphi_{sub,z}$ is obtained as the linear combination of four MRI phase images (see Equation (2.5c)). This combination will be shortly referred to as the “measured phase” and will be denoted by φ_{meas} . As also indicated by Equation (2.5c), φ_{meas} is obtained as

$$\varphi_{meas} = \left\{ \frac{\varphi^+(x, y) - \varphi^-(x, y)}{2} \right\}_{\sigma=\sigma_0} - \left\{ \frac{\varphi^+(x, y) - \varphi^-(x, y)}{2} \right\}_{\sigma=0} \quad (4.13)$$

where σ_0 is the conductivity of the imaging phantom. It is known that the noise in a MRI phase image has Gaussian distribution for which the standard deviation equals the inverse of the signal-to-noise-ratio (SNR) measured from the MRI magnitude image of the same measurement [55]. Therefore $u(\varphi_{meas})$ can be obtained using law of error propagation as

$$u(\varphi_{meas}) = \frac{\sqrt{2}}{2} \sqrt{\frac{1}{SNR_{\sigma=\sigma_0}^2} + \frac{1}{SNR_{\sigma=0}^2}} \quad (4.14)$$

where $SNR_{\sigma=\sigma_0}$ denote the SNR of the MRI magnitude image of the imaging phantom and $SNR_{\sigma=0}$ denote the SNR of the magnitude image for the non-conductive phantom.

4.3 Experimental Methods

The experiments described in this Chapter are performed in order to determine the uncertainty level of $\varphi_{sub,z}$ and to understand if this uncertainty is sufficiently low for accurate conductivity reconstruction. For the experiments, three homogeneous cylindrical phantoms of the radius 7 cm and height 19 cm are constructed

by using agar-saline gels which contain 18 gr/l agar, 1.5 gr/l CuSO_4 and different concentrations of NaCl (6, 9, and 0 gr/l for the first, second and third phantoms respectively). The agar-saline gels were solid enough to neglect flow artifacts. The conductivity of the three phantoms are measured as 1.3, 1.6 and 0.2 S/m using the phase-based MREPT technique proposed by Voigt et al. [24]. Although this technique estimates the conductivity at the Larmour frequency (123.2 MHz for our scanner), it has been reported that the conductivity of agar-saline gels do not change significantly in the range 10 Hz to 200 MHz [57]-[59]. Therefore these estimates are also representative at low frequencies. Although the third phantom is intended to be nonconductive, we have obtained a conductivity of 0.2 S/m due to agar.

Experiments are performed using a 3T MRI scanner (Magnetom Trio, Siemens Healthcare). The proposed pulse sequence (refer to Figure 2.1) is implemented in the MRI scanner software such that the parameters like the polarity of the z-gradient field, and the duration of the excitation and refocusing RF pulses are accessible from the user interface. For transmit and receive, the quadrature birdcage body coil of the MRI scanner is used. The phantoms are placed along the z-direction (the direction of B_0 is assumed as the z-direction). The slice orientation is transverse and the reference (center) slice is 2 cm away from the base of the phantom. The imaging slice is chosen as the $z=0.13$ m plane and other imaging parameters are summarized in Table 4.2. By constructing a platform on the patient table of the scanner, it is assured that the phantoms are fixed at the same position in all measurements, and thus artifacts due to phantom misalignments are negligible.

Two important remarks:

- (i) The amplitude of the z-gradient during excitation (G_z^{exc}) and refocusing (G_z^{rfc}) are 15.66 and 4.8 mT/m (see Table 4.2 and Figure 2.1). Given that the slice thickness and the flip angle are kept the same, if the z-gradient is increased, the bandwidth of the RF pulses should be increased by applying narrower RF

pulses in time which requires higher output voltage of the RF amplifier. For the MRI scanner used in this study, the z-gradient values of 15.66 mT/m and 4.8 mT/m are constrained by the output voltage of the RF amplifier rather than the maximum allowed z-gradient.

(ii) The slew rate is same in every edges of the z-gradient field and it is equal to 160 T/m/s. Note that if the slew rate increases, the instantaneous subject eddy field increase while the ramp times decrease. Therefore, the phase accumulated due to the subject eddy field remains the same since it is found by the time integral of subject eddy field (see Equation (2.3)). In other words, the accumulated phase during one ramp is determined by the end-value of the gradient field rather than its slew rate.

Parameter	Setting
Field of View (mm)	256×256
Image Matrix Size	128×128
Voxel Size (mm)	2×2×5
Imaging Slice (Transverse)	$z = 0.13m$
Echo Time (ms)	10
Repetition Time (ms)	1000
Flip angle (°)	90
Number of Acquisition	16
Total Imaging Time (min)	34.1×4
Bandwidth per Pixel (Hz/pix)	500
G_x Readout (mT/m)	5.9
G_z^{exc} Excitation (mT/m)	15.66
G_z^{rfc} Refocusing (mT/m)	4.8
Slew Rate of the z-gradient (T/m/s)	160
Excitation Ramp Time $\tau_{exc}(\mu s)$	98
Refocusing Ramp Time $\tau_{rfc}(\mu s)$	30

Table 4.2: The experimental parameters

Measurement of SNR in MRI Magnitude Images

SNR values are measured using the “ SNR_{mult} ” method which is based on acquiring multiple acquisitions [60]. MRI magnitude images acquired in a series of K acquisitions can be stated in the presence of noise as

$$S_N(\mathbf{r}, k) = S(\mathbf{r}) + N(\mathbf{r}, k) \quad (4.15)$$

where $S_N(\mathbf{r}, k)$ is the magnitude image of the k th acquisition, $\mathbf{r} = (x, y, z)$, $S(\mathbf{r})$ is the true magnitude, and $N(\mathbf{r}, k)$ is the noise image. It is known that $N(\mathbf{r}, k)$ has Gaussian distribution provided that SNR is larger than 3 which is true in most of the cases [55]. The SNR at each pixel of an MRI image can be stated as

$$SNR(\mathbf{r}) = \frac{S(\mathbf{r})}{std(N(\mathbf{r}, k))} = \frac{mean_K(S_N(\mathbf{r}, k))}{std_K(S_N(\mathbf{r}, k))} = \frac{m_K(\mathbf{r})}{s_K(\mathbf{r})} \quad (4.16)$$

where $std(N(\mathbf{r}, k))$ denote standard deviation of the noise, $mean_K(S_N(\mathbf{r}, k))$ and $std_K(S_N(\mathbf{r}, k))$ denote the mean and standard deviation of K acquisitions ($S_N(\mathbf{r}, 1), \dots, S_N(\mathbf{r}, k)$) for the pixel at the position $\mathbf{r}$. Note that Equation (4.16) provides an SNR distribution. However, most often, SNR is defined for an region-of-interest (ROI). The SNR of an ROI is obtained using Equation (4.16) as

$$SNR = \frac{mean_{ROI}(m_K(\mathbf{r}))}{mean_{ROI}(s_K(\mathbf{r}))} \quad (4.17)$$

where $mean_{ROI}$ denote the mean of pixel values from different positions within the ROI. In order to calculate SNR accurately, the spatial variation of $S(\mathbf{r})$ should be negligible inside the ROI. Since the experimental phantoms used in this thesis are homogeneous, the ROI is chosen as the whole region which stays inside the phantom. This region corresponds to a circle since transverse slices are used in cylindrical phantoms that are placed along the z-direction.

4.4 Results and Discussion

In Section 2.3, a method based on a novel spin-echo pulse sequence was described for measuring the phase accumulated by subject eddy fields. In order to understand the level of expected phase accumulation, simulations are performed by modeling the experimental phantoms in the Comsol Multiphysics and solving the forward problem (refer to Section 3.2.1). The position and geometry of the gradient coil are the same as in the case shown in Figure 3.1, and the phantom is assumed at the same position. The accumulated phase ($\varphi_{sub,z}$) is calculated by assuming that the slew rate of the z-gradient is 160 T/m/s at all edges of the z-gradient (see Figure 2.1). Figures 4.2a and b show the distributions of the subject eddy current magnitude and the subject eddy field at the imaging slice ($z=0.13$ m plane) for the first experimental phantom ($\sigma=1.3$ S/m). The subject eddy field ($B_{sub,z}$), which is constant in time during the gradient ramp, has a maximum magnitude of 30 nT. The accumulated phase is calculated by using Equation (2.3) with the ramp times (τ_{exc} and τ_{rfc}) given in Table 4.2. The maximum magnitudes of the expected $\varphi_{sub,z}$ are found to be 1.3×10^{-3} rad (0.075°) and 1.6×10^{-3} rad (0.092°) for the first and second phantoms respectively.

In the experiments, which are performed using the proposed pulse sequence (Figure 2.1) and the experimental phantoms, the SNR of the MR magnitude images (when either of the G_z^+ and G_z^- is used) are calculated as 160, 116 and 240 for the first, second, and third phantoms respectively. Using these SNR values in Equation (4.14), $u(\varphi_{meas})$ is estimated as 5.3×10^{-3} and 6.1×10^{-3} rad for the first and second phantoms respectively. Indeed, these values can be thought to be indicating the noise level in the measured phase. The maximum magnitudes of the expected $\varphi_{sub,z}$ (see Figure 4.2b) are about four times lower than these uncertainties which points that $\varphi_{sub,z}$ is below the noise level. Furthermore, for achieving an uncertainty of 0.1 S/m in the reconstructed conductivity, the maximum uncertainty allowed in $\varphi_{sub,z}$, which is denoted by $u(\varphi_{sub,z})_{max}$, is

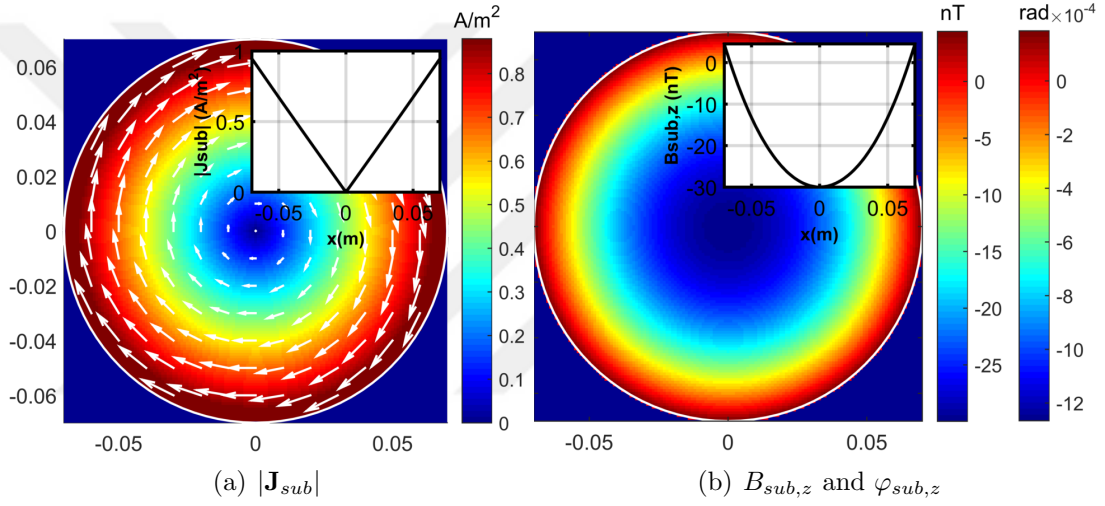


Figure 4.2: Simulation results for the first experimental phantom ($\sigma = 1.3$ S/m) at the imaging slice ($z=0.13$ m plane) when a linear gradient ramp with a slew rate of 160 T/m/s is assumed. (a): The distribution, vector plot and profile of the subject eddy current magnitude. The profile is plotted along the $y=0$ line. (b): The distribution and profile of the z-component of the subject eddy field ($B_{sub,z}$). The profile is plotted along the $y=0$ line. The phase accumulated due to $B_{sub,z}$ is calculated using Equation (2.3) with the ramp times (τ_{exc} , and τ_{rfc}) given in Table 4.2. The scale of this phase distribution is represented by the rightmost color bar.

calculated as 3.8×10^{-6} rad using Equation (4.12) with the experimental parameters given in Table 4.2 (0.1 S/m is assumed to be an acceptable uncertainty for the reconstructed conductivity). Since the $u(\varphi_{meas})$ values of the two phantoms are three orders of magnitude larger than $u(\varphi_{sub,z})_{max}$, we conclude that subject eddy fields cannot be measured with a fidelity sufficient for accurate conductivity reconstruction.

4.5 Appendix

Savitzky-Golay filters are based on locally fitting a polynomial to data. Once the coefficients of the polynomial is determined, data can be smoothed by replacing each data point with the value of its fitted polynomial. More interestingly, the coefficients of the polynomial can also be used for calculating first and second derivatives of data which is called "Savitzky-Golay differentiation". The original Savitzky-Golay filter was for one-dimensional data [53]. However extension to two or three-dimensional data is straight-forward as we shall see. Assume that we want to calculate the kernel elements of a 5x5x3 Savitzky-Golay filter which uses second-order polynomials. Therefore the data should be fitted to a second-order polynomial using the data in total of $5 \times 5 \times 3 = 75$ neighboring points. The polynomial function is given by

$$f(x, y, z) = c_1x^2 + c_2y^2 + c_3z^2 + c_4xy + c_5xz + c_6yz + c_7x + c_8y + c_9z + c_{10} \quad (4.18)$$

where $c_1, c_2, \dots, c_{10}$ denote the coefficients of polynomial function. Equation (4.18) can be written for each of the 75 neighboring points using local coordinates. For example $(x, y, z) = (0, 0, 0)$ at the center, $(x, y, z) = (\Delta x, 0, 0)$ at one point right from the center, $(x, y, z) = (0, 0, \Delta z)$ at one point up from the center, and vice versa. These equations can be stated in the matrix form as $\mathbf{A}_{75 \times 10} \mathbf{c}_{10 \times 1} = \mathbf{b}_{75 \times 1}$ where $\mathbf{A}$ matrix is constructed using local coordinates, $\mathbf{c} = [c_1, c_2, \dots, c_{10}]^T$, and $\mathbf{b}$ consists of data values at 75 points. Note that the number of equations are larger

than the number of unknowns ($75 > 10$) and thus this matrix system should be solved in the least-squares sense. It is known that the least square sense solution of this matrix system is obtained by $(\mathbf{A}^T \mathbf{A})^{-1} \mathbf{A}^T \mathbf{b} = \mathbf{c}$. It is important to note that the $\mathbf{F} = (\mathbf{A}^T \mathbf{A})^{-1} \mathbf{A}^T$ term does not depend on the data but its elements are functions of Δx , Δy and Δz . The 1st, 2nd and 3rd rows of $\mathbf{F}$ corresponds to x^2 , y^2 , and z^2 respectively. Since $\nabla^2 f = 2(c_1 + c_2 + c_3)$ (refer to Equation (4.18)), these rows are added to each other and multiplied by 2 so that 75 elements of the 5x5x3 Laplacian kernel is obtained. Equation (4.5) shows this kernel.

Chapter 5

Modeling Artifacts in the Measured Phase

For measuring subject eddy fields, a modified spin-echo pulse sequence was proposed by which the contribution of subject eddy fields to MR phase images is determined (refer to Section 2.3). As discussed in the previous chapter, it is observed that the noise in the measured phase is intolerably high and thus accurate conductivity reconstruction is not possible. In addition to the random noise, some bias artifacts were also observed in the phase measurements. In the current chapter, these artifacts are analyzed and modeled by considering the effects of undesired magnetic fields due to system imperfections during readout.

5.1 Theory

As discussed in Section 2.1, electrical currents are induced on the metallic system components of an MRI scanner due to switching of gradient fields. These currents were referred to as "system eddy currents" and the field they generate was referred

to as "system eddy field". After switching gradient fields off, the generated system eddy fields decay exponentially with multiple time constants ranging from a few to hundreds of milliseconds [42, 43]. Therefore, system eddy fields still exist during the readout (data acquisition). Furthermore, the field due to main magnetic field inhomogeneity (B0) always exist in the imaging volume. System eddy fields and B0 inhomogeneity manifest themselves with geometric distortions such as shifting, scaling, or shearing in the reconstructed image since they exist during readout [61, 47]. Among these fields, the z-component of the system eddy field due to switching of the z-gradient will be referred to as $B_{sys,z}$ and the z-component of other undesired magnetic fields including system eddy fields due to switching of x- and y-gradients and the B0 inhomogeneity will be referred to as $B_{other,z}$. It can be safely assumed that $B_{sys,z}$ and $B_{other,z}$ are constant in time during the short readout window ($\sim 1-2$ ms). Including the effects of geometric distortions, the phase images in Equations (2.4a) and (2.4b) become [61]

$$\varphi^+(x^+, y) = \varphi^+ \left(x + \frac{B_{other,z}(x, y)}{G_x} + \frac{B_{sys,z}(x, y)}{G_x}, y \right) \quad (5.1a)$$

$$\varphi^-(x^-, y) = \varphi^- \left(x + \frac{B_{other,z}(x, y)}{G_x} - \frac{B_{sys,z}(x, y)}{G_x}, y \right) \quad (5.1b)$$

where $\varphi^+(x^+, y)$ and $\varphi^-(x^-, y)$ are the phase images with geometric distortions, the readout direction is assumed to be the x-direction, and G_x is the readout gradient field. Since $\varphi^+(x^+, y)$ and $\varphi^-(x^-, y)$ are not aligned due to $B_{sys,z}(x, y)/G_x$ term, their difference contains bias artifacts. For cylindrical phantoms with uniform conductivity, these artifacts can be modeled by considering the terms given in Equations (2.4a) and (2.4b). For this purpose, similar to the approach employed by Mandija et al. [39], φ_{RF} is approximated with a quadratic function [62], i.e. $\varphi_{RF}(x, y) = b_1^{\sigma=\sigma_0} + b_2^{\sigma=\sigma_0}(x^2 + y^2)$ where σ_0 is the conductivity of the phantom (the coefficients scale with the conductivity of the phantom [62]). Substituting x^+ or x^- for x in $\varphi_{RF}(x, y)$, the difference between $\varphi^+(x^+, y)$ and

$\varphi^-(x^-, y)$ are expressed as

$$\begin{aligned} & \left\{ \frac{\varphi^+(x^+, y) - \varphi^-(x^-, y)}{2} \right\}_{\sigma=\sigma_0} \\ &= \frac{\varphi_{sub,z}^{sum}}{2} + \frac{\varphi_{sys,z}^{sum}}{2} + \frac{\varphi_{other}^{diff}}{2} + 2b_2^{\sigma=\sigma_0} \left(x + \frac{B_{other,z}}{G_x} \right) \frac{B_{sys,z}}{G_x} \end{aligned} \quad (5.2)$$

where $\varphi_{sub,z}^{sum} = \varphi_{sub,z}(x^+, y) + \varphi_{sub,z}(x^-, y)$, $\varphi_{sys,z}^{sum} = \varphi_{sys,z}(x^+, y) + \varphi_{sys,z}(x^-, y)$ and $\varphi_{other}^{diff} = \varphi_{other}(x^+, y) - \varphi_{other}(x^-, y)$. Because of the misregistration between $\varphi^+(x^+, y)$ and $\varphi^-(x^-, y)$, additional terms appear in Equation (5.2) compared with the terms in Equation (2.5a).

As discussed in Section 2.3, φ^+ and φ^- should also be measured for a non-conductive phantom in order to obtain $\varphi_{sub,z}$ (refer to Equation (2.5c)). However, preparing a phantom material with zero conductivity may not be practical. Therefore, we assume that a low-conductive phantom is used instead of a nonconductive phantom. Considering Equation (5.2) for the low-conductive phantom, $\varphi_{sys,z}^{sum}$ and φ_{other}^{diff} are the same as in the conductive phantom, whereas $\varphi_{sub,z}^{sum}$ and the last term in Equation (5.2) are different since they depend on the conductivity. Assuming that $\varphi_{sub,z}^{sum}/2 \cong \varphi_{sub,z}$ (see the Appendix at the end of this chapter for the validation), the measured phase (φ_{meas}), which would ideally equal $\varphi_{sub,z}$, can be expressed as (compare with Equation (2.5c))

$$\begin{aligned} \varphi_{meas} &= \left\{ \frac{\varphi^+(x^+, y) - \varphi^-(x^-, y)}{2} \right\}_{\sigma=\sigma_0} - \left\{ \frac{\varphi^+(x^+, y) - \varphi^-(x^-, y)}{2} \right\}_{\sigma=\sigma_{low}} \\ &\cong \varphi_{sub,z}^{\sigma_0-\sigma_{low}} + 2(b_2^{\sigma=\sigma_0} - b_2^{\sigma=\sigma_{low}}) \left(x + \frac{B_{other,z}}{G_x} \right) \frac{B_{sys,z}}{G_x} \end{aligned} \quad (5.3)$$

where σ_{low} is the conductivity of the low-conductive phantom, and $\varphi_{sub,z}^{\sigma_0-\sigma_{low}} = \{\varphi_{sub,z}\}_{\sigma=\sigma_0} - \{\varphi_{sub,z}\}_{\sigma=\sigma_{low}}$. Since the second term in Equation (5.3) is related to the RF phase that could not be eliminated, it will be referred to as the "RF leakage" as also done by Mandija et al. [39]. Note that the RF leakage scales with $(b_2^{\sigma=\sigma_0} - b_2^{\sigma=\sigma_{low}})$ and it, thereby, also scales with the phantom conductivity difference $(\sigma_0 - \sigma_{low})$ [62].

5.2 Experimental Methods

The experiments described in this chapter are performed for investigating RF leakage using the three cylindrical experimental phantoms described in Section 4.3. The experimental parameters are summarized in Table 5.1. In these experiments, large voxels of size 7x7x5 mm are used for assuring low $u(\varphi_{meas})$ so that the RF leakage is not obscured by noise in φ_{meas} . Specifically, using Equation (4.14) and the measured SNR values, which are 1960, 1421, and 2940 for the first, second and third phantoms, $u(\varphi_{meas})$ is estimated as 4.3×10^{-4} rad and 5.5×10^{-4} rad for the first and second phantoms respectively. These uncertainties are sufficiently lower than the level of measured RF leakages shown in Figures 5.2a and b (We will elaborate on these figures in the next section). For measuring SNR, the SNR_{mult} method described in Section 4.3 is used.

The RF leakage in the measured phase scales with the $(b_2^{\sigma=\sigma_0} - b_2^{\sigma=0.2})$ coefficient as evident from Equation (5.3). This coefficient is measured by fitting a quadratic function to the difference $\{\varphi^+(x, y)\}_{\sigma=\sigma_0} - \{\varphi^+(x, y)\}_{\sigma=0.2}$ (see Equation (2.5a)). Since the same z-gradient polarity is used, there is no misregistration between the phase images and the terms other than φ_{RF} cancel each other in the difference ($\varphi_{sub,z}$ is negligible compared to φ_{RF} (see Figure 4.2b)). Therefore, this difference equals $b_0^{\sigma=\sigma_0} - b_0^{\sigma=0.2} + (b_2^{\sigma=\sigma_0} - b_2^{\sigma=0.2})(x^2 + y^2)$. The fitted $(b_2^{\sigma=1.3} - b_2^{\sigma=0.2})$ coefficient is 271 rad/m² for the first experimental phantom ($\sigma = 1.3$ S/m) whereas it is 339 rad/m² for the second experimental phantom ($\sigma = 1.6$ S/m).

5.3 Results

In this section, we will demonstrate bias artifacts in φ_{meas} which are thought to be associated with the RF leakage. Figures 5.1a-c show the MR phase images at

Parameter	Setting
Field of View (mm)	224×224
Image Matrix Size	32×32
Voxel Size (mm)	7×7×5
Imaging Slice (Transverse)	$z = 0.13m$
Echo Time (ms)	10
Repetition Time (ms)	1000
Flip angle (°)	90
Number of Acquisition	16
Total Imaging Time (min)	8.5×4
Bandwidth per Pixel (Hz/pix)	500
G_x Readout (mT/m)	1.7
G_z^{exc} Excitation (mT/m)	15.66
G_z^{rfc} Refocusing (mT/m)	4.8
Slew Rate of the z-gradient (T/m/s)	160
Excitation Ramp Time $\tau_{exc}(\mu s)$	98
Refocusing Ramp Time $\tau_{rfc}(\mu s)$	30

Table 5.1: The experimental parameters

the imaging slice ($z=0.13$ m) of the three phantoms when G_z^+ is used (the phase images for G_z^- are not shown). For the three phantoms, Figures 5.1d-f show half the difference between the MRI phase images acquired using G_z^+ and G_z^- . These difference images, which are labelled as $\varphi_{diff}^{\sigma=1.3}$, $\varphi_{diff}^{\sigma=1.6}$ and $\varphi_{diff}^{\sigma=0.2}$, may be modeled by using Equation (5.2). Among the terms of Equation (5.2), $\varphi_{sub,z}^{sum}$ is not observable with the scale of these figures since it is in the order of 10^{-3} rad (see Figure 4.2b) and the $\varphi_{sys,z}^{sum}$ and φ_{other}^{diff} terms are the same for all the phantoms since they do not depend on conductivity. Therefore if it were only the first three terms of Equation (5.2), we would have observed same distributions for $\varphi_{diff}^{\sigma=1.3}$, $\varphi_{diff}^{\sigma=1.6}$ and $\varphi_{diff}^{\sigma=0.2}$, but that is not the case. It may be hypothesized that these differences are accounted for the last term in Equation (5.2) which is the RF leakage term. Figure 5g shows the difference between $\varphi_{diff}^{\sigma=1.3}$ and $\varphi_{diff}^{\sigma=0.2}$ while Figure 5h shows the difference between $\varphi_{diff}^{\sigma=1.6}$ and $\varphi_{diff}^{\sigma=0.2}$. These differences, which are defined as φ_{meas} , are modeled using Equation (5.3). The levels of φ_{meas} are in the order

of 10^{-2} rad, indicating that the contribution of $\varphi_{sub,z}^{\sigma_0-\sigma_{low}}$ is not dominant (see Figure 4.2b). Therefore φ_{meas} expected to be proportional to the coefficients $(b_2^{\sigma=1.3} - b_2^{\sigma=0.2})$ and $(b_2^{\sigma=1.6} - b_2^{\sigma=0.2})$. It is indeed observed that the pattern of φ_{meas} is very similar for two phantoms and the ratio between their levels is about 0.8 which equals the experimentally calculated ratio of $\frac{(b_2^{\sigma=1.3} - b_2^{\sigma=0.2})}{(b_2^{\sigma=1.6} - b_2^{\sigma=0.2})} = \frac{271}{339} = 0.8$. Therefore we may argue that the theory of RF leakage expressed through Equations (5.2) and (5.3) is consistent with our observations.

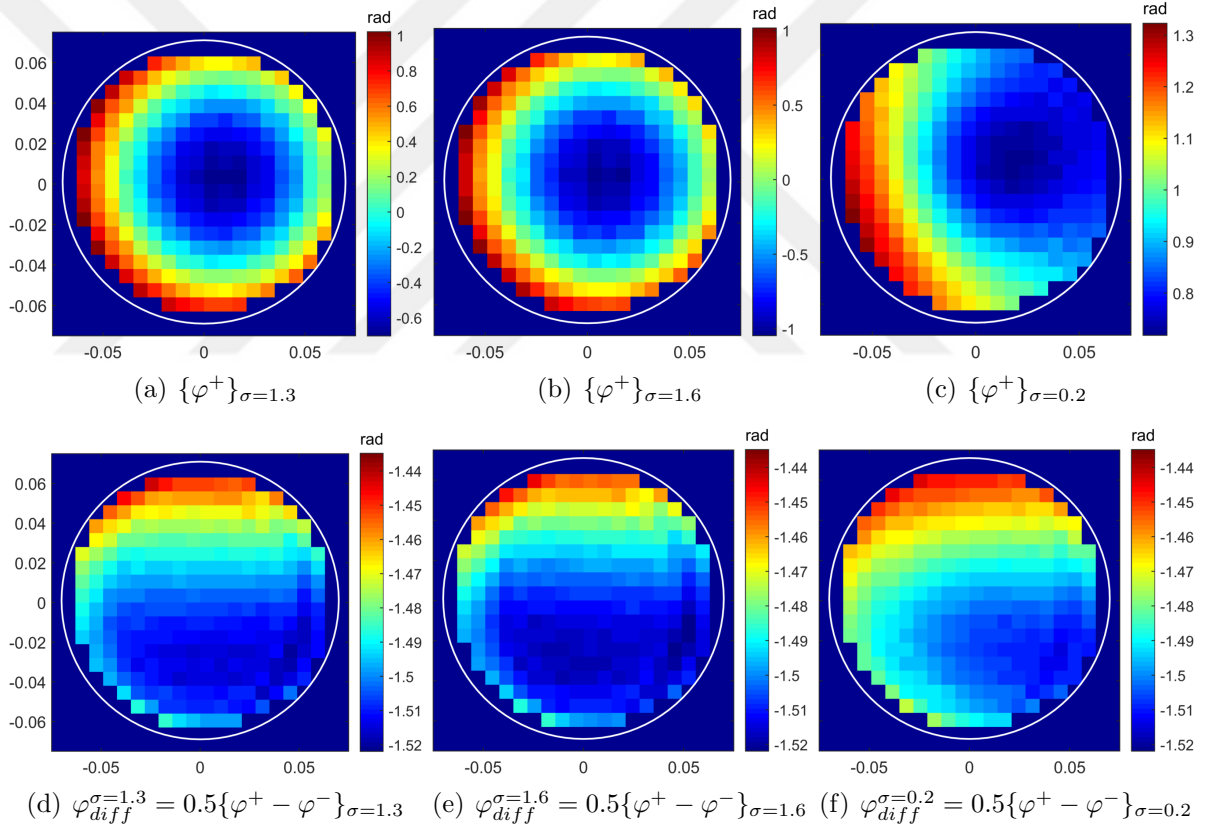


Figure 5.1: Experimental results regarding the demonstration of the RF leakage at the imaging slice ($z=0.13$ m plane) of the experimental phantoms (The units of x-axis (horizontal) and y-axis (vertical) are meters): (a-c): The MR phase images of the first ($\sigma = 1.3$ S/m), second ($\sigma = 1.6$ S/m), and third ($\sigma = 0.2$ S/m) phantoms respectively when the polarity of the z-gradient is positive (see G_z^+ in Fig. 1). (d-f): The half of the difference between the phase images acquired using positive and negative z-gradient polarities for the three phantoms respectively ($\varphi_{diff}^{\sigma=1.3}$, $\varphi_{diff}^{\sigma=1.6}$, and $\varphi_{diff}^{\sigma=0.2}$).

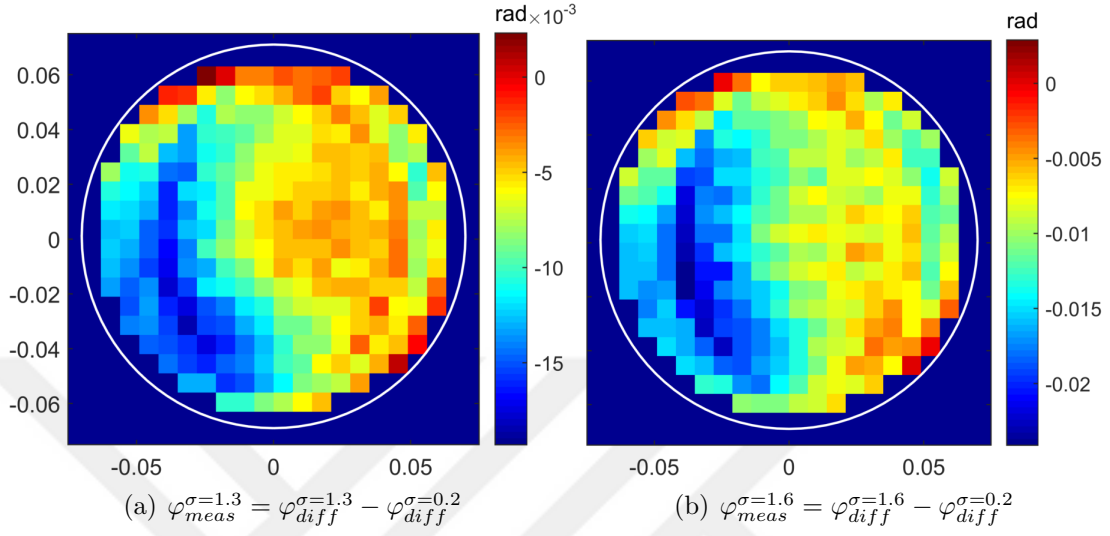


Figure 5.2: Experimental results regarding the demonstration of the RF leakage at the imaging slice ($z=0.13$ m plane) of the experimental phantoms (The units of x-axis (horizontal) and y-axis (vertical) are meters): (a): The measured RF leakage phase for the first phantom ($\varphi_{meas}^{\sigma=1.3} = \varphi_{diff}^{\sigma=1.3} - \varphi_{diff}^{\sigma=0.2}$). (b): The measured RF leakage phase for the second phantom ($\varphi_{meas}^{\sigma=1.6} = \varphi_{diff}^{\sigma=1.6} - \varphi_{diff}^{\sigma=0.2}$).

5.4 Discussion

In this chapter, bias artifacts observed in φ_{meas} are investigated by developing a theoretical model which hypothesizes that these artifacts are caused by the RF phase which could not be eliminated due to misregistration between $\varphi^+(x^+, y)$ and $\varphi^-(x^-, y)$. The developed model suggests that these artifacts, which are referred to as RF leakage, scale with conductivity of phantoms. Indeed, such scaling is also observed in our experiments which supports the validity of the model. Therefore, even if $u(\varphi_{meas})$ may be sufficiently lowered by some innovative means, there are still non-random RF leakage artifacts which must be handled in order to accurately measure $\varphi_{sub,z}$ and reconstruct conductivity. On the other hand, the pattern of RF leakage is hard to predict since it requires exact knowledge of B0 inhomogeneity and system eddy fields during readout. The complete verification of the RF leakage hypothesis, therefore, requires further study.

Measurement of subject eddy fields due to switching of gradients has been investigated in other studies as well [32]-[40]. In a recent study, Mandija et al. have investigated the measurement of the subject eddy field due to switching of readout (x- or y-) gradients [39]. They propose measuring the phase accumulated due to this subject eddy field by taking the difference of two phase images acquired using spin-echo pulse sequences of opposite readout gradient polarities (φ^+ and φ^-). In another recent study, Gibbs et al. have investigated the phase accumulated due to the subject eddy field induced by the falling edge of a gradient pulse which is applied immediately before the excitation [40]. In the both studies, the level of accumulated phases is found to be below the noise level [39, 40], which is in line with our findings. Moreover, by applying sub-voxel shifts to φ^+ and φ^- via spatial interpolation, Mandija et al. have also shown that even minor sub-voxel misregistrations in φ^+ and φ^- can lead to RF leakages which dominate desired measurements and which scale with conductivity [40]. Our experimental findings about RF leakage are also in line with the findings of this study.

5.5 Appendix

For cylindrical phantoms with uniform conductivity, $\varphi_{sub,z}$ can be approximated with a quadratic function (see the profile in Figure 4.2b), i.e. $\varphi_{sub,z}(x, y) = u_1^{\sigma=\sigma_0} + u_2^{\sigma=\sigma_0}(x^2 + y^2)$. Substituting x^+ or x^- for x $\varphi_{sub,z}^{sum}/2$ can be expressed as (for definitions of x^+ and x^- see Equations (5.1a) and (5.1b))

$$\frac{\varphi_{sub,z}^{sum}}{2} = \varphi_{sub,z}(x, y) + u_2^{\sigma=\sigma_0} \left[2x \frac{B_{other,z}}{G_x} + \left(\frac{B_{other,z}}{G_x} \right)^2 + \left(\frac{B_{sys,z}}{G_x} \right)^2 \right] \quad (5.4)$$

Since $B_{other,z}/G_x$ and $B_{sys,z}/G_x$ is on the order of 0.005 or less [47], $(B_{other,z}/G_x)^2$ and $(B_{sys,z}/G_x)^2$ can safely be neglected compared to $(x^2 + y^2)$. Away from the origin, the $2xB_{other,z}/G_x$ term can also be neglected compared to $(x^2 + y^2)$ (around the origin, $u_1^{\sigma=\sigma_0}$ term is dominant in $\varphi_{sub,z}$ anyway). Therefore the artifacts due to misregistration of $\varphi_{sub,z}$ are negligible compared to $\varphi_{sub,z}$ itself, and

thus $\varphi_{sub,z}^{sum}/2 \cong \varphi_{sub,z}(x, y)$.



Chapter 6

Possible Directions for Feasible Subject Eddy Current based Conductivity Imaging

In Section 4.4, the maximum allowed uncertainty in $\varphi_{sub,z}$ is found to be 3.8×10^{-6} rad for an accurate conductivity reconstruction, i.e. $u(\varphi_{sub,z})_{max} = 3.8 \times 10^{-6}$ rad in Equation (4.12). On the other hand, it is also found in Section 4.4 that the uncertainty of φ_{meas} is in the order of 3×10^{-3} rad when the proposed pulse sequence shown in Figure 2.1 is used, i.e. $u(\varphi_{meas}) = 3 \times 10^{-3}$ rad. For feasible subject eddy current based conductivity imaging, $u(\varphi_{meas})$ should be smaller than $u(\varphi_{sub,z})_{max}$. Therefore, whether $u(\varphi_{meas})$ should be decreased or $u(\varphi_{sub,z})_{max}$ should be increased. Since $\varphi_{sub,z}$ is measured as the linear combination of four MRI phase images (see Equation (4.13)), its uncertainty depends on the parameters effecting the SNR of an MRI image such as voxel size, number of acquisitions, echo time, bandwidth per pixel, . . . etc. In the experiments, we have chosen voxel size of 2x2x5 mm and the total acquisition time was about two hours due to

16 acquisitions. If clinical applications are considered, the voxel size and imaging time are already at the upper limit of acceptable values. Furthermore, it is not preferable to decrease bandwidth per pixel, because this would decrease the readout gradient amplitude (G_x) and cause RF leakage to increase (see Equation (5.3)). Therefore, considering the fact that we want to study feasibility with realistic parameters, it is not desirable to play with these parameters in order to decrease $u(\varphi_{meas})$. Sections 6.1 and 6.2, therefore, concentrate on the other option which is to increase $u(\varphi_{sub,z})_{max}$.

As discussed in Chapter 5, undesired magnetic fields due to system imperfections during readout cause geometric distortions in the acquired images, which in turn cause RF leakage in the measured phase. Section 6.3 investigates if the RF leakage problem can be handled by correcting these geometric distortions.

6.1 Increased Gradient Strength

As discussed above, $u(\varphi_{sub,z})_{max} = 3.8 \times 10^{-6}$ rad while $u(\varphi_{meas}) = 3 \times 10^{-3}$ rad. Therefore, $u(\varphi_{sub,z})_{max}$ should be increased at least 800-fold so that $u(\varphi_{meas})$ becomes smaller than $u(\varphi_{sub,z})_{max}$ and an accurate conductivity reconstruction is assured. The relation for $u(\varphi_{sub,z})_{max}$ was expressed by Equation (4.12) which is restated below

$$u(\varphi_{sub,z})_{max} = u(\sigma)_{des} \frac{\gamma \mu_0 z_0 (G_z^{exc} + 2G_z^{rfc})}{rss(K_{eq})} \quad (6.1)$$

where $u(\sigma)_{des}$ is the desired uncertainty in reconstructed conductivity ($u(\sigma)_{des} = 0.1$ S/m), z_0 is the z-coordinate of the imaging slice (0.13 m), $G_z^{exc} = 15.66$ mT/m, $G_z^{rfc} = 4.8$ mT/m, and $rss(K_{eq}) = 28777$ (K_{eq} is the equivalent kernel obtained by the convolution of a 3x3x3 Gaussian kernel with a 5x5x3 Savitzky-Golay differentiation kernel). In Section 4.1, it was shown that RSS decreases as kernel size increase (see Table 4.1). However, larger kernel sizes also increase the spatial

resolution, and $rss(K_{eq})$ cannot be further decreased considering clinical applications. Furthermore, the z-coordinate of the imaging slice (z_0) is limited by the maximum field-of-view of MRI scanner and the value 0.13 is already close to the maximum value. Therefore, parameters that can provide significant increase in $u(\varphi_{sub,z})_{max}$ are only G_z^{exc} and G_z^{rfc} which are the magnitudes of slice-selection gradients during excitation and refocusing. In clinical MRI scanners, the performance of gradient systems are being gradually improved as some applications like diffusion weighted imaging demand highest possible gradient fields [63, 64]. Although 800-fold increase in the performance of clinical gradient systems is not expected due to limiting factors of peripheral nerve stimulation and acoustic noise, recent developments in gradient-systems allow gradient fields of 80 mT/m to be applied in all axes [65, 66]. Moreover, small-sized head gradient coils have even better performance and they can reach gradient fields greater than 90 mT/m [67]. Compared to the gradient field levels used in this study, only $\frac{90+90 \times 2}{15.66+4.8 \times 2} = 11$ -fold increase can be achieved in $u(\varphi_{sub,z})_{max}$ provided that the output voltage of the RF amplifier is sufficient to compensate for the narrower RF pulses (see Remark (i) in Section 4.3). It seems that it is not possible to make the subject eddy current based conductivity imaging feasible in clinical scanners by only increasing the gradient strength.

It is interesting to note that commercially available small-sized preclinical MRI scanners can reach gradient fields of up to 1000 mT/m [68, 69]. This would provide $\frac{1000+1000 \times 2}{15.66+4.8 \times 2} = 119$ -fold increase in $u(\varphi_{sub,z})_{max}$. For animal subjects or phantoms inside these small scanners, imaging time is not a critical issue and thus number of acquisitions can also be increased. Furthermore, if a larger voxel size of 3x3x5 mm is used then a total of 800-fold increase might be achieved in $u(\varphi_{sub,z})_{max}$. Therefore, using these kinds of MRI scanners, the methods developed in this thesis might be used to reconstruct conductivity in animal subjects or phantoms provided that the RF leakage problem is solved.

6.2 Multi-spin-echo Pulse Sequence

For increasing $u(\varphi_{sub,z})_{max}$, we have developed a multi-spin-echo pulse sequence such that the polarity of the z-gradient field is negated for every other refocusing RF pulse. Timing-diagram for the proposed multi-spin-echo pulse sequence is shown in Figure 6.1. Every slice-selection gradient lobe of refocusing RF pulses contribute to $\varphi_{sub,z}$ as seen in the waveform shown at the sixth row. Therefore, for this multi-spin-echo pulse sequence, $\varphi_{sub,z}$ can be stated as

$$\varphi_{sub,z} = \gamma B_{sub,z} (\tau_{exc} + 2N\tau_{rfc}) \quad (6.2)$$

where N is the number of refocusing pulses. Using Equation (6.2), Equation (6.1) is modified for the multi-spin-echo pulse sequence as

$$u(\varphi_{sub,z})_{max} = u(\sigma)_{des} \frac{\gamma \mu_0 z_0 (G_z^{exc} + 2NG_z^{rfc})}{rss(K_{eq})} \quad (6.3)$$

As evident from Equation (6.3), the number of refocusing RF pulses determines how much improvement can be achieved in $u(\varphi_{sub,z})_{max}$. It is known that the excitation RF field (B1) is perturbed by the electrical properties (dielectric permittivity and conductivity) of imaging subjects and thus the B1-field and flip angle are not homogeneously distributed inside imaging subjects. Therefore, in practice, a refocusing RF pulse with nominal flip angle of 180° does not flip spins 180° at every position. This “imperfect refocusing” and the transverse relaxation of MR signal limit the number of refocusing pulses as we will discuss in Section 6.2.3. Before that, we will introduce Extended Phase Graph (EPG) framework in Section 6.2.1 and, we will use this framework to analyze the proposed multi-spin-echo pulse sequence in Section 6.2.2.

6.2.1 Extended Phase Graph (EPG) Framework

Extended Phase Graph (EPG) is a tool for understanding and depicting magnetization response of pulse sequences by characterizing the effect of RF pulses and

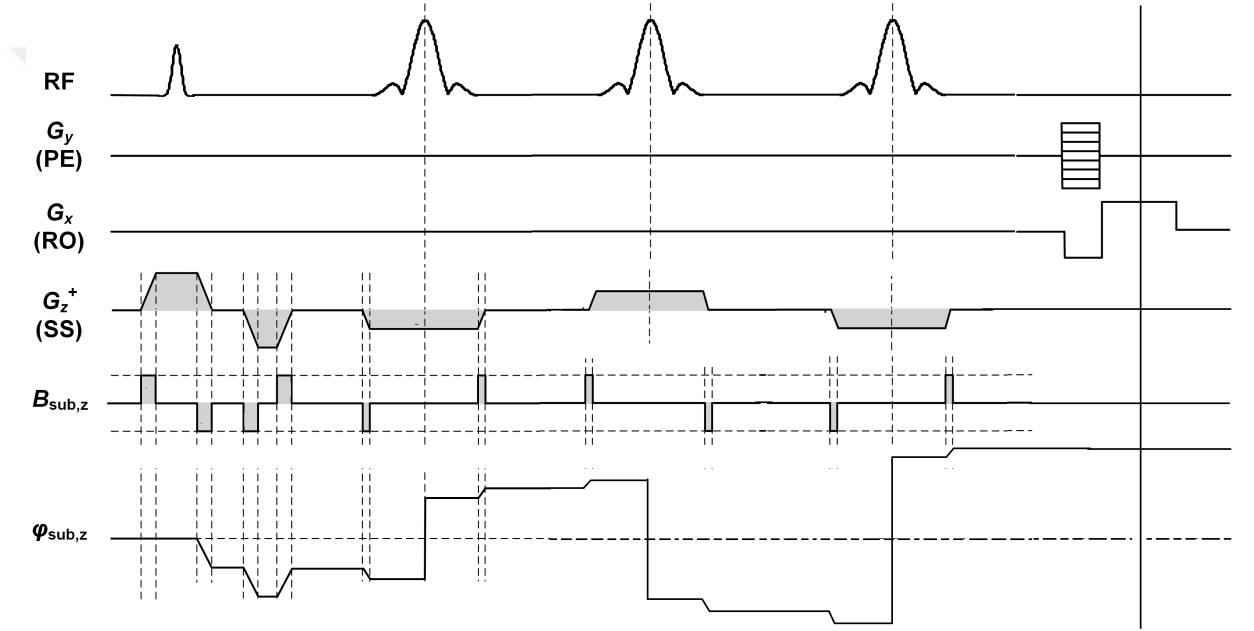


Figure 6.1: The timing diagram of the multi-spin-echo pulse sequence proposed for increasing $\varphi_{sub,z}$ (RF: radiofrequency field, PE: Phase Encoding, RO: Readout, SS: slice selection). The ramping times of the z-gradient field are exaggerated for a better visualization of $B_{sub,z}$. Two separate measurements, one using G_z^+ and one using G_z^- , are performed. Although not shown, G_z^- is the inverted version of G_z^+ . The waveforms of $B_{sub,z}$ and $\varphi_{sub,z}$ for the case of G_z^+ are shown at the fifth and sixth rows.

gradients [70, 71]. In this section, we will describe and briefly summarize EPG framework. In the next section, we will use EPG for analyzing the magnetization response of the proposed multi-spin-echo pulse sequence and elaborate how this magnetization response effects $\varphi_{sub,z}$ measurements.

A magnetization pathway, or simply a pathway, is a group of spins which share the same phase characteristics within a time interval, i.e. spins in a pathway have whether dephasing transverse magnetization (M_+), rephasing transverse magnetization (M_-), or longitudinal magnetization (M_z). For example, in an ideal spin-echo experiment, the excitation RF pulse generates a dephasing pathway in which spins gradually lose coherence. After the application of an ideal refocusing RF pulse, this dephasing pathway is converted to a rephasing pathway in which spins gradually gain coherence. This rephasing pathway forms an spin-echo at the time spins become fully coherent. In general, after the application of a non-ideal refocusing RF pulse, the dephasing pathway is not completely converted to a rephasing pathway but the magnetization is distributed among the newly generated dephasing, rephasing and longitudinal pathways depending on the actual flip-angle which is different than 180° . This is known as the “partitioning effect of a RF pulse” [72]. For quantitatively analyzing the partitioning effect, magnetizations of pathways are represented in the complex magnetization basis. The initial dephasing pathway (M_+) is obtained as

$$M_+ = M_x + iM_y = M_0 \sin \alpha \quad (6.4)$$

when the excitation RF pulse with flip angle α is applied in the y-axis (right-handed convention is adopted). Magnetizations of the pathways, which are generated by the refocusing RF pulse from this initial pathway, are obtained by the following relation [72]

$$\begin{aligned} M_+^+ &= M_+ \cos^2 \left(\frac{\beta}{2} \right) \\ M_-^+ &= (M_+)^* \sin^2 \left(\frac{\beta}{2} \right) \\ M_z^+ &= M_+ \cos(\beta) \end{aligned} \quad (6.5)$$

where subscripts + and - denote dephasing and rephasing pathways respectively, superscript + means right after the RF pulse, $(.)^*$ denotes complex conjugate, β is the flip angle of the refocusing RF pulse, M_+^+ , M_-^+ and M_z^+ are the magnetizations of the generated dephasing, rephasing and longitudinal pathways respectively. Each of the M_+^+ , M_-^+ and M_z^+ pathways will be split into three pathways by the next refocusing RF pulse. Magnetizations of these further generated pathways are obtained using the following general relations [72].

When the pathway to be split is dephasing or rephasing ($M_\pm$):

$$M_+^+ = M_\pm \cos^2 \left(\frac{\beta}{2} \right) \quad (6.6a)$$

$$M_-^+ = (M_\pm)^* \sin^2 \left(\frac{\beta}{2} \right) \quad (6.6b)$$

$$M_z^+ = -\frac{i}{2} M_\pm \sin(\beta) \quad (6.6c)$$

When the pathway to be split is longitudinal (M_z):

$$M_+^+ = -iM_z \sin(\beta) \quad (6.7a)$$

$$M_-^+ = iM_z \sin(\beta) \quad (6.7b)$$

$$M_z^+ = M_z \cos(\beta) \quad (6.7c)$$

Note that Equation (6.6)c indicates that longitudinal pathways can have complex magnetizations. Indeed, imaginary part of M_z represents the magnetization ‘stored’ in the longitudinal magnetization [70]. This stored magnetization forms an stimulated echo later, if another refocusing RF pulse is applied [73].

The partitioning effect of RF pulses, which is described by Equations (6.6) and (6.7), is the key for understanding EPG framework. Now we will elaborate on the EPG framework with an example. Figure 6.2 shows the EPG for a pulse sequence in which a 90_y° excitation RF pulse is followed by two 150_y° refocusing RF pulses (subscripts of flip-angles denote the axis in which RF pulses are applied). Rephasing and dephasing pathways are shown with solid lines, while longitudinal

Pathway	Magnetization
1	1.00-0.00i
2	0.07-0.00i
3	-0.00-0.25i
4	0.93+0.00i
5	0.00-0.00i
6	-0.00-0.02i
7	0.06+0.00i
8	-0.12+0.00i
9	0.00+0.22i
10	0.12+0.00i
11	0.06+0.00i
12	0.00-0.23i
13	0.87-0.00i

Table 6.1: Complex magnetizations of pathways shown in Figure 6.2

pathways are shown with dashed lines. Time-locations of the RF pulses are indicated with horizontal lines. The x-axis shows time in arbitrary units and the y-axis shows the phase difference within a voxel for spins in a pathway. If this difference is larger than 2π then the pathway is said to be completely dephased (no signal comes from spins in the pathway). Therefore, y-axis can be thought to be showing the degree of dephasing for the pathways. The RF partitioning effect can be easily observed in Figure 6.2. For example, 1st pathway, which is generated by the excitation RF pulse, is split into three pathways (2nd, 3rd, and 4th pathways) by the first refocusing RF pulse. The pathways, which share the same source pathway, are shown with same color and thus 2nd, 3rd, and 4th pathways are shown with red color. Complex magnetizations for these and all other pathways are calculated using Equations (6.6) and (6.7) and they are provided in Table 6.1. The number of generated pathways (N_p) is related to the number of refocusing RF pulses (N) as

$$N_p = \frac{1}{2} (3^{(N+1)} - 1) \quad (6.8)$$

Another important phenomena which can be observed in Figure 6.2 is the

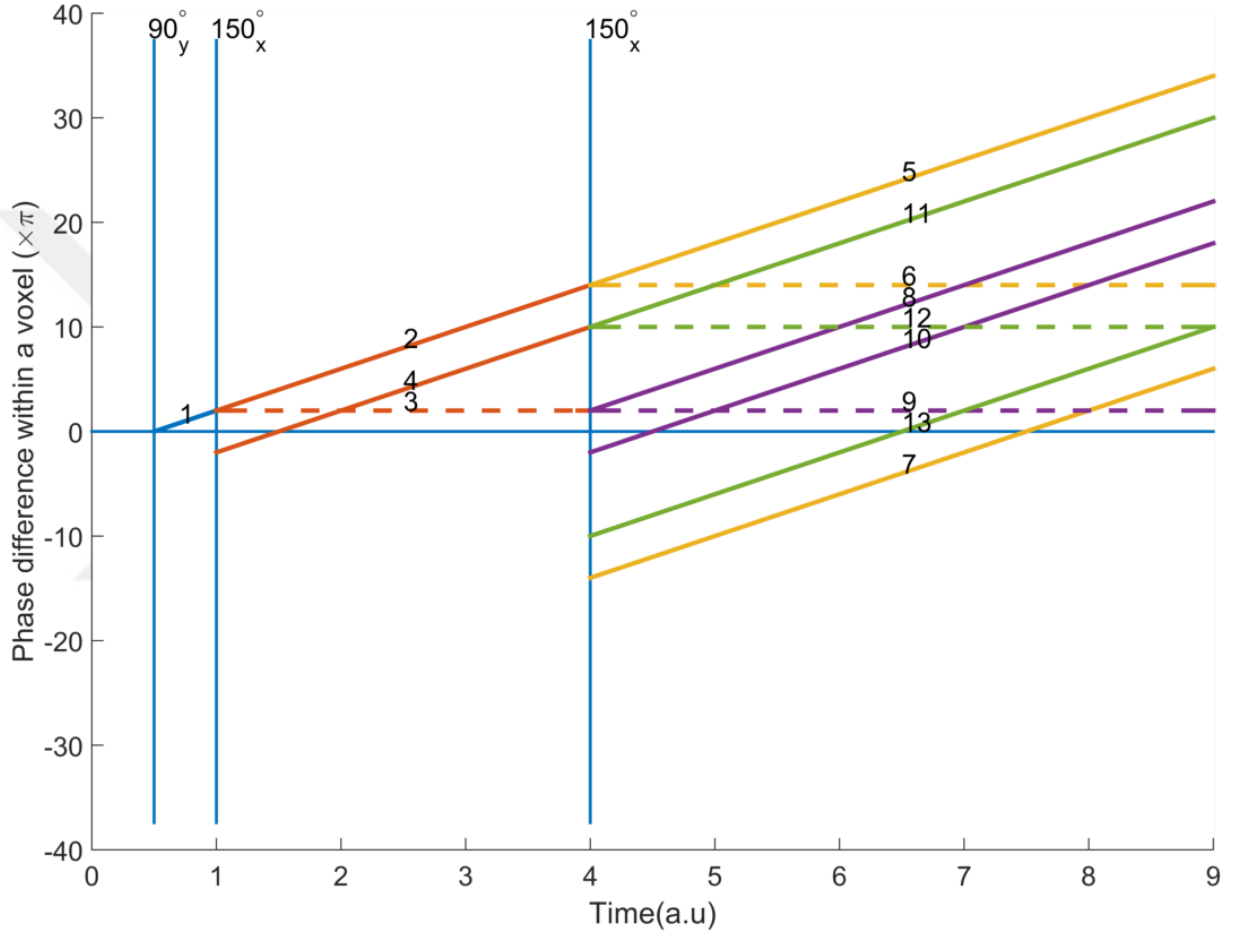
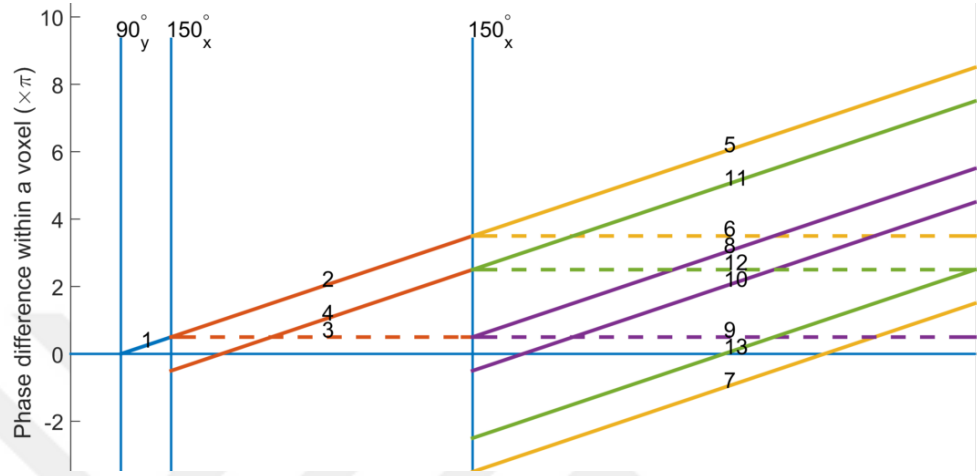


Figure 6.2: EPG for a pulse sequence in which a 90° excitation RF pulse is followed by two 150° refocusing RF pulses. Time-locations of RF pulses are indicated with horizontal lines. Subscripts of flip angles denote the axis in which RF pulses are applied. Rephasing and dephasing pathways are shown with solid lines, longitudinal pathways are shown with dashed lines. Pathways are numbered and colored with respect to their sourcing pathway. The x-axis shows time in arbitrary units (a.u.) and the y-axis shows the phase difference within a voxel for spins in a pathway.

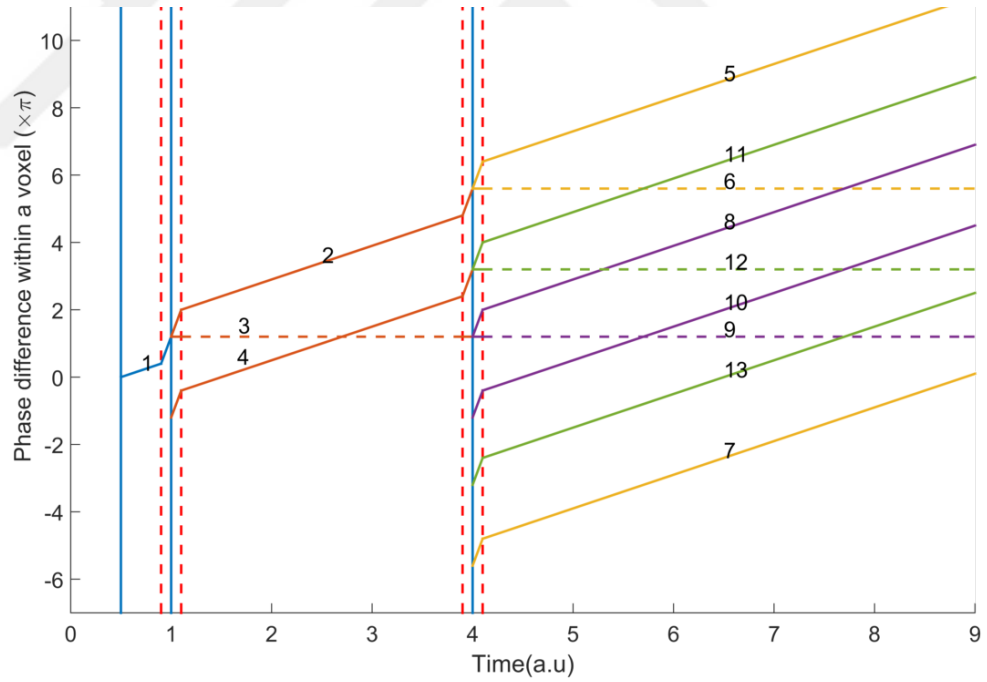
echo formation. A pathway is said to form an echo if the spins in the pathway become coherent, i.e. the phase difference of spins within a voxel becomes zero. Therefore, a pathway forms an echo once it passes through the x-axis on which the phase difference is zero and, in Figure 6.2, 4th, 10th, 13th and 7th pathways form an echo in different times. The echo of 4th pathway is a regular spin-echo which is formed by the refocusing of the first 150° RF pulse. Later, 4th pathway dephases again and it is refocused by the second 150° RF pulse and the echo of 13th pathway is formed. The echo of 7th pathway is formed by the refocusing of 2nd pathway which is not effected from the first 150° RF pulse. The echo of 10th pathway is an stimulated echo and it is formed by the 3rd pathway which is ‘stored’ as a longitudinal magnetization by the first 150° RF pulse and later refocused by the second 150° RF pulse to form 10th pathway and an stimulated echo [73]. The MRI signal for each of these echoes can be calculated using the magnetization of the pathway that generates the echo.

In obtaining Figure 6.2, we have assumed that, once pathways are generated by RF pulses, their magnetization dephases completely before they reach another RF pulse. This assumption is very important for the EPG concept in the sense that, with this assumption, all pathways other than the one passing through x-axis are dephased at the time an echo is generated. Therefore, the MRI signal during the echo-time comes from only a single pathway. In practice, however, the time between RF pulses is not long enough for a pathway to dephase completely. Therefore, most often, “crusher” gradients are used to dephase magnetization completely [74]. Crusher gradients are typically consists of two same gradient lobes, one applied before and one applied after refocusing RF pulses.

The effect of crusher gradients can also be analyzed using EPG. Figure 6.3a shows the same pulse sequence as in Figure 6.2 but the “natural” dephasing speed is 4-times lowered to obtain a more realistic diagram. Note that, at the time 13th pathway generates an echo, the phase difference for the 7th pathway is about 1π and thus it will also contribute to the acquired signal. Figure 6.3b shows the EPG



(a) Without crusher gradients



(b) With crusher gradients

Figure 6.3: EPG for a pulse sequence in which a 90° excitation RF pulse is followed by two 150° refocusing RF pulses: (a): When no crusher gradient is applied, (b): When crusher gradients, which provide 8-times faster dephasing, are used. The regions where crushers are effective are enclosed with two dashed lines.

when crusher gradients are applied before and after refocusing RF pulses. The regions where crushers are effective are enclosed with two dashed lines. In these regions, dephasing is 8-times faster than the natural dephasing speed. Note that, by means of the crusher gradients, the phase difference for 7th pathway is now larger than 2π at the time 13th pathway generates an echo and thus 7th pathway does not contribute to the acquired signal. Note also that the echo generated by 7th pathway itself is shifted in time. Indeed, crusher gradients can be used to shift time positions of echoes, so that desired echoes are included in the readout window while undesired echoes are sent away.

6.2.2 Analysis of Multi-spin-echo Sequence using EPG

We will now analyze the proposed pulse sequence shown in Figure 6.1 using the EPG framework. The EPG for this sequence is shown in Figure 6.4 when no crusher gradients are used. The flip-angles for the excitation and refocusing RF pulses are taken as 70_y° and 140_x° respectively. The proposed pulse sequence meets the following conditions: (i) The spacing between refocusing RF pulses are equal and this spacing is two-times the spacing between the excitation RF pulse and the first refocusing RF pulse. (ii) There is 90° phase-difference between the excitation and refocusing RF pulses, i.e. the excitation RF pulse is applied in y-axis while refocusing RF pulses are applied in x-axis. (iii) The net gradient area is equal at all intervals between refocusing RF pulses. These conditions are termed as “Carr-Purcell-Meiboom-Gill (CPMG)” conditions and it is known that, in sequences meeting CPMG conditions, certain pathways and echoes overlap, i.e. echoes occur at the same time position [74]. Although there should be $\frac{1}{2}(3^{3+1} - 1) = 40$ pathways in Figure 6.4 (see Equation (6.8)), only 20 distinct pathways are observable. The overlapping pathways labeled with group numbers G_1 to G_{20} and the pathways forming these groups and their magnetizations are provided in Table 6.2. The numbering convention of pathways is provided in Table 6.3 in which the source of each pathway can be read from the neighboring

cell on the left. Note that, the echo during readout (G_{17}) consists of pathways 20, 28, 31, 37 and 40 as highlighted in Table 6.2. In the most known CPMG sequences such as “Rapid Acquisition with Relaxation Enhancement (RARE)” (also known as fast spin-echo (FSE) or turbo spin-echo (TSE)), the contribution of multiple pathways to the acquired signal is desirable since the signal magnitude increases [71]. However, for the case of $\varphi_{sub,z}$ measurements, it is not desirable because the phase of each echo-forming pathway is effected differently from subject eddy fields. For example, as can be followed from Table 6.3, 28th pathway has 9th and 3rd longitudinal pathways as a source in its ‘history’. Since 3rd and 9th pathways are longitudinal, subject eddy fields cannot contribute to their phases. Therefore, the overall contribution of subject eddy fields to the phase of 28th pathway is different from, for instance, 31st pathway which has only one longitudinal pathway in its history. Similar arguments can be made for other echo-forming pathways. In conclusion, an echo which consists of several pathways is of no use for $\varphi_{sub,z}$ measurements. Starting from the next paragraph, we will discuss how an echo consisting of a single pathway can be obtained.

In order to obtain a single-pathway echo in the proposed multi-spin-echo pulse sequence, crusher gradients can be used to send undesired echoes away from the readout window. For this purpose, we propose the following crusher gradient scheme to be applied in the z-axis.

$$G_{cr}^{rel}(n) = \begin{cases} 3^{\frac{(N+1)}{2}-n} & \text{when } n \text{ is odd } N \text{ is odd} \\ -3^{\frac{(N+1)}{2}-n} & \text{when } n \text{ is odd } N \text{ is odd} \\ 3^{\frac{N}{2}-n} & \text{when } n \text{ is odd } N \text{ is even} \\ -3^{\frac{N}{2}-n} & \text{when } n \text{ is even } N \text{ is even} \end{cases} \quad (6.9)$$

where $G_{cr}^{rel}(n)$ denotes the relative gradient amplitude of the two equal gradient lobes to be applied before and after the n 'th refocusing RF pulse, and N is the total number of refocusing RF pulses. The actual crusher gradient amplitude

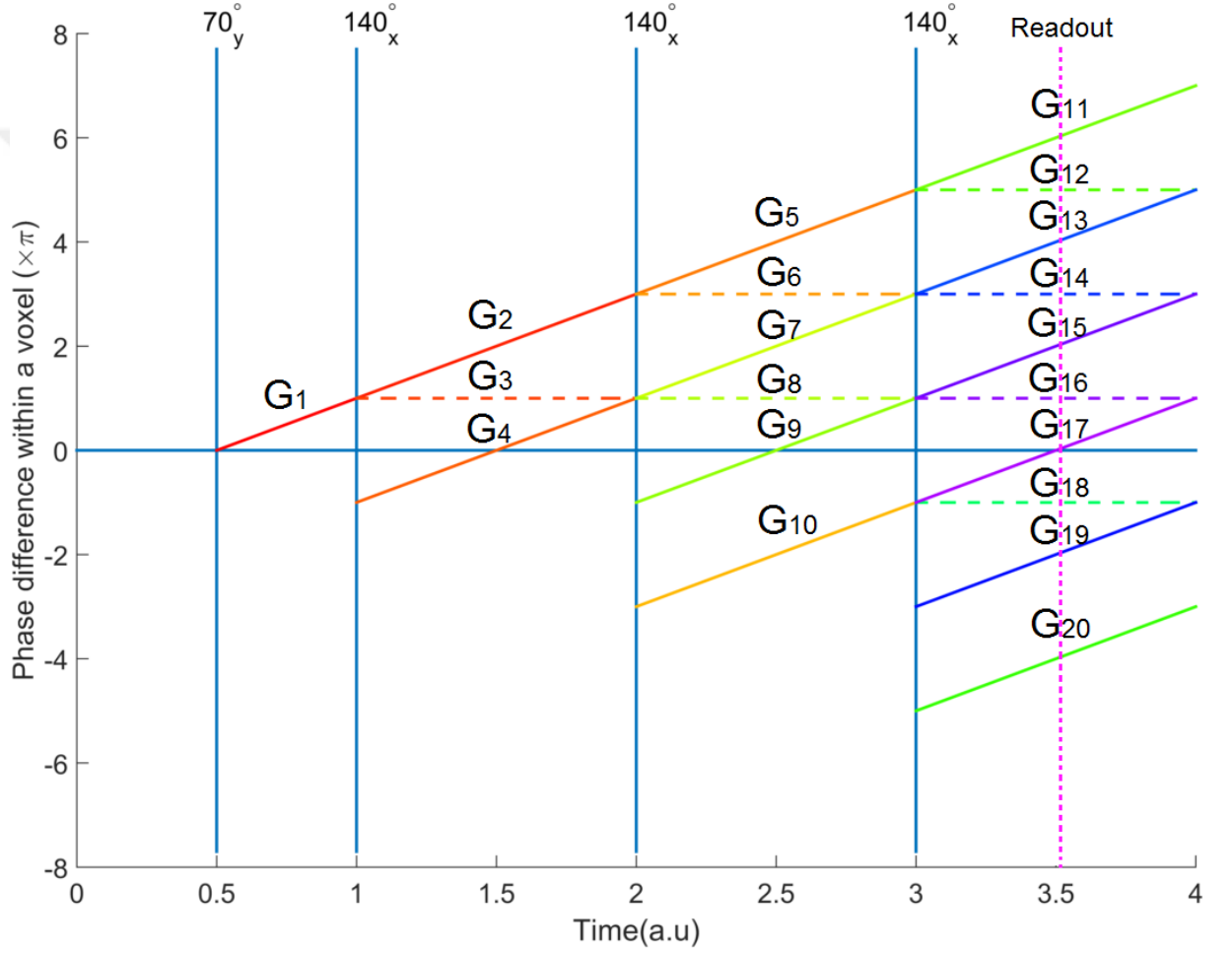


Figure 6.4: EPG for the proposed multi-spin-echo pulse sequence shown in Figure 2.1. The overlapping pathways labeled with group numbers G_1 to G_{20} (see Tables 6.2 and 6.3).

Pathway No.	Group	Magnetization	Pathway No.	Group	Magnetization
1	G_1	0.94-0.00i	22	G_{15}	0.09-0.00i
2	G_2	0.11-0.00i	26	G_{15}	0.15-0.00i
3	G_3	-0.00-0.30i	29	G_{15}	0.02+0.00i
4	G_4	0.83+0.00i	35	G_{15}	-0.17-0.00i
5	G_5	0.01-0.00i	38	G_{15}	0.09-0.00i
6	G_6	-0.00-0.04i	27	G_{16}	-0.00-0.18i
8	G_7	-0.19+0.00i	30	G_{16}	0.00-0.06i
11	G_7	0.10+0.00i	36	G_{16}	-0.00+0.20i
9	G_8	0.00+0.23i	39	G_{16}	-0.00-0.24i
12	G_8	0.00-0.27i	30	G_{16}	0.00-0.06i
10	G_9	0.19+0.00i	20	G_{17}	0.01+0.00i
13	G_9	0.73-0.00i	28	G_{17}	-0.15-0.00i
13	G_9	0.73-0.00i	31	G_{17}	0.17-0.00i
7	G_{10}	0.10+0.00i	37	G_{17}	0.17-0.00i
14	G_{11}	0.00-0.00i	40	G_{17}	0.65+0.00i
15	G_{12}	-0.00-0.00i	21	G_{18}	0.00-0.03i
17	G_{13}	-0.02+0.00i	19	G_{19}	0.02+0.00i
23	G_{13}	-0.02+0.00i	25	G_{19}	-0.17-0.00i
32	G_{13}	0.01+0.00i	34	G_{19}	0.09-0.00i
18	G_{14}	0.00+0.03i	16	G_{20}	0.01+0.00i
24	G_{14}	0.00+0.06i			
33	G_{14}	0.00-0.03i			

Table 6.2: Complex magnetizations of 40 pathways that are generated by the multi-spin-echo pulse sequence containing three refocusing RF pulses (refer to Figure 6.4).

1	2	5	14
			15
			16
		6	17
			18
			19
		7	20
	21		
	22		
	3	8	23
			24
			25
		9	26
			27
			28
		10	29
			30
			31
	4	11	32
			33
34			
12		35	
		36	
		37	
13		38	
		39	
		40	

Table 6.3: The numbering convention of the pathways in Table 6.2. The source of each pathway can be read from the neighboring cell on the left. Due to partitioning effect of RF pulses, each pathway sources three pathways which are dephasing, rephasing, and longitudinal. Cells for dephasing pathways are green, longitudinal pathways are yellow, and rephasing pathways are red.

N	G_{cr}^{rel}	G_{cr}^{act} (mT/m)
2	[1, -1]	[4.7, -4.7]
3	[3, -3, 1]	[14.1, -14.1, 4.7]
4	[3, -3, 1, -1]	[14.1, -14.1, 4.7, -4.7]
5	[9, -9, 3, -3, 1]	[42.3, -42.3, 14.1, -14.1, 4.7]
6	[9, -9, 3, -3, 1, -1]	[42.3, -42.3, 14.1, -14.1, 4.7, -4.7]
7	[27, -27, 9, -9, 3, -3, 1]	[126.8, -126.8, 42.3, -42.3, 14.1, -14.1, 4.7]
8	[27, -27, 9, -9, 3, -3, 1, -1]	[126.8, -126.8, 42.3, -42.3, 14.1, -14.1, 4.7, -4.7]
9	[81, -81, 27, -27, 9, -9, 3, -3, 1]	[380.5, -380.5, 126.8, -126.8, -42.3, 42.3, 14.1, -14.1, 4.7]

Table 6.4: The relative and actual gradient amplitudes for the proposed crusher gradient scheme which is applied in the z-axis (N : number of refocusing RF pulses, G_{cr}^{rel} : array of relative gradient amplitudes, G_{cr}^{act} : array of actual gradient amplitudes) The actual values are calculated using Equation (6.10) when $\Delta z = 5$ mm and $T_{cr} = 2$ ms. T_{cr} can be increased if one of the actual values is not implementable for the used MRI scanner.

($G_{cr}^{act}(n)$) can be calculated as [71, 74]

$$G_{cr}^{act}(n) = \frac{G_{cr}^{rel}(n)4\pi}{\gamma\Delta z T_{cr}} \quad (6.10)$$

where γ is the gyromagnetic ratio, Δz is the voxel size in the z-direction, and T_{cr} is the desired duration of a single gradient lobe. The factor of 4π comes from the fact that even the minimum crusher gradient lobe should provide at least 4π phase difference in a voxel for proper crushing [71]. The relative and actual gradient amplitudes, which are calculated using this equation when $\Delta z = 5$ mm and $T_{cr} = 2$ ms, are provided in Table 6.4. It is observed that the required gradient amplitudes are implementable with current clinical MRI scanners for up to 8 refocusing RF pulses (The value of 126.8 mT/m can be decreased by slightly increasing T_{cr}). For larger number of refocusing pulses, T_{cr} must be increased significantly to obtain implementable gradient amplitudes which, in turn, cause the spacing between refocusing RF pulses to be increased significantly and the MRI signal will decrease more due to T2-decay.

For the case when the proposed crusher gradient scheme is applied, the EPG

for the sequence shown in Figure 6.4 changes as shown in Figure 6.5. Overlapping pathways are separated and all 40 pathways are now observable in the EPG. It is observed that the degree of separation depends on how much two consecutive crusher gradient pairs are different from each other. For example, if power of 2 is used instead of power of 3 in Equation (6.9) then the pathways come closer to each other and if power of 4 is used they become more separated but it is harder to implement such high gradient amplitudes. Note that, magnetizations of the pathways do not change with the application of crusher gradients and Tables 6.2 and 6.3 are still valid. More importantly, there is now only one pathway (40th pathway) contributing to the MRI signal during readout. This pathway has the highest magnetization among the pathways generated by the last refocusing RF pulse and it is sourced by pathways which consecutively rephased by refocusing RF pulses. Indeed, as long as flip angle of the refocusing RF pulse is not significantly lower than 180° , the pathway which is formed by consecutive refocusing RF pulses has always the largest magnetization, and thus, always such pathways are chosen for $\varphi_{sub,z}$ measurements. Figures 6.6 and 6.7 show the EPG with crushers for the case when the number of refocusing RF pulses are 4 and 6 respectively. For these cases, the number of pathways are 121 and 1093 as calculated using Equation (6.8). It is observed that although the number of pathways are significantly increased, the echo at the readout still consists of a single pathway.

6.2.3 Optimum Number of Refocusing RF Pulses

As discussed in the previous section, the pathway which is formed by consecutive refocusing RF pulses is used for $\varphi_{sub,z}$ measurements. Equation (6.6) indicates that, this echo-forming pathway loses its magnetization by the ratio $\sin^2\left(\frac{\beta}{2}\right)$ every time an refocusing RF pulse is applied. Note that, in practice, the output voltage of the RF amplifier for a refocusing RF pulse is set exactly the two-times of the output voltage for the excitation RF pulse, i.e. $\beta = 2\alpha$ where α is the flip angle

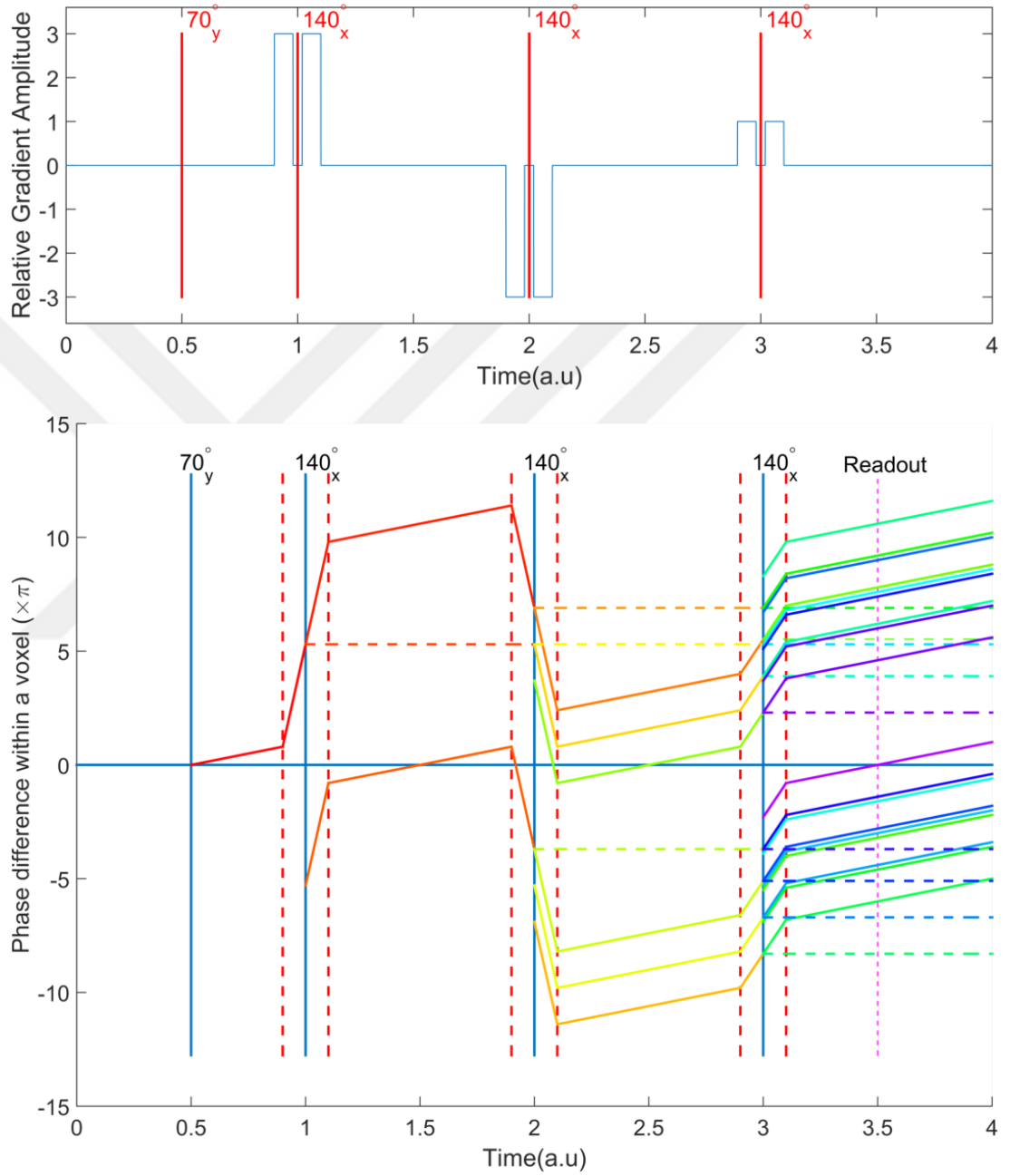


Figure 6.5: The EPG for the multi-spin-echo pulse sequence ($N = 3$) when the proposed crusher gradient scheme is used. The waveform for the crusher gradients are provided above the EPG. Pathways are separated and all 40 pathways are observable. Echo is generated by a single pathway during readout.

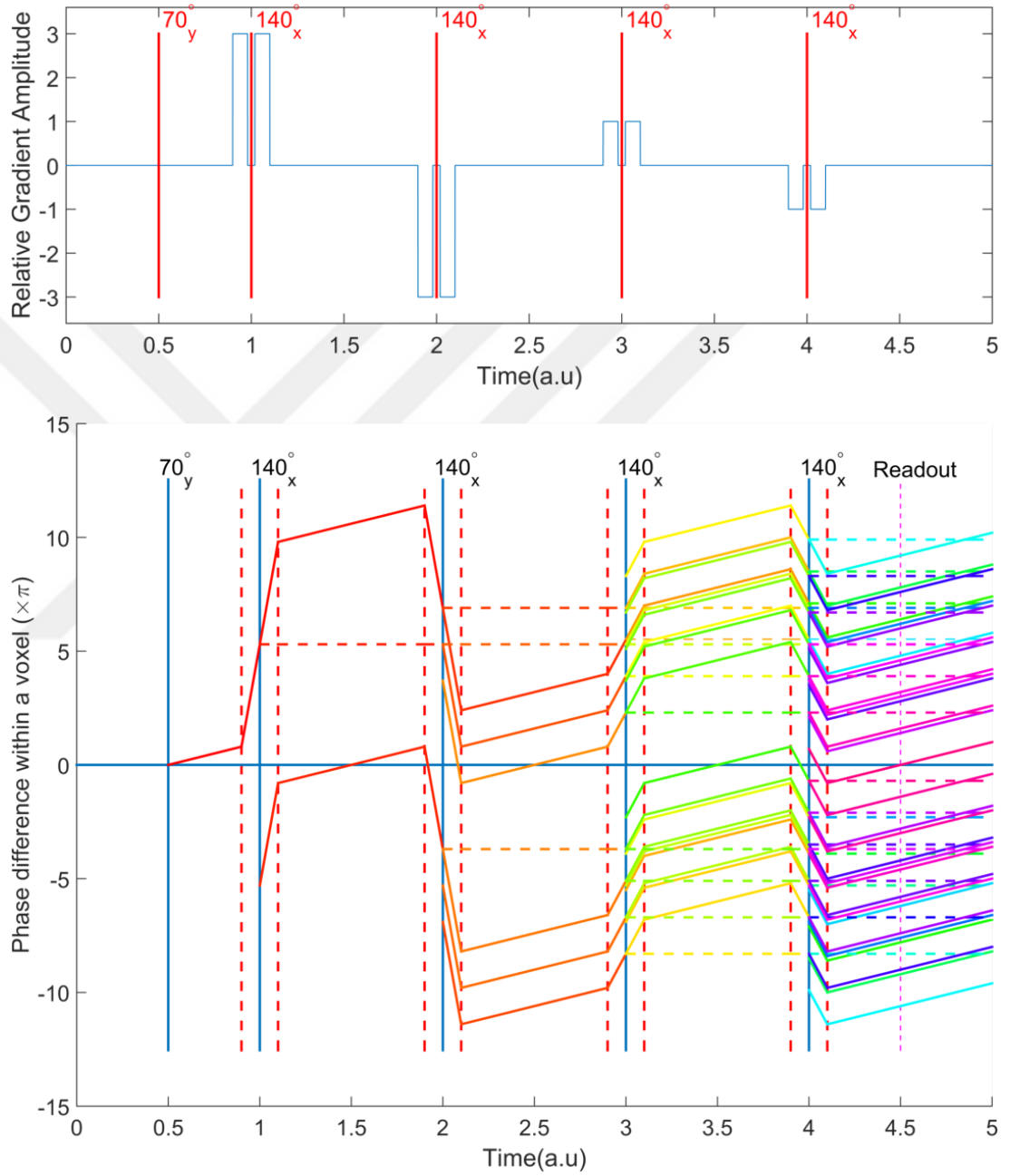


Figure 6.6: The EPG for the multi-spin-echo pulse sequence ($N = 4$) when the proposed crusher gradient scheme is used. The waveform for the crusher gradients are provided above the EPG. Although, there are total of 121 pathways, echo is still generated by a single pathway during readout.

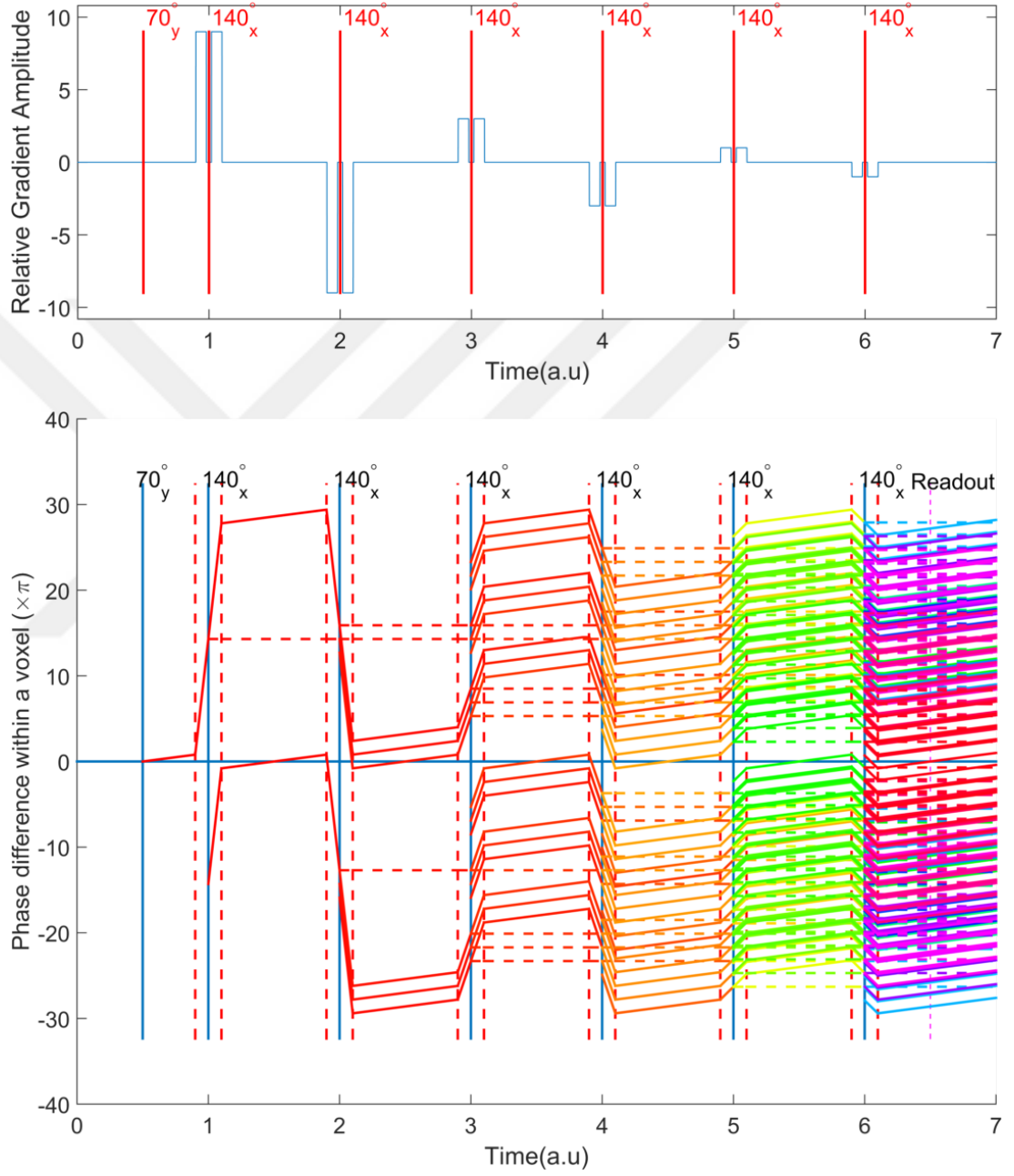


Figure 6.7: The EPG for the multi-spin-echo pulse sequence ($N = 6$) when the proposed crusher gradient scheme is used. The waveform for the crusher gradients are provided above the EPG. Although, there are total of 1093 pathways, echo is still generated by a single pathway during readout.

of the excitation RF pulse. Therefore, if a nominal 90° excitation RF pulse flips spins 75° at a region due to B1 inhomogeneity then refocusing RF pulse flips spins 150° at the same region. Consequently, we have the following relation for the MRI magnitude image that is denoted with $I(x, y)$.

$$I(x, y) \sim \sin(\beta/2)^{1+2N} \quad (6.11)$$

where N is the number of refocusing RF pulses. Furthermore, transverse relaxation (T_2) until readout also decreases $I(x, y)$ and thus we have

$$I(x, y) \sim \exp\left(-\frac{N\Delta_{rfc}}{T_2}\right) \sin(\beta/2)^{1+2N} \quad (6.12)$$

where Δ_{rfc} is the time-interval between two refocusing RF pulses. On the other hand, the accumulated $\varphi_{sub,z}$ was given by Equation (6.2) for the case of multi-spin-echo pulse sequence. The optimum number of refocusing RF pulses can be analyzed using Equations (6.11) and (6.2). As discussed at the beginning of this chapter, our purpose is to make the uncertainty of the measured $\varphi_{sub,z}$, which is denoted by $u(\varphi_{meas})$, smaller than the maximum allowed uncertainty in $\varphi_{sub,z}$, which is denoted by $u(\varphi_{sub,z})_{max}$. As discussed in Section 4.2 (see Equation (4.14)), $u(\varphi_{meas})$ is inversely proportional to the SNR of the magnitude images, and thereby it is inversely proportional to the term on the right-hand side of Equation (6.12). On the other hand, $u(\varphi_{sub,z})_{max}$ is proportional to $G_z^{exc} + 2NG_z^{rfc}$ as indicated in Equation (6.3). Consequently, the optimization problem that we need to solve is obtained as

$$\arg \max_{N \geq 1} \left[(G_z^{exc} + 2NG_z^{rfc}) \exp\left(-\frac{N\Delta_{rfc}}{T_2}\right) \sin\left(\frac{\beta}{2}\right)^{1+2N} \right] \quad (6.13)$$

The derivative of this argument can be calculated analytically and the optimum N which maximizes this argument is found as

$$N_{opt} = \frac{1}{\frac{\Delta_{rfc}}{T_2} - 2 \ln\left(\sin\left(\frac{\beta}{2}\right)\right)} - \frac{G_z^{exc}}{2G_z^{rfc}} \quad (6.14)$$

Using Equation (6.14), it is found that $N_{opt} = 8.22 \cong 8$ when $\Delta_{rfc} = 5$ ms, $T_2 = 100$ ms, $\beta = 150^\circ$, $G_z^{exc} = 15.66$ mT/m, and $G_z^{rfc} = 4.8$ mT/m. Figure

6.8 shows the argument of Equation (6.13) vs N . For a better interpretation of results, the argument is normalized by its value at $N = 1$. At the optimum N value of 8, an improvement of 3-fold is achieved. However, no significant improvement is achieved going from $N = 6$ to $N = 8$. Therefore, N can be chosen as 6 for easier implementation especially regarding the crusher gradients.

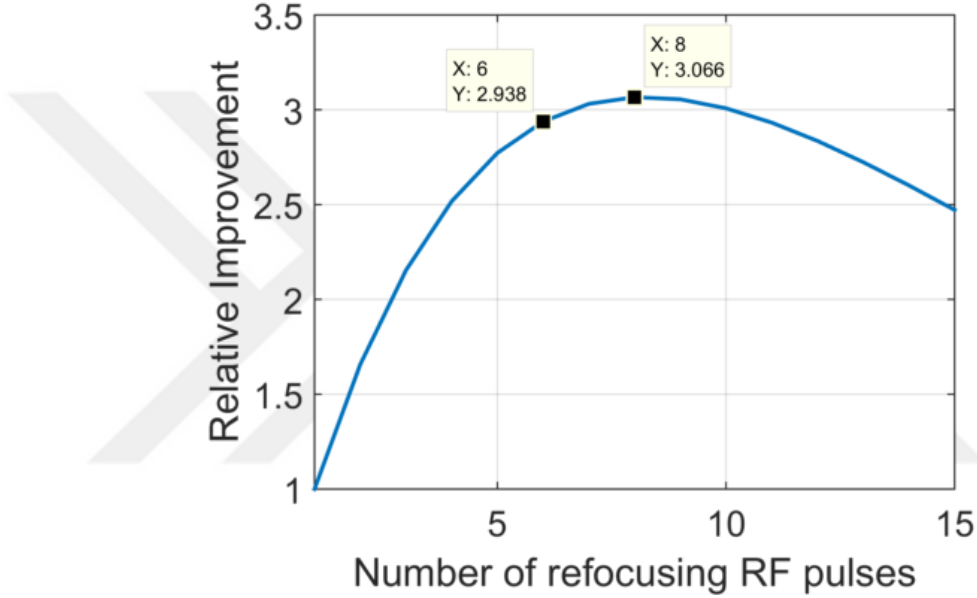


Figure 6.8: The argument of Equation (6.13) vs number of refocusing RF pulses (N). For a better interpretation of results, the argument is normalized by its value at $N = 1$. At the optimum N value of 8, an improvement of 3-fold is achieved. The improvement slightly decreases to 2.93 when $N = 6$.

In this section, a multi-spin-echo pulse sequence is proposed for measuring $\varphi_{sub,z}$ and its different aspects are analyzed. The imperfect refocusing of RF pulses causes extra pathways to be generated which distorts the $\varphi_{sub,z}$ measurements. For eliminating these extra pathways, a crusher-gradient scheme is designed. The imperfect refocusing also causes signal loss together with the transverse relaxation. Due to all these limiting factors, it is found that only 3-fold improvement is possible in $u(\varphi_{sub,z})_{max}$. In Section 6.1, it was found that, powerful gradient systems in recently developed clinical MRI scanners can provide 11-fold increase. If multi-spin-echo pulse sequence is used in such systems then

total of $11 \times 3 = 33$ -fold improvement is possible. However this improvement is still significantly smaller than the required improvement of 800-fold. On the other hand, it was argued in Section 6.1 that subject eddy current based conductivity imaging for animals or phantoms may be feasible if small-sized MRI scanners are used and if the RF leakage problem is solved. Considering these scanners, a total of $119 \times 3 = 357$ -fold improvement can be achieved if multi-spin-echo pulse sequences are used and the conductivity imaging, therefore, becomes more feasible.

6.3 Geometric Distortion Correction

In Section 5.1, it was shown that the z-component of the system eddy field due to switching of the z-gradient, which is denoted by $B_{sys,z}$, and the z-component of other undesired magnetic fields including system eddy fields due to switching of x- and y-gradients and the B0 inhomogeneity, which are denoted by $B_{other,z}$, cause geometric distortions in the MRI image such as scaling, shearing, and shifting. Including the effects of geometric distortions, the phase images was stated as

$$\varphi^+(x^+, y) = \varphi^+ \left(x + \frac{B_{other,z}(x, y)}{G_x} + \frac{B_{sys,z}(x, y)}{G_x}, y \right) \quad (6.15a)$$

$$\varphi^-(x^-, y) = \varphi^- \left(x + \frac{B_{other,z}(x, y)}{G_x} - \frac{B_{sys,z}(x, y)}{G_x}, y \right) \quad (6.15b)$$

where $\varphi^+(x^+, y)$ and $\varphi^-(x^-, y)$ are the phase images with geometric distortions, the readout direction is assumed to be the x-direction, and G_x is the readout gradient field. Since $\varphi^+(x^+, y)$ and $\varphi^-(x^-, y)$ are not aligned due to $B_{sys,z}(x, y)/G_x$ term, their difference contains bias artifacts due to the phase of the B1-field (RF phase) which would have been canceled after subtraction if geometric distortions did not exist. These artifacts were referred to as the ‘RF Leakage’. The expression for the RF leakage was indicated by Equation (2.5c) which is restated

as

$$\varphi_{meas} \cong \varphi_{sub,z}^{\sigma_0-\sigma_{low}} + 2(b_2^{\sigma=\sigma_0} - b_2^{\sigma=\sigma_{low}}) \left(x + \frac{B_{other,z}}{G_x} \right) \frac{B_{sys,z}}{G_x} \quad (6.16)$$

where the second term on the right-hand side is recognized as the RF leakage. As evident from Equations (6.15) and (6.16), the level of RF leakage depends on the extent of geometric distortions since this extent is determined by $B_{sys,z}/G_x$ and $B_{other,z}/G_x$. Therefore, the problem of RF leakage can be handled by correcting geometric distortions to the degree that the level of RF leakage becomes sufficiently low. Note that $B_{other,z}$ cause geometric distortions in the same direction for both $\varphi^+(x^+, y)$ and $\varphi^-(x^-, y)$ (see Equation (6.15)), and thus, indeed, only geometric distortions due to $B_{sys,z}$ needs to be corrected.

Some possible geometric distortion correction methods have been already proposed and thoroughly investigated in studies which aim at correcting the geometric distortions due to the switching of diffusion sensitizing gradients in the diffusion-weighted imaging [75, 61, 76, 47, 42]. However, before implementing one of these methods, one must first understand how accurate the corrections must be in order to make RF leakages sufficiently low. For instance, the RF leakage for the first experimental phantom was found to be in the level of 20×10^{-3} rad (see Figure 5.2). If $B_{other,z}/G_x$ is neglected and if $B_{sys,z}/G_x$ is assumed to be spatially constant, the RF leakage can be expressed as

$$2x (b_2^{\sigma=1.3} - b_2^{\sigma=0.2}) s_0 \quad (6.17)$$

where s_0 is the shift caused by constant $B_{sys,z}$ ($s_0 = B_{sys,z}/G_x$). Note that the RF leakage level of 20×10^{-3} rad can be reached with $s_0 \cong 0.5$ mm when x changes between -7 to 7 cm (radius of the phantom is 7 cm). Therefore, even small geometric distortions of 0.5 mm can generate RF leakages high enough to dominate $\varphi_{sub,z}$. Furthermore, the pattern of RF leakage indicates that these small distortions are not in the form of a simple shift but higher-order distortions exist, which are harder to detect. Note that the voxel size was 2x2x5 mm in the experiments, and thus it seems not possible to correct such small geometric distortions to the level that resulting RF leakage level is sufficiently low.

Chapter 7

Conclusions

The idea of imaging low-frequency conductivity of tissues by utilizing subject eddy currents has got attention of investigators since this technique eliminates the need of current injection that is impractical and that raises safety problems. In this thesis, two aspects of the feasibility of this technique are investigated. First aspect is to understand if the inverse problem of reconstructing conductivity from subject eddy fields is well-defined and solvable. For this aspect, an algorithm is developed for the solution of the inverse problem and it is shown by simulations that the algorithm is successful and the inverse problem is solvable.

The second aspect of the feasibility is the investigation of subject eddy field measurement. For measuring subject eddy fields, a novel MRI pulse sequence is developed in which the contribution of subject eddy fields to MRI phase is determined. Our criteria for feasibility is that the uncertainty of the measured contribution is smaller than the maximum uncertainty allowed for accurate conductivity reconstruction. In this manner, closed-form expressions are derived for the uncertainty of the measured contribution and the maximum allowed uncertainty. These expressions bring a measure to the fidelity by which subject eddy fields must be measured for accurately reconstructing conductivity. Furthermore,

low-pass filtering of input data and different differentiation kernels are also considered in deriving these expressions and, by this way, their effects to conductivity reconstruction is investigated by adopting a quantitative approach along with the other parameters. In the experiments that are conducted with representative objects, it is found that the uncertainty of the measured phase ($u(\varphi_{meas})$) is about three orders of magnitude larger than the uncertainty allowed for accurate conductivity reconstruction. Furthermore, $u(\varphi_{meas})$ is also found to be larger than the maximum magnitude of the expected $\varphi_{sub,z}$. In summary, the level of $u(\varphi_{meas})$ is not sufficiently low for accurate conductivity reconstruction, and it is not sufficiently low even for imaging $\varphi_{sub,z}$ itself. Indeed, in human experiments, $u(\varphi_{meas})$ will not be so different since the expected SNR is on the same order of magnitude as of the phantoms. This leads us to one of the key conclusions of this thesis that the measurement of subject eddy fields with an sufficiently low uncertainty is not feasible at least using the experimental setup we use.

Besides two mentioned aspects of the feasibility, RF leakage artifacts in the measured phase is also investigated since these artifacts must be eliminated for obtaining $\varphi_{sub,z}$ accurately. For the RF leakage artifact, a theoretical model is developed which hypothesizes that these artifacts are caused by the RF phase which could not be eliminated due to misregistration between the phase images obtained with G_z^+ and G_z^- . We were able to show through experiments that RF leakage scales with conductivity as suggested by the developed model. On the other hand, the pattern of RF leakage is hard to predict since it requires exact knowledge of B0 inhomogeneity and system eddy fields during readout. The complete verification of the RF leakage hypothesis, therefore, requires further study.

In the final part of the thesis, we have analyzed possible solutions to make the subject eddy current based conductivity imaging feasible. For increasing the span of the phase accumulated by subject eddy fields, the state-of-the-art clinical gradient systems are evaluated and it is found that these systems cannot provide

the needed increase. On the other hand, it is found that small-sized MRI scanners can provide the needed increase if the number of acquisitions and voxel size are increased. Therefore, subject eddy current based conductivity imaging for animals or phantoms may be feasible if small-sized MRI scanners are used and if the RF leakage problem is solved. As another option for increasing the accumulated phase, a multi-spin-echo pulse sequence is developed and different aspects of this pulse sequence are analyzed using the extended phase graph framework. It is found that the imperfect refocusing of RF pulses generates extra pathways which cause signal loss together with the transverse relaxation. Due to this limitation, it is found that only 3-fold improvement is possible which is not sufficient for the feasibility. The possibility of using geometric distortion correction methods for eliminating the artifacts in the measured phase is also evaluated. It is understood that even small geometric distortions (such as 0.5 mm shift) can cause RF leakages high enough to generate RF leakages higher than $\varphi_{sub,z}$. Since it is not possible to correct such small geometric distortions, the RF leakage level cannot be sufficiently lowered. In summary, although the very low span of the accumulated phase can be increased sufficiently at least using the small-sized scanners, the RF leakage problem is a lot more difficult problem to deal with.

The studies explained in Chapters 2 to 5 are published as a journal article and partly presented in the 23rd Annual Meeting of International Society for Magnetic Resonance in Medicine (ISMRM) [38, 41]. The study explained in Chapter 3 was also partly presented in 21st Annual Meeting of ISMRM and it was awarded with *Magna Cum Laude Merit Award* [33].

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