

A NOVEL HYBRID MAGNETIC PARTICLE IMAGING AND LOW-FIELD MAGNETIC RESONANCE IMAGING SCANNER

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

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ABSTRACT

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Magnetic particle imaging (MPI) is an emerging medical imaging modality, in which the spatial distribution of the magnetic nanoparticles (MNPs) are imaged using their non-linear magnetization curve. Since biological tissues do not exhibit such magnetic behavior, MNPs serve as the sole source of the MPI signal, making it a promising in vivo imaging modality with high contrast and sensitivity. However, anatomical information is also essential for many applications. To address this issue, MPI can be combined with other imaging modalities, such as computed tomography (CT) or magnetic resonance imaging (MRI), using standalone or hybrid systems. It is particularly advantageous to combine MPI with MRI, given that they are both non-ionizing imaging modalities. Moreover, since both MPI and MRI utilize magnetic fields, a hybrid system that integrates these modalities can potentially reduce costs via shared utilization of hardware. This thesis introduces a novel preclinical-size hybrid MPI and low-field (LF) MRI scanner. The proposed system features an MPI mode with a field free line (FFL) topology and a selection field gradient of 0.25 T/m, alongside a LF-MRI mode with a B_0 field strength of 50 mT. The primary advantage of this hybrid system lies in the interchangeable use of coil groups between MPI and LF-MRI modes, facilitating the generation of a multimodal image that features high sensitivity and contrast imaging of MNP distribution by MPI, alongside anatomical information from LF-MRI. Additionally, the coil configuration of this hybrid system features an open-sided design, with the exception of the Tx/Rx coil of MRI, which utilizes a solenoid design for experimental studies. This coil can be substituted with a surface coil, facilitating the development of an open-sided hybrid system. First, the feasibility of multimodal imaging with the proposed hybrid

scanner is evaluated by characterizing the magnetic fields in the system. Next, the effects of system-induced deviations on image quality are investigated via an in-house MRI simulator. The experimental imaging results demonstrate that the proposed preclinical-size hybrid MPI and LF-MRI scanner can successfully perform multimodal imaging.



Keywords: Magnetic particle imaging, magnetic resonance imaging, low field, field free line, hybrid imaging, multimodal imaging.

ÖZET

ÖZGÜN BİR HİBRİT MANYETİK PARÇACIK GÖRÜNTÜLEME VE DÜŞÜK ALANLI MANYETİK REZONANS GÖRÜNTÜLEME TARAYICISI

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Manyetik parçacık görüntüleme (MPG), manyetik nanoparçacıkların (MNP) uzamsal dağılımının doğrusal olmayan manyetizasyon eğrileri kullanılarak görüntülendiği, görece yeni bir tıbbi görüntüleme tekniğidir. Biyolojik dokular bu tür bir manyetik davranış sergilemediği için, MNP'ler MPG sinyalinin tek kaynağıdır. Bu özellik MPG'yi yüksek kontrast ve hassasiyete sahip, umut verici bir in vivo görüntüleme yöntemi haline getirmekte; ancak, birçok uygulama için gerekli olan anatomik bilginin elde edilememesine sebep olmaktadır. Bu bilgiyi elde etmek için MPG, bilgisayarlı tomografi (BT) ve manyetik rezonans görüntüleme (MRG) gibi diğer görüntüleme teknikleriyle bağımsız veya hibrit sistemler kullanarak birleştirilmektedir. Hem MPG hem de MRG'nin iyonlaştırıcı radyasyon içermeyen yöntemler olmaları, bu iki tekniğin birleştirilmesini avantajlı kılmaktadır. Ayrıca, hem MPG hem de MRG yönteminde manyetik alanların kullanılması, bu yöntemlerin entegre edildiği hibrit bir sistemdeki donanımların ortak kullanımı sayesinde, sistem maliyetini azaltma potansiyeline sahiptir. Bu çalışmada, özgün bir prelinik boyutlu hibrit MPG ve düşük alanlı (DA) MRG sistemi sunulmaktadır. Önerilen sistem, 0.25 T/m seçim alanı gradyanı ile manyetik alansız çizgi (MAÇ) topolojisine sahip MPG modunu ve 50 mT B_0 alan büyüklüğüne sahip DA-MRG modunu içermektedir. Bu sistemin başlıca avantajı, MPG ve MRG modları arasında bobin gruplarının ortak kullanımına olanak sağlamasıdır. Bu sayede, MPG modu ile MNP'lerin yüksek hassasiyet ve kontrast ile görüntülenmesine, MRG modu ile ise anatomik bilginin elde edilmesine imkan sağlamaktadır. Buna ek olarak, bu hibrit sistemin bobin konfigürasyonu, MRG deneysel çalışmaları için kullanılan solenoid şeklindeki alıcı/verici bobin

dışında, açık kenarlı bir tasarıma sahiptir. MRG alıcı/verici bobininin yüzey bobini tasarımı ile değiştirilmesi, hibrit sistemin tamamen açık kenarlı hale getirilmesini sağlayacaktır. Öncelikle önerilen sistemin hibrit görüntülemeye uygulanabilirliğini değerlendirmek amacıyla sistem karakterizasyonu yapılmıştır. Sonrasında, sistem kaynaklı problemlerin MRG görüntü kalitesi üzerindeki etkileri, geliştirilen MRG simülatörü aracılığıyla incelenmiştir. Deneysel görüntüleme sonuçları, önerilen prelinik boyutlu hibrit MPG ve DA-MRG tarayıcısının başarılı bir şekilde multimodal görüntüleme gerçekleştirebildiğini göstermektedir.

Anahtar sözcükler: Manyetik parçacık görüntüleme, manyetik rezonans görüntüleme, düşük alan, manyetik alansız çizgi, hibrit görüntüleme, multimodal görüntüleme.



To my beloved family . . .

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Chapter 1

Introduction

Medical imaging modalities play a crucial role in modern healthcare, allowing clinicians to visualize the internal structures and functions of the human body for diagnostic and therapeutic purposes. These modalities can be categorized into two main types: (1) anatomy-based imaging such as magnetic resonance imaging (MRI), computed tomography (CT), X-ray imaging, and ultrasound imaging and (2) tracer-based imaging such as positron emission tomography (PET). In anatomy-based imaging, the contrast in the images arises from the inherent properties of the human anatomy. On the other hand, tracer-based imaging utilizes an imaging tracer introduced externally into the body, which generates image contrast without background signal from the surrounding tissue. Tracer-based imaging results in higher sensitivity and improved contrast; however, it often lacks anatomical information. To address this limitation, a combined approach can be employed, integrating both tracer and anatomy-based imaging modalities. In this way, anatomical information is obtained from the anatomy-based imaging modality, while tracer-based imaging provides high contrast and sensitivity [1]. This combination enhances diagnostic capabilities by offering both detailed anatomical context and excellent imaging sensitivity and contrast.

Magnetic particle imaging (MPI) is an emerging tracer-based imaging modality that utilizes magnetic nanoparticles (MNPs) as tracers to produce images

without using ionizing radiation [2]. MPI effectively captures the concentration distribution of the MNPs based on their the non-linear magnetization response. Since biological tissues do not exhibit such magnetic behavior [3], MNPs serve as the only source of MPI signal, making it a promising in vivo imaging modality with high contrast and sensitivity. However, anatomical information via another imaging modality is needed to determine where the MNPs are relative to the human body. In many studies, MPI is combined with CT scans [4, 5, 6, 7], taking advantage of the high spatial and temporal resolution of CT. Yet, given that MPI does not use ionizing radiation, it may be preferable to combine it with another non-ionizing modality, such as MRI. Previous work has demonstrated the combination of MPI and MRI using standalone systems [8], but the fusion of images from separate MPI and MRI systems may not be a preferred solution in practice due to patient movement-related artifacts in the overlaid images [9].

Hybrid MPI-MRI systems have been developed to address these challenges. The first design for a hybrid MPI-MRI scanner that allows sequential data acquisition was introduced in 2013 [10, 11]. A subsequent study has detailed the system’s design, implementation, and characterization, showcasing a selection field gradient of 2.2 T/m for MPI in a field free point topology, and a B_0 field of up to 0.5 T for MRI [12]. In this system, a dual-mode coil was employed to generate B_0 field of the MRI, while applying the selection field for MPI, with additional coil groups dedicated to each modality. The performance of the system was analyzed through experimental 3D hybrid phantom studies.

Another hybrid MPI-MRI system integrates traveling wave MPI (TWMPI) with a 4 T/m magnetic field gradient and pre-polarized low-field (LF) MRI [13]. For the LF-MRI, a 30 mT pre-polarizing pulse is applied before scanning, while a B_0 field of 1.1 mT is used during the scan. In this hybrid system, a common receive coil is used for both modalities, while other components are allocated specifically for each modality. Later, enhancements to the system were introduced, employing a dynamic linear gradient array (dLGA) for the TWMPI in dual mode to generate a B_0 field of 235 mT for the MRI mode [14]. The performance of this improved system was assessed through 2D TWMPI and 1D MRI experiments on a hybrid phantom.

These previously proposed hybrid systems employed close-bore configurations, which provide high magnetic field efficiency, but may restrict patient access and cause discomfort such as claustrophobia. Additionally, in these systems, the coil group responsible for generating the gradient fields for MRI is dedicated exclusively to MRI usage.

Recently, an open-sided MPI scanner capable of electronically scanning a field-free-line (FFL) was proposed [15]. The performance of the prototype system was analyzed via both simulations [16, 17] and experiments [18]. In this thesis study, we present a novel preclinical-size hybrid MPI and LF-MRI scanner, based on the aforementioned prototype system which features an MPI mode with FFL topology and a selection field gradient of 0.25 T/m, alongside a low-field MRI mode with a B_0 field strength of 50 mT. The coil groups of the system are utilized interchangeably for both MPI and LF-MRI data acquisition. Only the transmit/receive (Tx/Rx) coil of MRI and the receive coil of MPI are dedicated to their respective modalities. Additionally, the coil configuration of the system follows an open-sided design, except for the Tx/Rx coil of the LF-MRI mode, where a solenoid coil is utilized for experimental studies. This coil can be replaced with a surface coil [19], enabling the development of an open-sided hybrid system.

This thesis is organized into six chapters. Chapter 2 presents the fundamentals of MRI and MPI imaging modalities and includes a brief introduction to LF-MRI. In Chapter 3, the prototype system is characterized to assess its suitability for performing LF-MRI. Chapter 4 demonstrates, through a proof-of-concept simulation study of the prototype system, that it can successfully conduct MPI and LF-MRI with the appropriate selection of B_0 field strength and pulse sequence parameters. Chapter 5 analyzes the imaging performance of the prototype hybrid system through experimental studies, demonstrating its capability to perform multimodal imaging with MPI and LF-MRI modes.

Chapter 2

Background

2.1 Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) is a non-invasive medical imaging modality that employs magnetic fields and radiofrequency (RF) pulses to produce high-resolution images of soft tissues, organs, and various anatomical features without exposing patients to ionizing radiation. MRI enables the visualization of tissues containing MRI-active atoms by generating signals in response to externally applied magnetic fields. A key characteristic of these atoms is their nuclear spin angular momentum, which can be conceptualized as electrically charged spheres rotating around their axes; this is why they are also referred to as spins. The movement of electrical charge associated with each spin creates a magnetic moment, and the magnetic moments for an ensemble of spins form a magnetization. Through the interaction of this magnetization with externally applied magnetic fields, MRI signal is obtained. Hydrogen atoms are commonly used as MRI-active species due to their abundance in the human body and high gyromagnetic ratio.

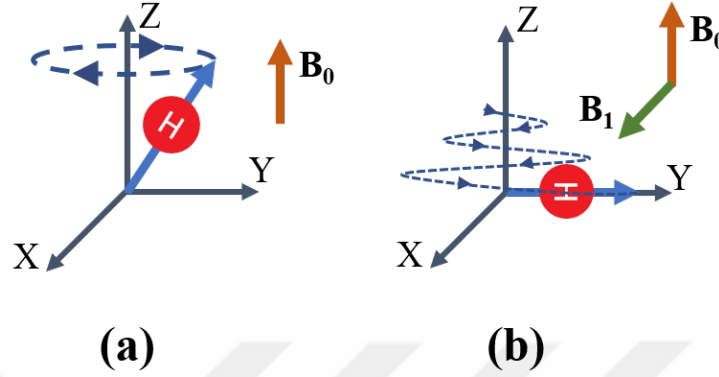


Figure 2.1: (a) Precessional motion of the spins in the presence of B_0 field. (b) The magnetization is rotated into the transverse plane due to the applied RF field.

2.1.1 Magnetic Fields in MRI

2.1.1.1 B_0 Field

The magnetic moments of hydrogen atoms within the body are randomly oriented, which prevents the formation of net magnetization. For these magnetic moments to align in a specific direction and produce net magnetization, they must be placed within a strong static field, known in MRI as the main static field or B_0 field. By convention, the direction of the B_0 field is the z -direction, referred to as the longitudinal direction. As the magnitude of the B_0 field increases, the resultant net magnetization also increases, contributing to a stronger MRI signal. The B_0 field not only aligns the spins in the same direction but also induces precessional (oscillatory) motion, as illustrated in Fig. 2.1(a). This precessional movement occurs at the Larmor frequency, which varies based on the gyromagnetic ratio specific to each spin and the magnitude of the B_0 field.

$$\omega_0 = \gamma B_0, \quad (2.1)$$

where ω_0 is the Larmor frequency and γ is the gyromagnetic ratio, which is equal to $\gamma/(2\pi) = 42.58 \text{ MHz/T}$ for Hydrogen spins. For example, for 3 T MRI systems, $f_0 = \omega_0/(2\pi) = 127.74 \text{ MHz}$.

The synchronized precession of the spins at the same frequency is crucial for exciting the spins and acquiring spatial information in MRI, as will be discussed in subsequent sections. Therefore, the B_0 field must be highly homogeneous.

2.1.1.2 RF Field

To obtain an MRI signal from spins aligned in the same direction as the B_0 field (i.e., the z -direction), the magnetization created by these spins must be rotated into the xy -plane (i.e., the transverse plane). This rotation is achieved by applying an RF pulse, also known as B_1 field, at the Larmor frequency ω_0 in the xy -plane (see Fig. 2.1(b)). The duration and amplitude of the applied RF pulse determine the rotation angle, α , as follows:

$$\alpha = \gamma \int_0^{\tau_p} B_1^e(\tau) d\tau, \quad (2.2)$$

where $B_1^e(t)$ and τ_p denotes the envelope and the duration of the RF pulse, respectively.

The spins flipped to the xy -plane induce a voltage on the receiver coil due to Faraday's law of electromagnetic induction on an RF coil sensitive to the xy -plane, forming the MRI signal. The magnitude of the signal decays exponentially because the spins start to realign with the B_0 field, a phenomenon known as relaxation. As a result, this MRI signal is referred to as Free Induction Decay (FID). During this relaxation process, spins gain longitudinal magnetization in the z -direction with a time constant T_1 , called the longitudinal relaxation time. At the same time, they lose their transverse magnetization in the xy -plane with a time constant T_2 , called the transverse relaxation time. These time constants, along with the density of spins, differ from tissue to tissue and are the fundamental sources of contrast in MRI images.

2.1.1.3 Gradient Fields

Using the B_0 and B_1 fields mentioned previously, the spins generate an MRI signal, enabling us to determine the presence of a specific nuclei. However, to generate an image, spatial information is also required, which is obtained through the usage of gradient fields (see Fig. 2.2).

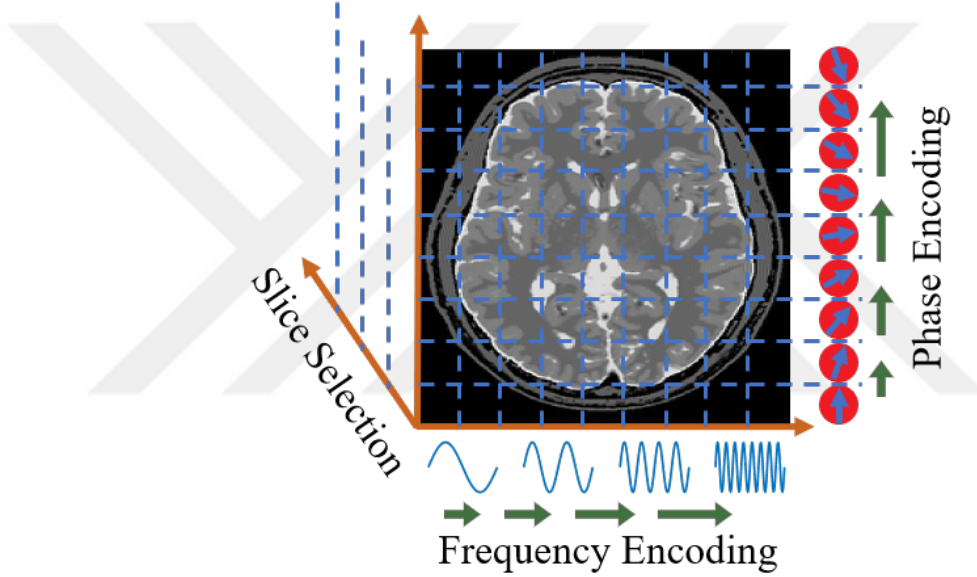


Figure 2.2: Gradient fields are applied in three dimensions. The magnetic field vectors for all three cases are aligned in the longitudinal direction (z -direction), with spatial gradients in the x -, y -, and z - directions. The gradient field in the z -direction functions as the slice selection gradient, whereas the other two are used for in-plane spatial encoding.

In MRI, images are formed by selecting a slice of specific thickness in the z -direction. This slice selection process involves applying a gradient field G_z in the same direction, causing the frequency of the spins to vary linearly along that axis. When an RF pulse with the same frequency as the spins in the selected slice is applied, only those spins are excited, resulting in an MRI signal that originates solely from that slice. Under the assumption of a small tip-angle excitation, the relationship between the applied RF pulse and slice profile can be expressed using

via 1D Fourier transform as follows [20]:

$$M_{xy}(z) = i\gamma M_0 F_{1D} \left\{ B_1^e(t + \frac{\tau_p}{2}) \right\} \Big|_{f=-\frac{\gamma}{2\pi} G_z z} \quad (2.3)$$

where M_0 denotes the equilibrium magnetization in the longitudinal direction achieved through the applied B_0 field. In addition, $M_{xy} = M_x + iM_y$ is the complex representation of the transverse magnetization (in this case, right after the RF pulse and the subsequent refocusing gradient). Here, $M_{xy}(z)$ can be interpreted as the slice profile.

Spatial information for the spins within the slice in the xy -plane is encoded through the application of gradient fields in those directions. Before the MRI signal is collected, a gradient field applied in the y -direction, G_y , causes the spins to have different phases. This process of encoding the y -position of the spin into its phase is called phase encoding. The gradient field applied in the x -direction, G_x , is applied during data acquisition to ensure that the spins possess different frequencies or rotation. This process of encoding the x -position of the spin into its frequency is called frequency encoding. As a result, the phase and frequency values of the spins contain their position information. In other words, spatial information is encoded in the phase and frequency of the spins.

2.1.2 Signal Model of MRI

The derivations for the MRI signal model are adapted from [20] and repeated here for completeness. To accurately represent the MRI signal, it is essential to model the dynamics of the magnetization vector ($\mathbf{M}$). The behavior of $\mathbf{M}$ under an externally applied magnetic field is described using the Bloch equations, given as follows:

$$\frac{d\mathbf{M}}{dt} = \mathbf{M} \times \gamma \mathbf{B} - \frac{M_x \mathbf{i} + M_y \mathbf{j}}{T_2} + \frac{(M_z - M_0) \mathbf{k}}{T_1}, \quad (2.4)$$

where $\mathbf{i}$, $\mathbf{j}$, and $\mathbf{k}$ are the unit vectors in the x -, y -, and z -directions, respectively, and M_x , M_y , and M_z are the components of $\mathbf{M}$ in x -, y -, and z -directions, respectively. In addition, $\mathbf{B}$ is the vector of the total externally applied magnetic field (i.e., the vector sum of B_0 , RF, and gradient fields).

By solving Equation (2.4) equation, we can understand the behavior of the magnetization vector. Following an RF excitation, this equation can be solved separately for the longitudinal (M_z) and transverse ($M_{xy} = M_x + iM_y$) components of the $\mathbf{M}$ vector, yielding the following solutions:

$$M_z(t) = (M_z(0) - M_0) e^{-t/T_1} + M_0 \quad (2.5)$$

$$M_{xy}(t) = M_{xy}(0) e^{-t/T_2} e^{-i\omega_0 t} e^{-i \int_0^t \gamma \Delta B(\tau) d\tau} \quad (2.6)$$

Here, $t = 0$ indicates the time point right after RF excitation and $\Delta B(t)$ is the applied magnetic fields apart from the B_0 field. If we consider the applied gradient fields, we can define it as $\Delta B(t) = G_x(t)x + G_y(t)y$. Therefore, Equation (2.6) can be rewritten as:

$$M_{xy}(t) = M_{xy}(0) e^{-t/T_2} e^{-i\omega_0 t} e^{-i \int_0^t \gamma (G_x(\tau)x + G_y(\tau)y) d\tau} \quad (2.7)$$

The received signal is generated from the contributions of all precessing transverse magnetizations within the volume, so it can be modeled as follows:

$$s_r(t) = \iiint_V M_{xy}(x, y, z, t) dx dy dz \quad (2.8)$$

Combining Equations (2.7) and (2.8) gives us

$$s_r(t) = \iiint_V M_{xy}(x, y, z, 0) e^{-t/T_2(x,y,z)} e^{-i\omega_0 t} e^{-i \int_0^t \gamma (G_x(\tau)x + G_y(\tau)y) d\tau} dx dy dz \quad (2.9)$$

For the selected slice of thickness Δz centered at z_0 , we can define the object to be imaged as

$$m(x, y) = \int_{z_0 - \Delta z/2}^{z_0 + \Delta z/2} M_{xy}(x, y, z, 0) e^{-t/T_2(x,y,z)} dz \quad (2.10)$$

$$\cong M_{xy}(x, y, z_0) e^{-t/T_2(x,y,z_0)} \Delta z \quad (2.11)$$

Here, the latter approximation is performed assuming a sufficiently thin slice. Thus, Equation (2.9) can be rewritten as:

$$s_r(t) = \iint m(x, y) e^{-i\omega_0 t} e^{-i \int_0^t \gamma (G_x(\tau)x + G_y(\tau)y) d\tau} dx dy \quad (2.12)$$

This acquired signal is then demodulated at a frequency of ω_0 , which yields:

$$s(t) = \iint m(x, y) e^{-ix\gamma \int_0^t G_x(\tau) d\tau} e^{-iy\gamma \int_0^t G_y(\tau) d\tau} dx dy \quad (2.13)$$

Rewriting this equation as follows gives us the MRI signal model, where the MRI signal is equal to the 2D Fourier transform of the object to be imaged:

$$s(t) = \iint m(x, y) e^{-i2\pi(k_x x + k_y y)} dx dy \quad (2.14)$$

where

$$k_x = \frac{\gamma}{2\pi} \int_0^t G_x(\tau) d\tau \quad (2.15)$$

$$k_y = \frac{\gamma}{2\pi} \int_0^t G_y(\tau) d\tau \quad (2.16)$$

In MRI, the Fourier domain is referred to as the k-space.

As Equation (2.14) indicates, the acquired signal directly corresponds to the k-space information of the object to be imaged. The relevant element of the two-dimensional matrix representing the frequency space is calculated based on the applied gradient field magnitude and duration. Once all elements of the matrix have been computed, an inverse two-dimensional Fourier transform can be performed to reconstruct the image. The relationship between the image domain parameters and k-space coverage is as follows:

$$FOV_x = \frac{1}{\Delta k_x} \quad , \quad FOV_y = \frac{1}{\Delta k_y} \quad (2.17)$$

$$\delta_x = \frac{1}{W_{k_x}} \quad , \quad \delta_y = \frac{1}{W_{k_y}} \quad (2.18)$$

where FOV_x and FOV_y are the field-of-view (FOV), and δ_x and δ_y are the spatial resolution in x - and y -directions, respectively. In addition, Δk_x and Δk_y are the sampling distances, and W_{k_x} and W_{k_y} are the maximum extent of the k-space along k_x -axis and k_y -axis, respectively.

2.1.3 Pulse Sequence

An MRI pulse sequence refers to a series of programmed RF pulses, gradient fields, and data acquisition windows. By varying the timing, amplitude, and

orientation of the RF pulses and gradients, different imaging contrasts and tissue characteristics can be emphasized. Additionally, modifying the pulse sequence parameters can enhance robustness against certain artifacts. A variety of pulse sequences are employed in MRI. The two most commonly used pulse sequences are described below.

2.1.3.1 Gradient Echo (GRE) Pulse Sequence

The gradient echo (GRE) pulse sequence is a widely used MRI pulse sequence that utilizes magnetic field gradients to generate echoes, allowing for rapid imaging of tissues. The gradient field causes the spins to experience different precessional frequencies based on their position in the magnetic field. Over time, as the spins dephase due to these differences, a second gradient field (usually a reversal of the initial gradient field) is applied to rephase the spins back to a coherent state. This rephasing forms an echo called gradient echo at the echo time, TE. During the echo, the signal is recorded. It should be noted that the gradient echo amplitude decays with T_2^* relaxation, which accounts for both T_2 decay and dephasing effects due to magnetic susceptibility differences. The timing diagram of the GRE sequence is given in Fig. 2.3.

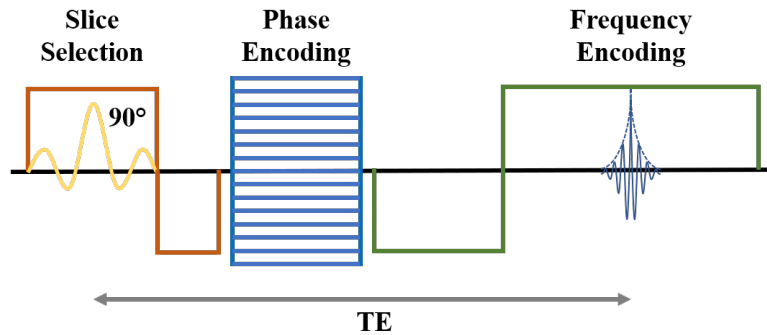


Figure 2.3: Timing diagram of the gradient echo (GRE) pulse sequence. In this example, the k-space is acquired in a line-by-line fashion.

2.1.3.2 Spin Echo (SE) Pulse Sequence

The spin echo (SE) pulse sequence is a fundamental MRI technique. The SE sequence begins with a 90° RF excitation pulse. After this pulse, the spins start to dephase, which means that the magnetic moments lose coherence over time due to inhomogeneities in the magnetic field and variations in their local magnetic environments. This dephasing process causes the signal to decay over time. To recover the loss of signal resulting from dephasing, a 180° RF pulse, called a refocusing pulse, is applied. This refocusing pulse effectively reverses the phase of the spins, allowing them to regain coherence, thereby producing an echo called a spin echo at TE. The use of the 180° RF pulse helps compensate for dephasing due to magnetic field inhomogeneities, making the spin echo sequence less susceptible to dephasing artifacts compared to the GRE sequence. Thus, the spin echo amplitude decays with T_2 relaxation instead of T_2^* relaxation. The timing diagram of the SE sequence is given in Fig. 2.4.

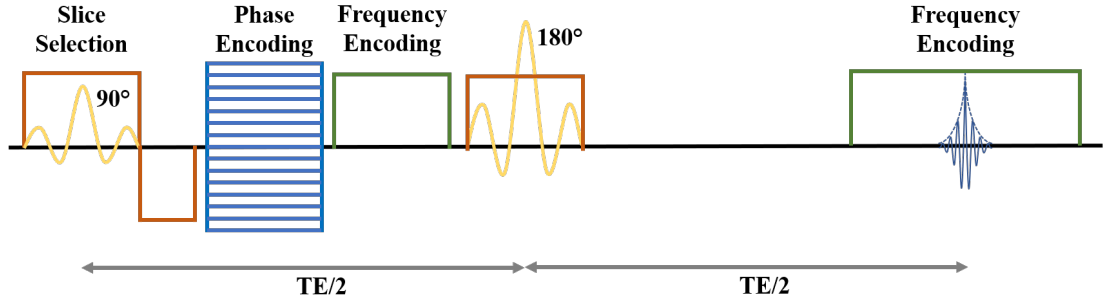


Figure 2.4: Timing diagram of the spin echo (SE) pulse sequence. In this example, the k-space is acquired in a line-by-line fashion.

2.2 Low-Field MRI (LF-MRI)

Although early MRI scanners employed lower B_0 field strengths such as 0.35 T and lower [21], advancements in MRI technology have led to a significant shift toward higher magnetic field strengths, aimed at enhancing signal quality and reducing scan times [22]. However, these benefits are countered by increased

installation and operational costs, which limit worldwide accessibility of the MRI technology. Additionally, high-field MRI scanners require specialized facilities, such as shielded rooms and cooling systems, which restrict their mobility.

Furthermore, studies indicate that imaging performance is influenced by factors beyond just B_0 field strength. For instance, a comparison of reconstructed brain images obtained from 1.5 T MRI scans in 1980 versus 2020 reveals that recent advancements in MRI technology have significantly improved the image quality, irrespective of B_0 field strength [23].

Considering the aforementioned factors, low-field MRI (LF-MRI) has attracted considerable interest in the recent years, as a means to make MRI more accessible and portable while achieving acceptable image quality.

2.2.1 Signal-to-Noise Ratio (SNR) in LF-MRI

The signal-to-noise ratio (SNR) is a fundamental measure of MRI image quality. In this section, the relationship between SNR and B_0 field strength is adapted from [20] and repeated here for completeness. The SNR in MRI can be defined as:

$$SNR = \frac{S}{\sigma}, \quad (2.19)$$

where S is the signal amplitude and σ is the standard deviation of noise, and both of these parameters depend on the B_0 field strength.

The signal amplitude is directly proportional to Larmor frequency and the equilibrium magnetization, which is given as

$$M_0 = \frac{N\gamma^2\hbar^2 I(I+1)B_0}{3k_B T} \quad (2.20)$$

Here, N is the number of nuclear spins per unit volume, $\hbar = h/(2\pi)$ is the reduced Planck's constant, and I is the spin operator in quantum mechanics. Equations (2.1) and (2.20) show that both the Larmor frequency and M_0 are directly proportional to B_0 . Therefore, the signal amplitude S is proportional to B_0^2 .

The Johnson noise is the dominant noise source in the MRI signal, with two contributors: sample (body) and coil resistance. The body resistance noise power is proportional to ω_0^2 (and hence to B_0^2), while the coil resistance noise power is proportional to $\omega_0^{1/2}$ (and hence to $B_0^{1/2}$). In the case of B_0 field strength higher than 1 T, the noise due to body resistance dominates [24]. Therefore, for the high-field MRI regime,

$$SNR_{high\ field} \propto \frac{B_0^2}{\sqrt{B_0^2}} = B_0 \quad (2.21)$$

For B_0 field strength lower than 0.1 T, the noise due to coil resistance dominates [24]. Therefore, for the low-field MRI regime,

$$SNR_{low\ field} \propto \frac{B_0^2}{\sqrt{B_0^{1/2}}} = B_0^{7/4} \quad (2.22)$$

Between 0.1–1 T, body and coil resistance are at a comparable level [24]. Note that, although the relationship between SNR and B_0 field strength can be summarized as in Equations (2.21) and (2.22), the actual SNR during imaging is influenced by the B_0 field strength in a complex manner due to the impact of other factors, such as relaxation time constants, which also depend on B_0 field strength.

2.2.2 Relaxation Time Constants in LF-MRI

In MRI, T_1 and T_2 time constants describe the relaxation processes of nuclear spins after they have been tilted by an RF pulse. These relaxation times are crucial for understanding how different tissues respond to MRI and directly impact image contrast. The relaxation time constants are also influenced by the B_0 field strength: the longitudinal relaxation time (T_1) increases with the B_0 field strength, whereas the apparent transverse relaxation time (T_2^*) decreases with B_0 [25]. In LF-MRI, the decrease in T_1 provides higher contrast in T_1 -weighted images and allows shorter scan times for T_2 -weighted images, while the increase in T_2 is advantageous in terms of SNR [21].

2.2.3 Specific Absorption Rate (SAR) in LF-MRI

Specific absorption rate (SAR) is a critical parameter in MRI that quantifies the rate at which energy is absorbed by a unit mass of tissue when exposed to RF fields. It is particularly relevant in ensuring patient safety during MRI procedures, as it helps to assess the thermal effects of RF energy on biological tissues. The relationship between SAR and B_0 field strength is as follow [24]:

$$SAR \propto \omega_0^2 \propto B_0^2 \quad (2.23)$$

Therefore, the SAR values in low-field MRI are significantly lower than those in high-field MRI, reducing the risk of tissue heating.

2.2.4 Off-resonance Effects in Low-Field MRI

In the context of LF-MRI, the restrictions related to magnetic field inhomogeneity are relaxed compared to conventional MRI systems. This is primarily due to the lower Larmor frequency associated with the diminished B_0 field strength. As the Larmor frequency decreases, the phase accumulation of spins due to off-resonance effects also becomes less pronounced, even when subjected to the same level of inhomogeneity. Consequently, this reduction in phase accumulation allows for greater tolerance of B_0 field variations. For example, it was shown that MRI images can be obtained successfully for an inhomogeneity level of up to 2400 ppm for a B_0 field strength of 50.4 mT [26].

The displacement in the frequency encoding direction due to off-resonance effects can be expressed as follows [20]:

$$\Delta x = \frac{\Delta\omega}{\gamma G_x} \quad (2.24)$$

where Δx represents the displacement in the frequency encoding direction, and $\Delta\omega$ denotes the off-resonance frequency. In addition, G_x is the amplitude of the readout gradient, which is assumed to remain constant during the data acquisition and can be written as:

$$G_x = \frac{2\pi BW}{\gamma FOV_x} \quad (2.25)$$

where BW indicates the readout bandwidth. Combining Equations (2.24) and (2.25) yields

$$\Delta x = \frac{FOV_x \Delta \omega}{2\pi BW} = \frac{FOV_x \Delta f}{BW} \quad (2.26)$$

Here, $\Delta f = \Delta \omega / (2\pi)$ is the off-resonance frequency in Hz. We can observe that a higher readout bandwidth results in lower distortion along the readout direction, since faster data acquisition reduces phase accumulation between successive data points along the k_x -direction.

2.3 Magnetic Particle Imaging (MPI)

Magnetic particle imaging (MPI) is a relatively new imaging modality, in which the spatial distribution of magnetic nanoparticles (MNPs) is imaged with high sensitivity and contrast [2].

2.3.1 MPI Signal Equation

The MPI signal is based on the highly nonlinear magnetization response of superparamagnetic iron oxide nanoparticles (SPIONs), which can be modeled using the Langevin function [27]:

$$s(t) = -\frac{\partial}{\partial t} \mu_0 m \int_V c(\mathbf{r}) \mathcal{L}(\beta |\mathbf{H}(\mathbf{r}, t)|) \frac{\mathbf{H}(\mathbf{r}, t)}{|\mathbf{H}(\mathbf{r}, t)|} \cdot \mathbf{p}(\mathbf{r}) dV \quad (2.27)$$

where $\mathbf{r}$ is the position vector, μ_0 is free space magnetic permeability, $c(\mathbf{r})$ is the concentration distribution of the SPIONs, $\mathcal{L}(\cdot)$ is the Langevin function, $\mathbf{H}(\mathbf{r}, t)$ is the total applied magnetic field, $\mathbf{p}(\mathbf{r})$ is the receive coil sensitivity. In addition, $m = M_{sat} V$, where M_{sat} is the saturation magnetization and V is the volume of the particle, and $\beta = m\mu_0 / k_B T$, where k_B is the Boltzmann's constant and T is particle temperature.

2.3.2 Magnetic Fields in MPI

2.3.2.1 Drive Field

To obtain the MPI signal experimentally, a time-varying homogeneous magnetic field, referred to as the drive field, is applied to the region of interest (ROI), while the received signal is simultaneously captured. If MNPs are not present in the ROI, the receive coil captures only the direct feedthrough signal from the drive field, resulting in a pure sinusoidal signal. However, when MNPs are present in the ROI, the received signal also includes contributions from the MNPs, characterized by the presence of higher harmonics due to the nonlinear magnetization response of MNPs. Since almost all human tissues are diamagnetic [3], they cannot produce MPI signals, making MPI a promising in vivo imaging modality with high contrast and sensitivity.

By analyzing the received signal, we can determine whether MNPs are present in the region of interest (ROI). However, to create an accurate image, spatial information about the distribution of MNPs within the ROI is also necessary, which can be obtained by applying the selection and focus fields of MPI.

2.3.2.2 Selection Field

Selection field is a static inhomogeneous magnetic field that includes a region where the magnetic field is zero, called as the field free region (FFR). The MNPs within the FFR can respond to the drive field and generate signal since their magnetization is still in the dynamic region of the magnetization curve. In contrast, the magnetization of the MNPs outside the FFR are saturated, so they cannot respond to the drive field and contribute to the signal (see Fig. 2.5). By scanning the position of the FFR within the ROI, MPI images can be obtained.

As in the first MPI scanner in the literature [2], when the shape of the FFR is a point, it is called a field free point (FFP). Imaging using FFP enables 3D

imaging with 3D resolution. For improved sensitivity, the volume of the FFP can be enlarged to increase the number of responsive particles. For example, the FFR can be made in the shape of a line called a field free line (FFL) [28]. FFL scanners exhibit higher sensitivity than FFP scanners [28, 29], and they are well-suited for the larger imaging volumes necessary for clinical applications. One downside to imaging using an FFL scanner is that it provides projection format images (i.e., 2D resolution only).

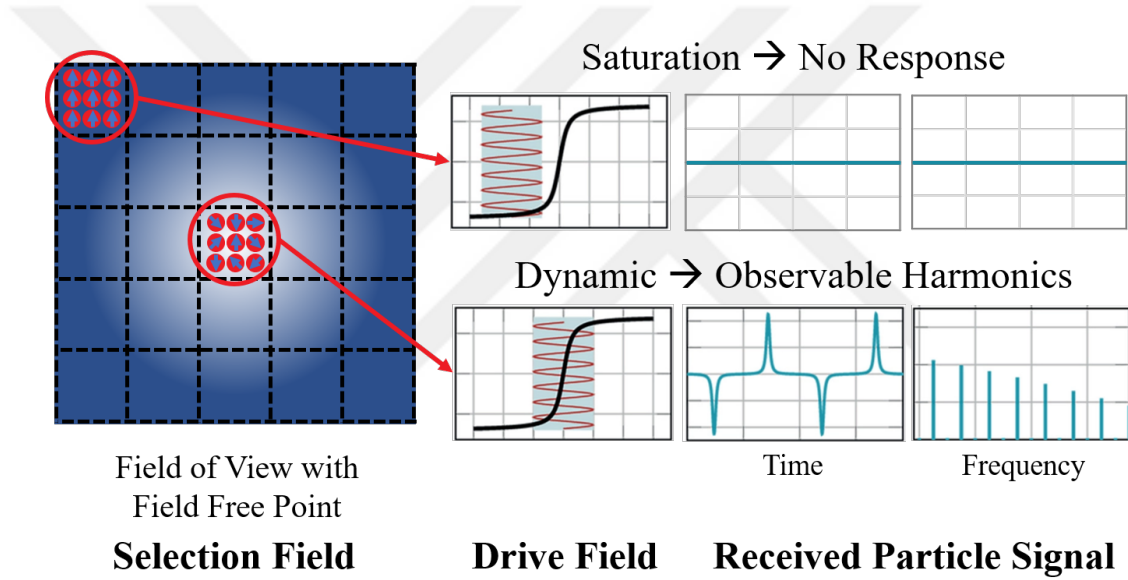


Figure 2.5: SPIONs are positioned within an FOV where a selection field with an FFP is applied. The SPIONs outside the FFP become saturated due to the selection field, preventing them from contributing to the MPI signal. In contrast, SPIONs within the FFP can respond to the drive field and generate a detectable particle signal. This response indicates the presence of SPIONs inside the FFP. By scanning the FFP throughout the FOV, an MPI image can be produced.

2.3.2.3 Focus Field

The application of the drive field serves not only to provide excitation but also to facilitate the movement of the FFR. However, hardware limitations, as well as SAR and peripheral nerve stimulation (PNS) limits, restrict the amplitude of the

drive field, allowing only a few centimeters to be scanned [27, 30]. To address this limitation, a time-varying homogeneous magnetic field called focus field has been introduced. Because the frequency of the focus field is much lower than that of the drive field, it can accommodate larger magnetic fields and enlarge the FOV, without causing safety issues.

2.3.3 Image Reconstruction in MPI

In MPI, two different techniques are commonly used for image reconstruction: X-space reconstruction and system matrix reconstruction. For a detailed explanation of X-Space reconstruction method, interested readers may refer to [27]. In this thesis study, the system matrix reconstruction technique is employed.

2.3.3.1 System Matrix Reconstruction Method

In the system matrix reconstruction technique, the system is first characterized by creating a system matrix via a calibration process. For the generation of the system matrix, a three-dimensional system matrix phantom is used. This phantom typically has the same shape as a single voxel of the image. This calibration phantom is positioned at a voxel within the imaging field-of-view (FOV), and the collected MPI signal is placed in the corresponding column of the system matrix. This process is repeated for each voxel in the FOV, one by one. Then, the MPI signal for actual object to be imaged is acquired and the MNP distribution that caused the received MPI signal is determined using inverse problem techniques:

$$\mathbf{A} \mathbf{x} + \mathbf{n} = \mathbf{b}, \quad (2.28)$$

Here, $\mathbf{A} \in \mathbb{C}^{M \times N}$ is the system matrix, $\mathbf{b} \in \mathbb{C}^{M \times 1}$ is the received signal, $\mathbf{x} \in \mathbb{R}^{N \times 1}$ is the vectorized version of the MPI image, and $\mathbf{n} \in \mathbb{C}^{M \times 1}$ represents the noise term. In addition, N is the number of voxels, and M is the number of frequency components included in image reconstruction.

2.4 Magnetic Fields Used in MRI & MPI

While MRI and MPI are fundamentally different imaging modalities, both utilize magnetic fields. A summary of the characteristics of the magnetic fields used in MRI and MPI is presented in Table 2.1.

Table 2.1: Magnetic Fields utilized in MRI and MPI

Modality	Magnetic Field	Field Pattern	Field Type
Magnetic Resonance Imaging (MRI)	B_0 Field	Homogeneous	Static
	RF Field	Homogeneous	Dynamic ($\sim$ MHz)
	Gradient Fields G_x, G_y, G_z	Linearly Varying (in x, y, z -directions)	Dynamic ($\sim$ Hz-kHz)
Magnetic Particle Imaging (MPI)	Selection Field	Inhomogeneous (with FFP or FFL)	Static
	Drive Field	Homogeneous	Dynamic ($\sim$ kHz)
	Focus Field	Homogeneous	Dynamic ($\sim$ Hz)

Chapter 3

Hybrid MPI and Low-Field MRI System

Parts of this chapter are based on following publications:

S. Karaca, D. A. Soydan, E. U. Saritas, and C. B. Top, "Open-bore hybrid mpi-mri scanner: a proof-of-concept simulation study," *Proceedings of the 32nd annual meeting of the international society for magnetic resonance in medicine*, 2023, Abstract 4561.

S. Karaca, D. A. Soydan, C. B. Top, and E. U. Saritas, "A simulation study for an open-sided hybrid mpi-mri scanner," *International Journal on Magnetic Particle Imaging IJMPI*, vol. 9, no. 1 Supply 1, 2023.

S. Karaca, D. A. Soydan, C. B. Top, and E. U. Saritas, "Proof-of-concept simulation study: An open-sided hybrid mpi and low-field mri scanner," *International Journal on Magnetic Particle Imaging IJMPI*, vol. 10, no. 1 Supply 1, 2024.

This chapter presents the design and characterization of the proposed hybrid MPI and LF-MRI system, shown in Fig. 3.1. This hybrid system design starts from a pre-existing prototype FFL MPI system [18], which is then empowered with the capability to perform LF-MRI.

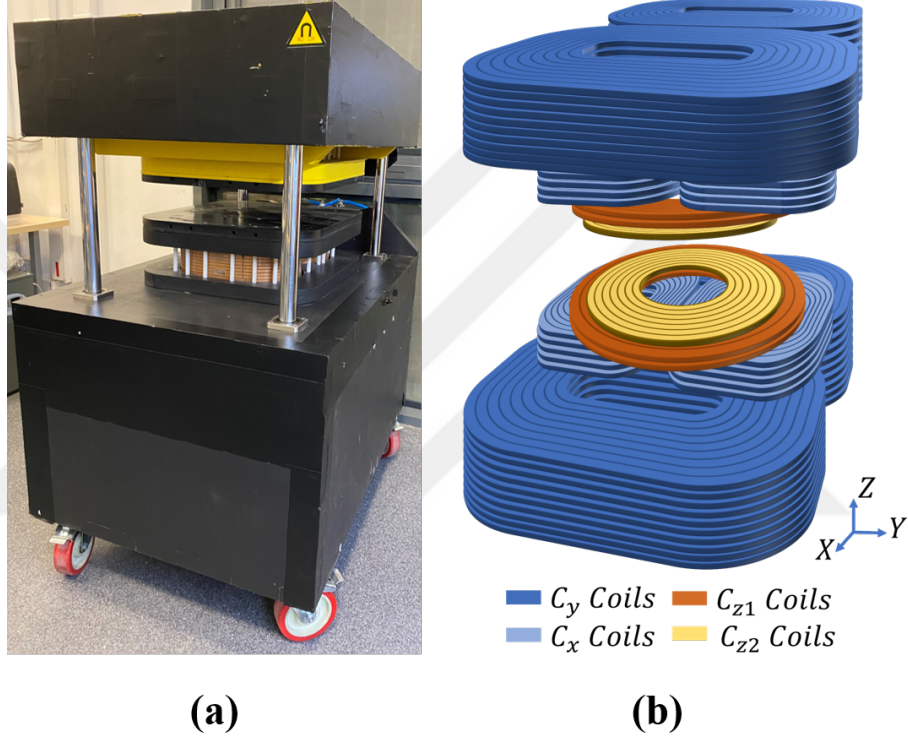


Figure 3.1: (a) Prototype hybrid MPI and LF-MRI system and (b) its coil topology. The Tx/Rx coil of LF-MRI and the receive coil of MPI are not shown.

3.1 MPI Performance of the Prototype Hybrid System

The prototype system features an open-sided MPI scanner with an electronically scanned FFL [15]. In the previous studies of our group, the MPI performance of this prototype system was analyzed in detail via both simulations [16, 17] and experiments [18]. Example simulation and experimental results are shown in the Figs. 3.2 and 3.3, respectively.

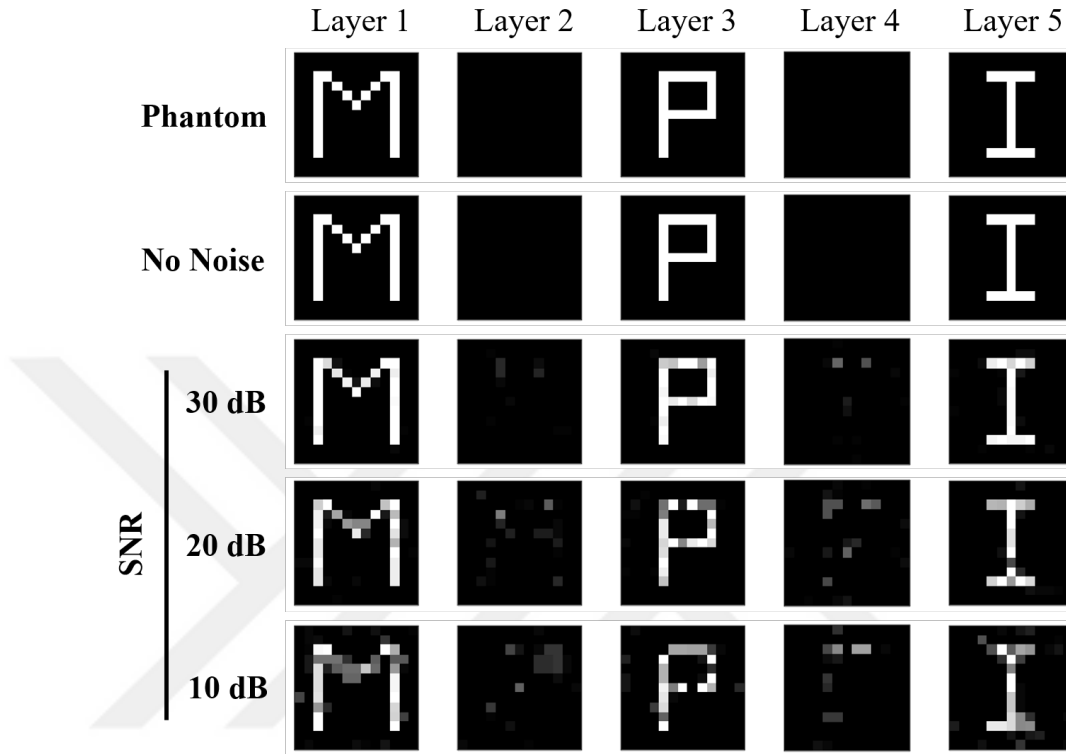


Figure 3.2: Example 3D simulation results for the MPI mode of the prototype system. The MPI phantom contains three letters in different imaging planes, which can be identified by visual inspection. The presence of noise leads to misplacement of the reconstructed particle distribution among the successive layers. This effect becomes more pronounced for the lower SNR cases. For these simulations, imaging FOV was $26 \times 26 \times 10 \text{ mm}^3$, discretized into $2 \times 2 \times 2 \text{ mm}^3$ grids. This figure is adapted from [17].

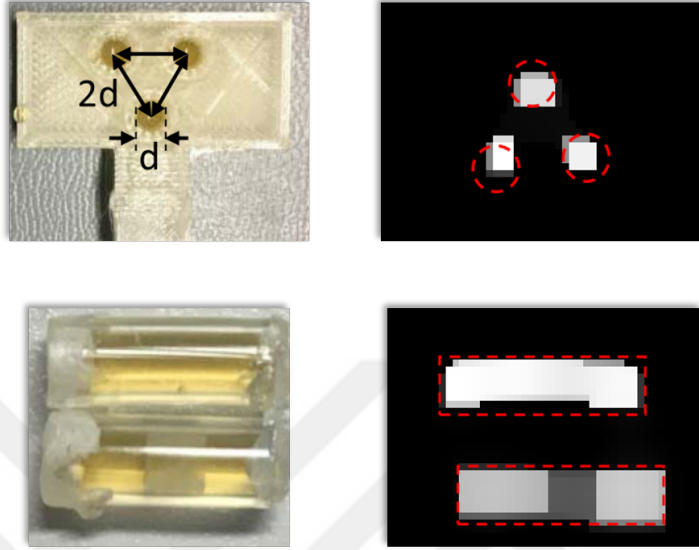


Figure 3.3: Experimental results for the MPI mode of the prototype system for phantoms filled with MNP solutions. [Top] A phantom with three dots and [Bottom] a phantom containing two parallel tubes, where the lower tube contains a blockage to mimic stenosis in a blood vessel. The reconstruction result for the three-dot phantom demonstrates high-resolution separation of the dots. Additionally, the vessel phantom reconstruction result indicates a clear observation of the stenosis region in the image, whereas the tube that mimics healthy blood vessel exhibits an almost uniform distribution. For these experiments, the system matrix was obtained for an FOV of $34 \times 18 \text{ mm}^2$, acquired on $2 \times 2 \text{ mm}^2$ grids. This figure is adapted from [18].

3.2 Coil Topologies of the Hybrid System

The prototype hybrid system along with its corresponding coil configuration is illustrated in Fig. 3.1. Each coil group within the system is described in the following sections. A detailed description of the system when used as an FFL MPI scanner can be found at [18].

3.2.1 C_x and C_y Coil Groups

The bi-planar gradient coil group denoted as C_y , is positioned at the outermost part of the system. This coil group functions to generate a gradient field in the x -direction. It is important to highlight that while the magnetic field itself is oriented in the z -direction, its gradient is directed along the x -axis. Similarly, a 90° rotated version of the C_y coil group labeled as C_x is utilized to produce a gradient field in the y -direction. In this case, the magnetic field itself is again in the z -direction, while the gradient is now in the y -direction. The coil groups (see Fig. 3.4) are constructed with hollow conductors to facilitate water cooling and are custom produced by Danfysik (Denmark). The characteristics of the coils in the C_x and C_y coil groups are presented in Table 3.1.

Table 3.1: Properties of individual coils in the C_x and C_y coil groups (each coil group is composed of four identical coils) [18].

Parameter	C_x Coils	C_y Coils
Inductance (mH @ 20Hz)	0.435 ± 0.005	2.900 ± 0.015
Resistance (m Ω)	22.0 ± 0.1	47.8 ± 0.2
Number of Turns	7×9	12×12
Outer Dimensions (cm^3)	$16 \times 21 \times 5$	$25 \times 34 \times 10$

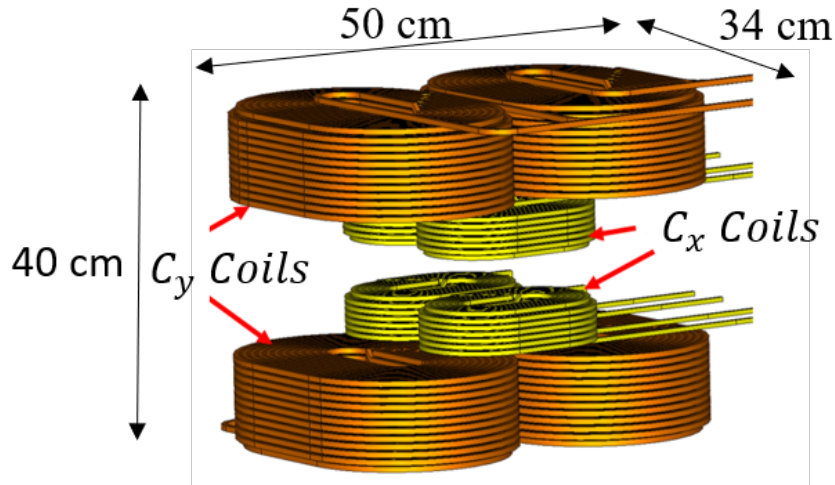


Figure 3.4: Schematic of C_x and C_y coil groups, showing dimensions of the overall structure.

The C_x and C_y coil groups operate separately to generate a FFL along the x - and y -directions with gradient fields in the y - and x -directions, respectively (see Fig. 3.5(a)-(b)). These coil groups can be employed together to produce gradient field at an arbitrary angle (see Fig. 3.5(c)).

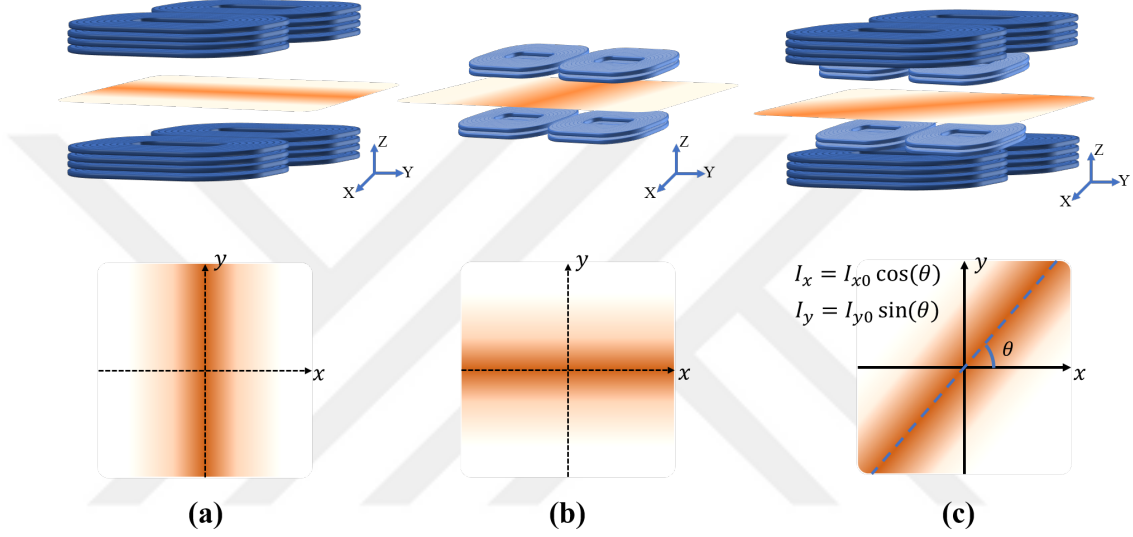


Figure 3.5: (a) C_y and (b) C_x coil groups can independently generate gradient fields in the x - and y -directions, respectively. (c) When operated together, the C_x and C_y coil groups can produce a gradient field at any arbitrary angle. The corresponding current values for C_x and C_y coil groups are given to rotate the gradient field by θ° .

3.2.2 C_{z1} and C_{z2} Coil Groups

Two bi-planar circular coil groups, labeled as C_{z1} and C_{z2} , are positioned on the inner side of the C_x coil group (see Fig. 3.1). In these coil groups, when the upper and lower coils are fed to generate a magnetic field in the same direction (i.e., in Helmholtz configuration), a homogeneous magnetic field can be produced in the z -direction. Conversely, if the coils are fed to create magnetic fields in opposite directions (i.e., in Maxwell configuration), a gradient field is formed along the z -direction. In this case, both the magnetic field itself and the gradient are oriented in the z -direction. The C_{z1} coil group is made with hollow conductors to enable

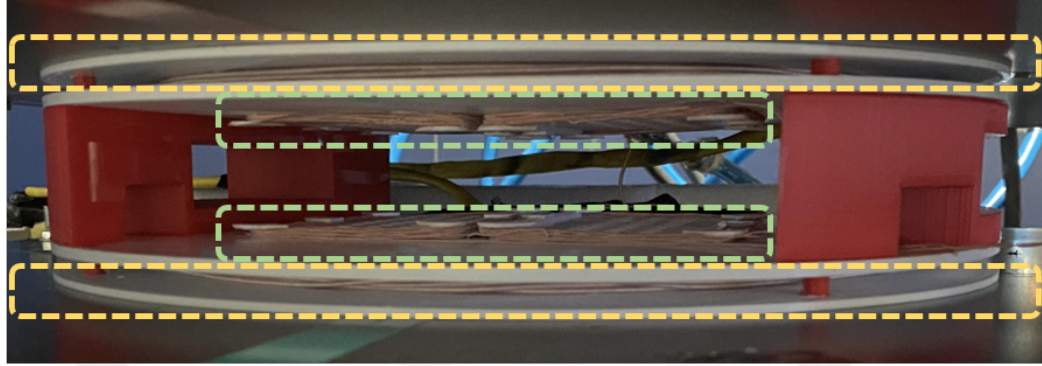
water cooling, custom produced by Tesla Engineering Ltd (England), as shown in Fig. 3.6. The C_{z2} coil group (see Fig. 3.7) is wound around a 3D-printed housing using a 200-strand AWG 41 Litz wire (Rupalit V155, Rudolf Pack GmbH & Co., Germany). The parameters for the C_{z1} and C_{z2} coil groups are detailed in Table 3.2.

Table 3.2: Properties of the C_{z1} and C_{z2} coil groups.

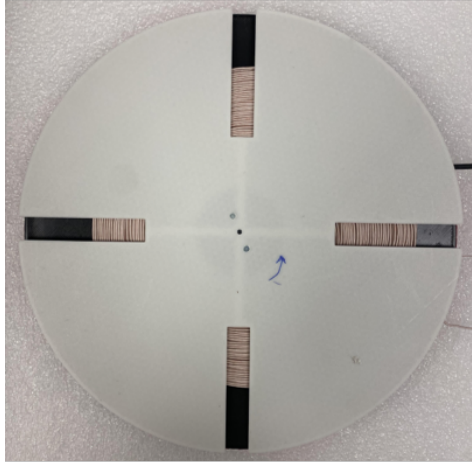
Parameters	C_{z1} Coils	C_{z2} Coils
Inductance (mH)	0.68 (@ 100 Hz)	1.95 (@ 25 kHz)
Resistance (Ω)	0.058	18
Number of Turns	14×3	57×3
Dimensions (cm) (D_{in} , D_{out} , height)	(12, 26, 2)	(6, 22, 0.5)



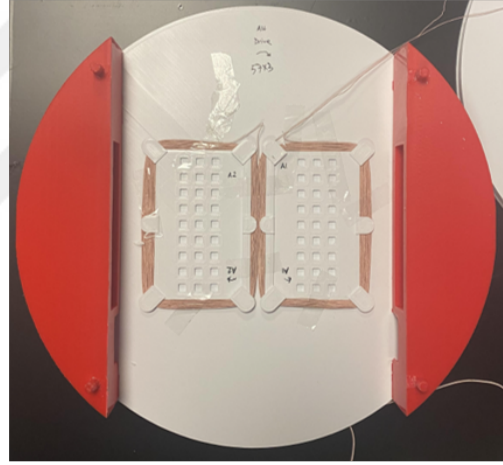
Figure 3.6: C_{z1} coil group. The 3D-printed supports are used to align upper and lower coils.



(a)



(b)



(c)

Figure 3.7: (a) The C_{z2} coil group, indicated with yellow dashed line and receive coil of the MPI, indicated with green dashed line are wound to single-piece 3D printed housing. (b) The top-view of the C_{z2} coil group and (c) the receive coil of the MPI, which features an aperture of 3 cm.

3.2.3 Common Deployment of Coil Groups in the Hybrid System

Fig. 3.8 shows the coil configuration and the functions of each coil group for both the MPI and LF-MRI modes:

- The C_{z1} coil group is operated in Helmholtz configuration to generate the focus field in MPI mode and the B_0 field in LF-MRI mode.
- The two bi-planar gradient coil groups, denoted as C_x and C_y , generate FFL along the x - and y directions, respectively, for the selection field of MPI in FFL topology. Adjusting the currents in these two coil groups enables electronic rotation of the FFL along a desired angle. These coils generate magnetic field gradients in the y - and x -directions, respectively, and hence can be used to form the G_y and G_x gradient fields in LF-MRI mode. Note that the C_x coil generates the G_y gradient fields and the C_y coil generates the G_x gradient fields.
- The C_{z2} coil group generates the drive field in MPI mode when coils are fed in-phase (i.e., in Helmholtz configuration); and generates the G_z gradient field in LF-MRI mode when coils are fed out-of-phase (i.e., in Maxwell configuration).

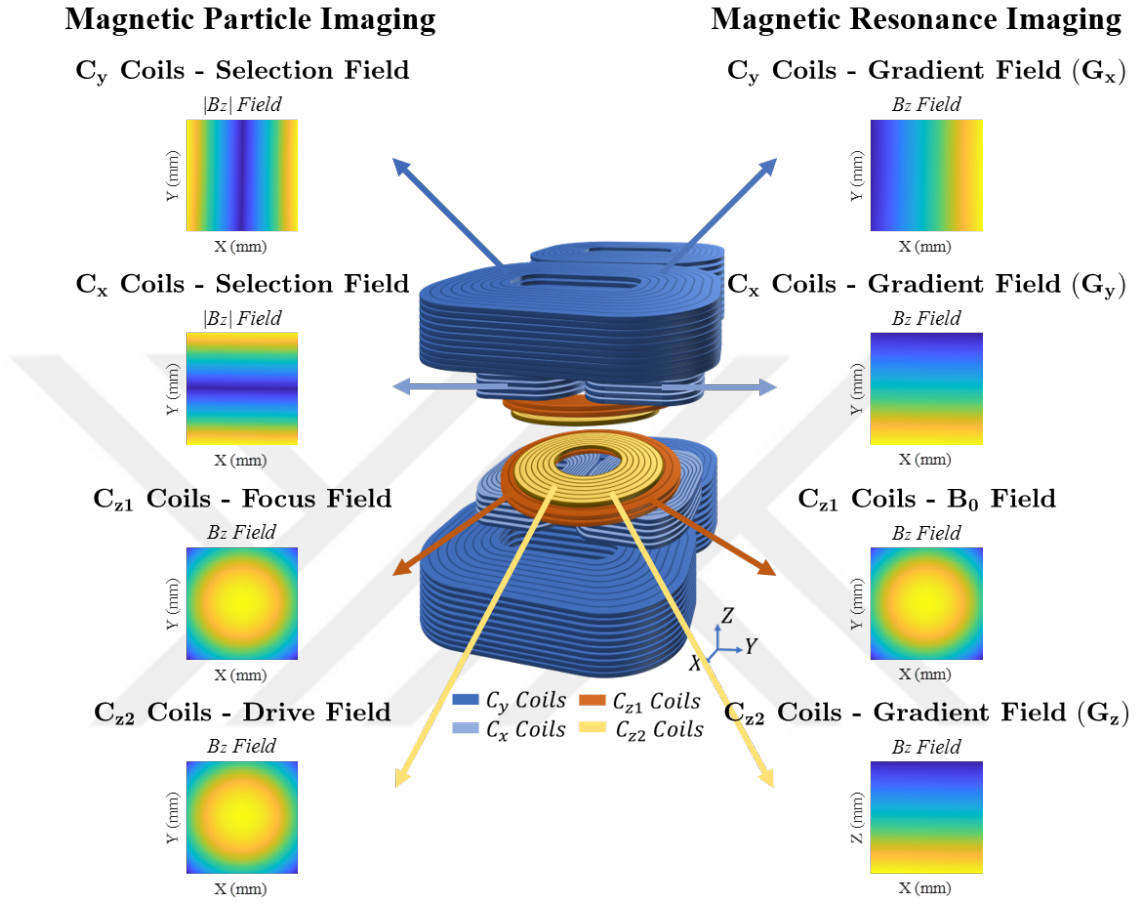


Figure 3.8: Magnetic field maps produced by each coil group for MPI and LF-MRI modes of the hybrid system. The C_y and C_x coil groups are utilized to generate the FFL of the selection field for MPI mode, and the G_x and G_y gradient fields for LF-MRI mode. The C_{z1} coil group is responsible for generating the focus field in MPI mode and the B_0 field in LF-MRI mode. Lastly, the C_{z2} coil group produces the drive field for MPI mode and the G_z gradient field for LF-MRI mode.

3.2.4 Receive Coil of MPI

The receive coil for MPI mode consists of two rectangular Helmholtz coils in a gradiometer configuration in the y -direction (see Fig. 3.7), providing an FOV up to $6 \times 9 \text{ cm}^2$. Each rectangular coil contains 36 turns, constructed with a 75-strand AWG 46 Litz wire on a 3D-printed housing.

3.2.5 Tx/Rx Coils of LF-MRI

A single solenoid coil (Pure Devices GmbH, Germany) serves dual purposes for transmission (Tx) and reception (Rx) in LF-MRI mode, facilitated by a customized switch operating around 2 MHz and surrounded by an electromagnetic shield. The Tx/Rx coil is tuned to 2.13 MHz, corresponding to the Larmor frequency at a B_0 field of 50 mT. The photograph and the dimensions of the coil with mechanical housing are given in Fig. 3.9.

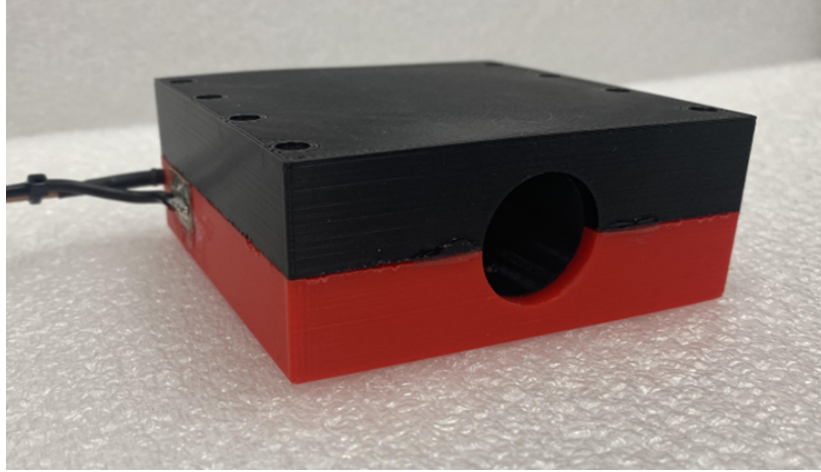


Figure 3.9: A single solenoid coil (Pure Devices GmbH, Germany) functions for both transmission and reception. It features a bore size of 2.5 cm, and the dimensions of the mechanical housing are $10 \times 10 \times 4 \text{ cm}^3$.

3.3 System Characterization for LF-MRI Mode

3.3.1 Magnetic Field Map Simulations and Measurements

Determining the fidelity of the magnetic fields is a fundamental step for characterizing the performance of the system, which is crucial for ensuring accurate spatial encoding and image quality. The related simulations and measurements provide a detailed spatial representation of the magnetic fields generated by each coil group.

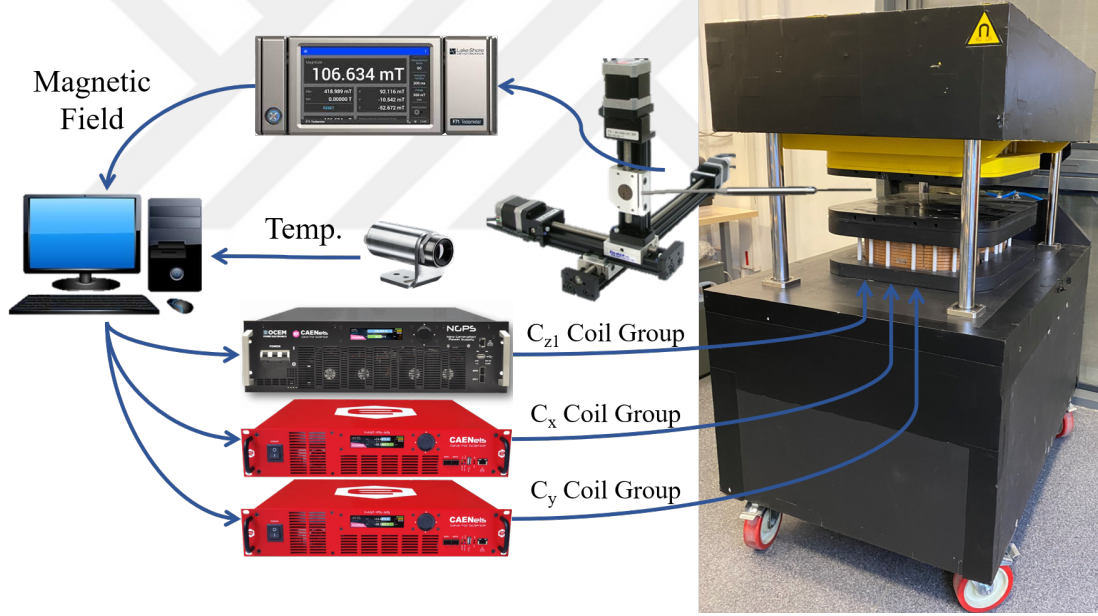


Figure 3.10: Setup for magnetic field map measurements.

Measurement Setup: The magnetic field maps of the C_x , C_y , and C_{z1} coils are measured using the setup shown in Fig. 3.10. In this setup, the C_{z1} coil group that generates the B_0 field is driven by a 10 kW unipolar power supply (NGPS, Caen Els S.R.L., Italy). In addition, C_x and C_y coil groups that generate G_y and G_x gradient fields, respectively, are driven via 1.5 kW bipolar power supplies (FAST-PS-1K5, Caen Els S.R.L., Italy). All of the power supplies are controlled via MATLAB (Mathworks). Magnetic field measurements are conducted using a multi-axis teslameter (F71, Lake Shore Cryotronics Inc., OH, USA.) equipped

with a three-axis Hall effect probe. This probe is mounted on a three-axis mechanical robot (Velmex Inc., NY, USA) to scan the region of interest (ROI). Additionally, the temperature of the coils and the cooling water are monitored during measurements via temperature probe (SI Analytics GmbH, Germany) and thermal camera (Xi400, Optris, Germany) to ensure the coils do not overheat.

3.3.1.1 B_0 Field

For these measurements, B_0 field of 50 mT is targeted based on the literature [31]. A current of 146 A is applied to the C_{z1} coil group to produce a 50 mT B_0 field, corresponding to a coil efficiency of approximately 0.34 mT/A. The 3D B_0 field map is measured within a ROI of $32 \times 32 \times 8$ mm³, discretized with $4 \times 4 \times 4$ mm³ grids. Then, this 3D data is interpolated to $1 \times 1 \times 1$ mm³ grids. In addition, the C_{z1} coil group is modeled in Maxwell (Ansys Electromagnetics Suite, Ansys Inc., USA), and the magnetic field map is computed via magnetostatic simulations for a coil current of 160 A, which generates $B_0 = 50$ mT. The measurement and simulation results are presented in Fig. 3.11, demonstrating a high level of agreement.

Furthermore, the B_0 inhomogeneity map generated using the measured B_0 field map is provided in Fig. 3.12. The B_0 field inhomogeneity for the circular of FOV of 20 mm diameter shown in this figure is computed in units of parts-per-million (ppm) as follows:

$$\Delta B_0(ppm) = \frac{B_0(r=0) - B_0(r=10\text{ mm})}{B_0(r=0)} \times 10^6 \quad (3.1)$$

B_0 at the center (i.e., at $r=0$) is measured as 50.0370 mT. B_0 gets smaller away from the center of the FOV, reaching the lowest value of 49.9378 mT on the circumference of the circle (i.e., at $r=10$ mm). This level of deviation corresponds to approximately $\Delta B_0 = 2000$ parts-per-million (ppm) inhomogeneity in B_0 , while the simulated B_0 field map displays an inhomogeneity level of approximately 4000 ppm. This difference may be caused by practical considerations, such as

slight variations in the winding patterns and differences in the spacings among coil windings during manufacturing compared to the simulated model.

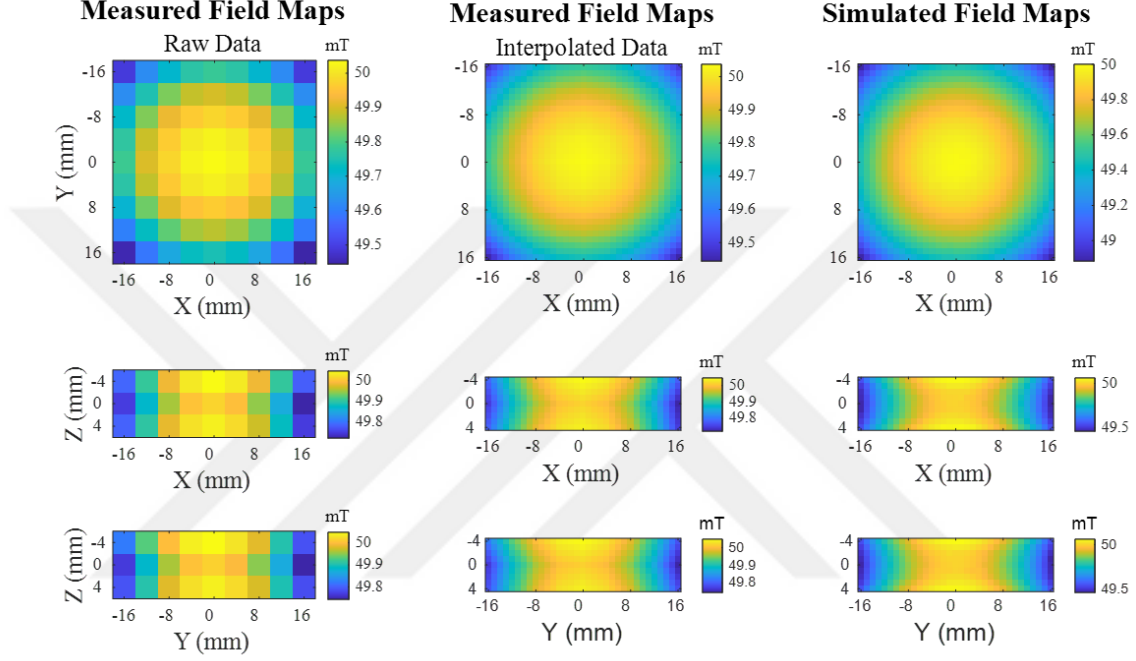


Figure 3.11: B_0 field map from the C_{z1} coil group for a $32 \times 32 \times 8$ mm³ ROI. [Left] Measured raw data on a $4 \times 4 \times 4$ mm³ grid, [Middle] measured data interpolated to a $1 \times 1 \times 1$ mm³ grid, and [Right] simulation results for a $1 \times 1 \times 1$ mm³ grid. The results are shown for [Top] xy -plane at $z = 0$, [Middle] xz -plane at $y = 0$, and [Bottom] yz -plane at $x = 0$. Fields along the z -direction (B_z) are shown. Note the narrow display ranges for these maps.

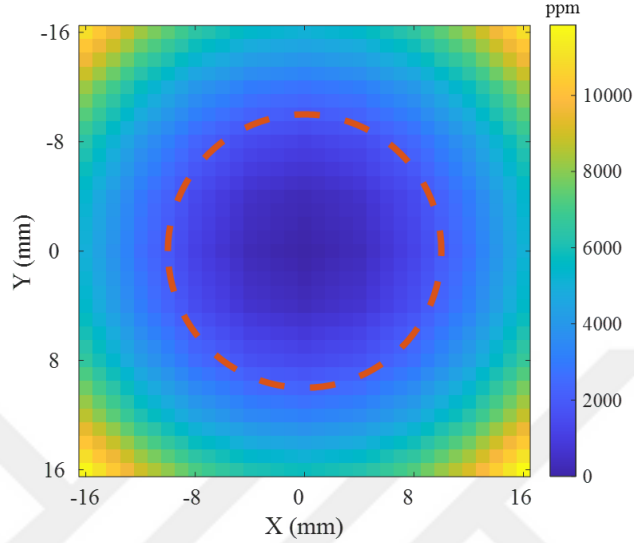


Figure 3.12: B_0 inhomogeneity map derived from the measured B_0 field map in Fig. 3.11. The red dashed circle indicates a circular FOV of 20 mm diameter showing approximately a maximum of 2000 parts-per-million (ppm) inhomogeneity in B_0 .

3.3.1.2 Gradient Fields

C_x and C_y Coil Groups: A current of 10 A is applied to the C_x coil group, while 2 A is applied to the C_y coil group. The 2D field maps are measured within a ROI of 32×32 mm², discretized into 4×4 mm² grids. Then, this 2D data is interpolated to 1×1 mm² grids. In addition, the C_x and C_y coil groups are modeled in MATLAB, and the magnetic field maps are computed using the Biot-Savart law. As shown in Fig. 3.13, the measured and simulated field maps display a high level of agreement. While the range of gradients field values match closely between the measured and simulated gradient field maps as shown in Fig. 3.14, there are also some discrepancies between the two, potentially related to the accuracy of the field measurements and practical considerations in coil winding.

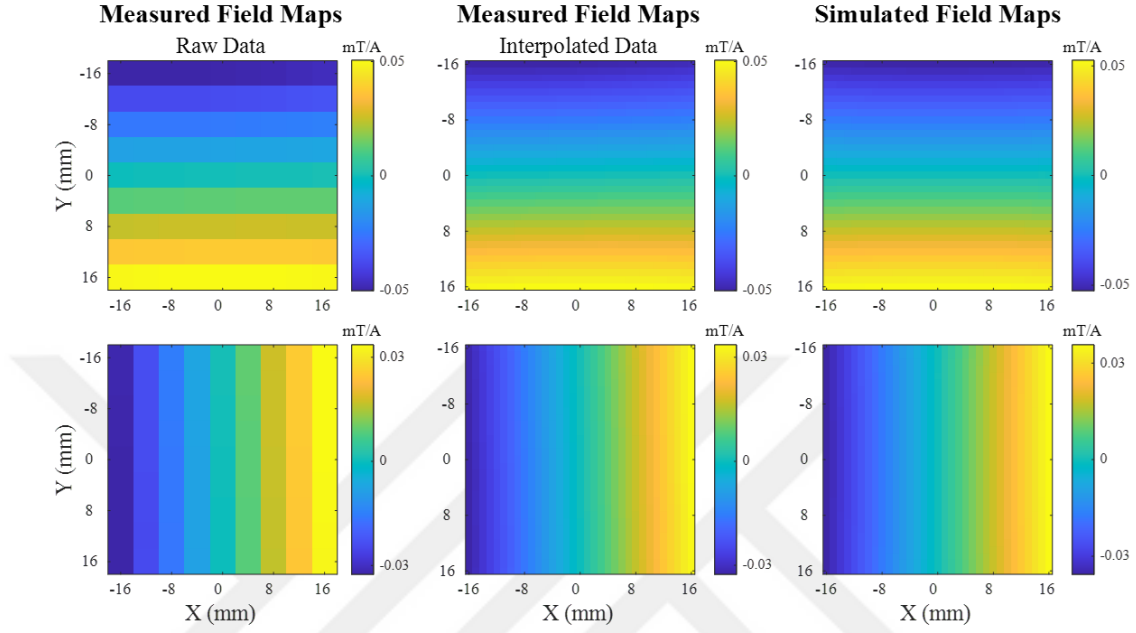


Figure 3.13: Field maps for [Top] C_x coil group that generates the G_y gradients and [Bottom] C_y coil group that generates the G_x gradients, for a $32 \times 32 \times 8$ mm³ ROI. [Left] Measured raw data on a $4 \times 4 \times 4$ mm³ grid, [Middle] measured data interpolated to a $1 \times 1 \times 1$ mm³ grid, and [Right] simulation results for $1 \times 1 \times 1$ mm³ grid. Fields along the z -direction (B_z) are displayed per unit current through each coil group.

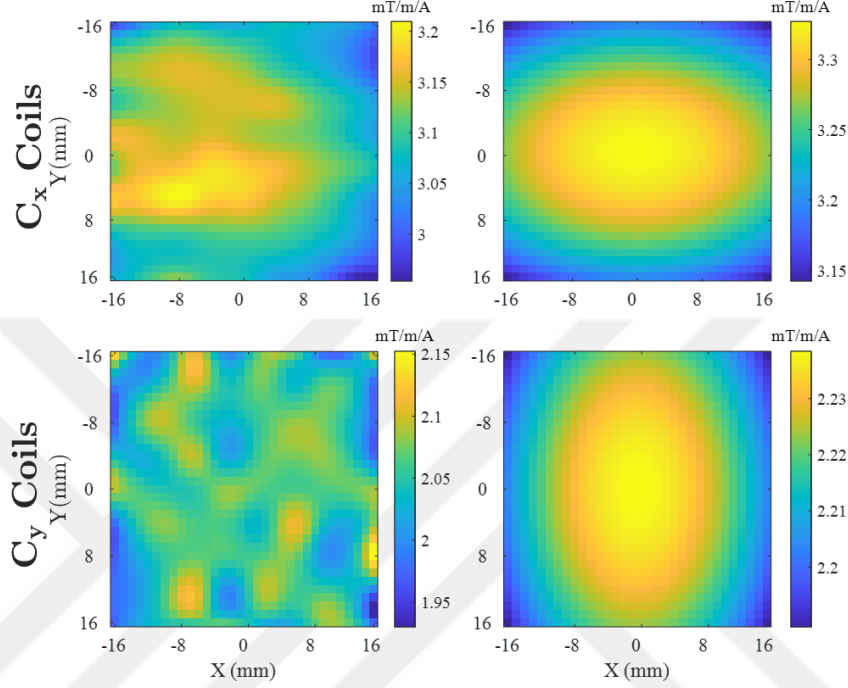


Figure 3.14: [Left] Measured and [Right] simulated gradient field efficiency maps, showing $G_y = \frac{\partial B_z}{\partial y}$ for C_x coil group and $G_x = \frac{\partial B_z}{\partial x}$ for C_y coil group, normalized to unit current. Note the narrow display ranges for these maps.

While Fig. 3.14 shows gradient field efficiency maps (i.e., gradient field per unit current) as a function of position, average values for the FOV of interest are also calculated. Accordingly, the average gradient field efficiencies for a FOV of 20 mm are calculated using the central axes of the measured field maps (see Fig. 3.15) as follows:

$$G_{x,eff} (\text{mT m}^{-1} \text{ A}^{-1}) = \frac{G_x}{I_{C_y}} = \frac{B_{C_y}(10 \text{ mm}, 0) - B_{C_y}(-10 \text{ mm}, 0)}{0.020 \text{ m} \times I_{C_y} (\text{A})} \quad (3.2)$$

$$G_{y,eff} (\text{mT m}^{-1} \text{ A}^{-1}) = \frac{G_y}{I_{C_x}} = \frac{B_{C_x}(0, 10 \text{ mm}) - B_{C_x}(0, -10 \text{ mm})}{0.020 \text{ m} \times I_{C_x} (\text{A})} \quad (3.3)$$

where $G_{x,eff}$ and $G_{y,eff}$ represents the average gradient field efficiencies for the x - and y -directions, while B_{C_y} and B_{C_x} denote the field maps of the C_y and C_x

coil groups, respectively. In addition, G_x and G_y are the gradients when currents I_{C_y} and I_{C_x} are applied to the C_y and C_x coil groups, respectively.

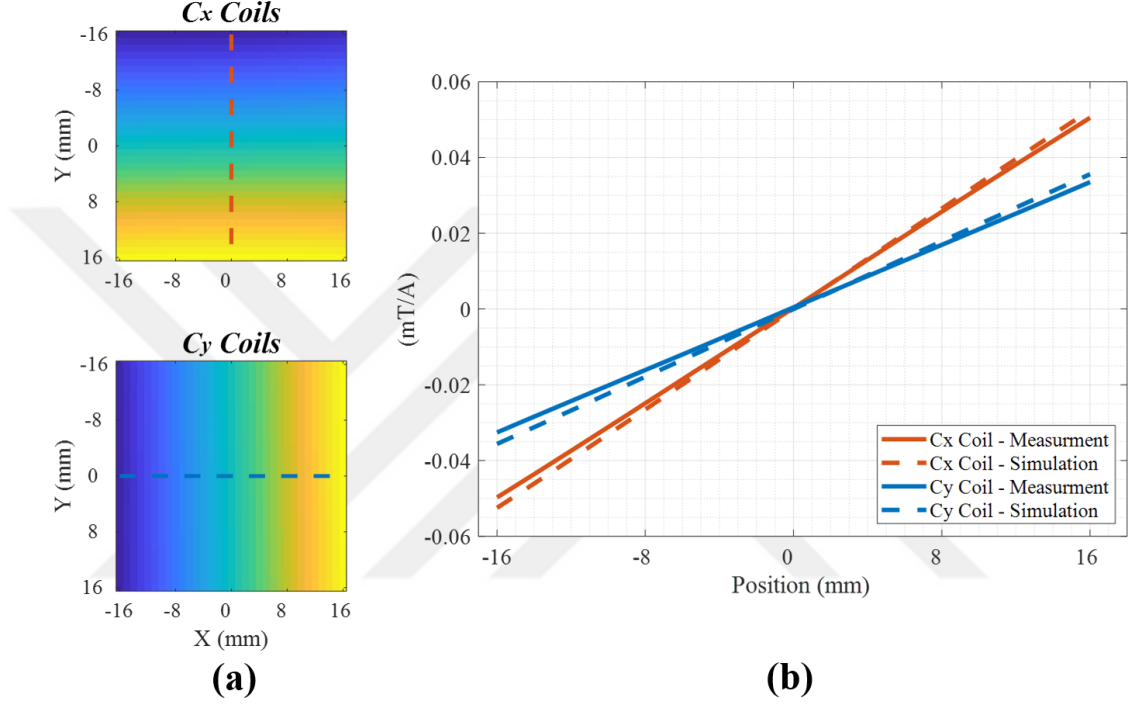


Figure 3.15: (a) Measured field maps of C_x and C_y coil groups. The central axes marked by orange and blue dashed lines are used to calculate gradient field efficiencies. (b) 1D field plots for the C_x and C_y coil groups, displaying both measured and simulated data. The slopes of these lines are used to determine the gradient field efficiencies.

When $I_{C_y} = 2$ A is applied to the C_y coil group, the magnetic field strength as a function of x -position is measured as 0.042 mT at $x = 10$ mm and -0.040 mT at $x = -10$ mm, resulting in $G_{x,eff} = 2.1$ mT m $^{-1}$ A $^{-1}$. Additionally, when $I_{C_x} = 10$ A is applied to the C_x coil group, the magnetic field strength as a function of y -position is measured as 0.320 mT at $y = 10$ mm and -0.312 mT at $y = -10$ mm, yielding $G_{y,eff} = 3.2$ mT m $^{-1}$ A $^{-1}$. In comparison, simulated field maps indicate average gradient efficiencies of $G_{x,eff} = 2.2$ mT m $^{-1}$ A $^{-1}$ and $G_{y,eff} = 3.3$ mT m $^{-1}$ A $^{-1}$, closely matching the experimental values.

The maximum gradient amplitudes of $G_{x,max} = 210 \text{ mT m}^{-1}$ and $G_{y,max} = 320 \text{ mT m}^{-1}$ can be achieved in the x - and y -directions, respectively, within the 100 A maximum current capacity of the power supplies (FAST-PS-1K5, Caen Els S.R.L., Italy). These maximum gradient amplitude values are more than sufficient for successful imaging in MRI. However, assessing the gradient coil performance in MRI also requires consideration of the slew rate [32].

C_{z2} Coil Group: The C_{z2} coil group is modeled in Maxwell configuration in MATLAB, and its magnetic field map is computed using the Biot-Savart law. The corresponding simulation results are given in Fig. 3.16. Since the dimensions of the Tx/Rx coil for the LF-MRI mode are incompatible with the C_{z2} coil group, slice-selection gradients are not applied in the experimental studies (see Chapter 5). Therefore, magnetic field map measurements were not performed for the C_{z2} coil group.

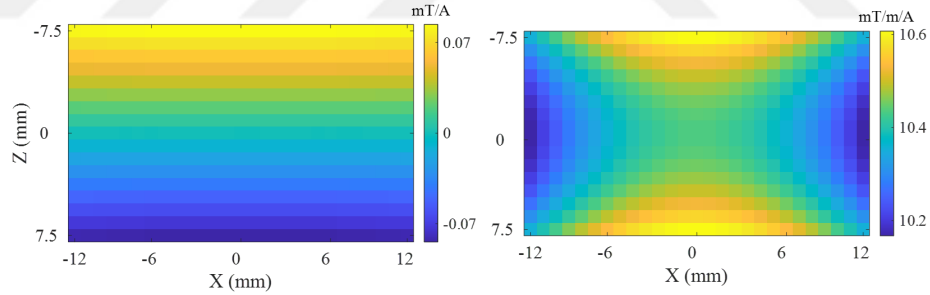


Figure 3.16: [Left] Simulated field map of C_{z2} coil group that generates the G_z gradients, shown in $y = 0$ plane. Field along the z -direction (B_z) is displayed per unit current through the coil group. [Right] The corresponding gradient field efficiency map, showing $G_z = \frac{\partial B_z}{\partial z}$, normalized to unit current. Note the narrow display range for this map.

3.3.2 Slew Rate Measurements

The slew rate of a gradient coil in MRI refers to the speed at which the gradient coil can ramp up or ramp down the gradient field strength. The slew rate is a critical parameter because it affects the ability of the MRI system to quickly and

accurately turn on/off the gradient fields, which is essential for spatial encoding, image resolution, and scan time.

Measurement Setup: The slew rates of the C_x and C_y coil groups are assessed to determine their suitability for LF-MRI imaging, using the measurement setup outlined in Fig. 3.17. In this setup, gradient coils are powered via 1.5 kW bipolar power supplies (FAST-PS-1K5, Caen Els S.R.L., Italy). A square pulse waveform is defined for the power supplies and generated following a trigger signal from a waveform generator (33500B, Keysight Technologies, CA, USA). The same signal triggers the data acquisition card (NI-6363 USB, National Instruments, USA), which records the current waveform measured via current probe (1146B, Keysight Technologies, CA, USA).

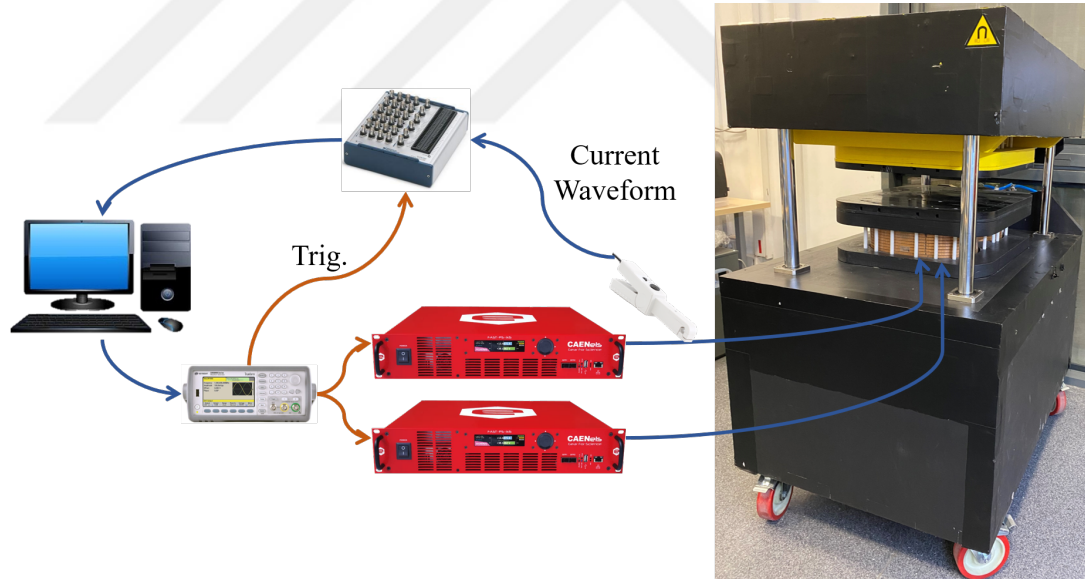


Figure 3.17: Setup for slew rate measurements.

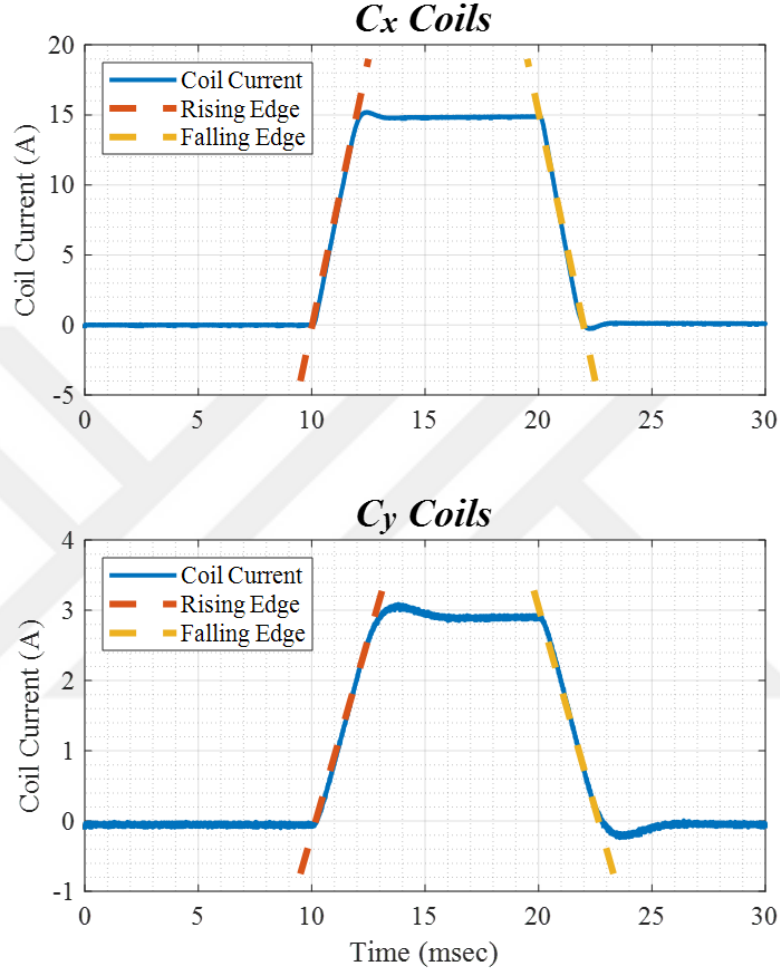


Figure 3.18: Slew rate measurements for [Top] the C_x coil group and [Bottom] C_y coil group. Lines are fitted to both the rising and falling edges of the current waveforms, and the slopes of these lines are used to calculate the slew rates.

Slew Rates for Gradient Fields: The measured coil currents for C_x and C_y coils are shown in Fig. 3.18. These current waveforms are utilized to calculate the slew rates of the gradient coils, taking into account the measured gradient field efficiencies as follows:

$$SR_{rising} = |Slope_{rising}| \times G_{eff} = \left| \frac{I_{90\%} - I_{10\%}}{t_{90\%} - t_{10\%}} \right| \times G_{eff} \quad (3.4)$$

$$SR_{falling} = |Slope_{falling}| \times G_{eff} = \left| \frac{I_{10\%} - I_{90\%}}{t_{10\%} - t_{90\%}} \right| \times G_{eff} \quad (3.5)$$

Here, I is the coil current, and SR_{rising} and $SR_{falling}$ are the slew rates for the rising and falling edges of the current waveform. The rising and falling slopes of the current waveform are computed using the 10% to 90% values.

The slopes of the rising and falling edges of the current waveform for the C_x coil group are calculated as 7.26 and -7.81 A msec⁻¹, respectively, resulting in slew rates of 23 and 25 mT m⁻¹ msec⁻¹. On the other hand, for the C_y coil groups, the absolute value of the slopes for both edges are computed as 1.03 A msec⁻¹, leading to slew rate of 2.2 mT m⁻¹ msec⁻¹.

The measurement results for C_x and C_y coil groups are summarized in Table 3.3.

Table 3.3: Measured gradient efficiencies, maximum gradient amplitudes, and slew rates for the G_y and G_x gradient fields generated by C_x and C_y coil groups, respectively

Coil Group	Gradient Field	Gradient Efficiency (mT/m/A)	Max. Gradient Amplitude (mT/m)	Slew Rate (mT/m/msec)	
				Rising	Falling
C_x	G_y	3.2	320	23	25
C_y	G_x	2.1	210	2	2

3.3.3 Discussion

The measured B_0 field map is aligned with the expected behavior, as predicted by the coil geometries and simulation results. However, it is noted that the magnetic field in the measured data exhibits a slightly slower reduction in B_0 field away from the center of the coil group, potentially arising from practical considerations in the coil production process. The measured B_0 field inhomogeneity is found as approximately 2000 ppm, which is acceptable for LF-MRI compared with the related work in the literature [26]. The measured B_0 field map can be used for unwarping algorithms to reduce off-resonance induced warping artifacts for future studies.

The measured field maps for gradient fields also exhibited the expected behavior based on the coil geometries and simulation results. Moreover, the gradient field efficiencies are used to determine the currents to be applied to gradient coil groups to generate corresponding fields according to the required gradient fields. Furthermore, these field maps can be utilized in post-processing algorithms to enhance image quality by correcting artifacts caused by gradient non-linearity in future studies.

While the slew rates of the gradient coils are lower than those in typical clinical MRI systems, they are at a sufficient level compared with the LF-MRI scanners reported in the literature [33]. The slew rate and gradient efficiency of the C_x coil group is higher than those of the C_y coil group. Considering these factors, the C_x coil group is selected to create frequency-encoding gradient field (i.e., chosen as G_x coil).

Additionally, the 10 kW unipolar power supply (NGPS, Caen Els S.R.L., Italy) is tested for driving the gradient coil groups during the measurements. However, because this power supply is not bipolar, it resulted in significantly different rise and fall times for the coil current waveform (results not shown). Particularly, the resulting fall time is too long for effective use in MRI experiments. Thus, 1.5 kW bipolar power supplies (FAST-PS-1K5, Caen Els S.R.L., Italy), which provide approximately equal rise and fall time performances, are employed for

the gradient field generation.

Notably, during MPI measurements, since the FFL is rotated and data is acquired for successive angle steps, the current waveform exhibits smoother transitions [15], enabling the use of the 10 kW unipolar power supplies (NGPS, Caen Els S.R.L., Italy) to power the C_y coils in the MPI mode. The usage of the 10 kW power supplies is also advantageous for achieving higher gradient field amplitudes, which directly impacts image resolution in MPI [27].

Chapter 4

Simulation Studies

Parts of this chapter are based on following publications:

S. Karaca, D. A. Soydan, E. U. Saritas, and C. B. Top, "Open-bore hybrid mpi-mri scanner: a proof-of-concept simulation study," *Proceedings of the 32nd annual meeting of the international society for magnetic resonance in medicine*, 2023, Abstract 4561.

S. Karaca, D. A. Soydan, C. B. Top, and E. U. Saritas, "A simulation study for an open-sided hybrid mpi-mri scanner," *International Journal on Magnetic Particle Imaging IJMPI*, vol. 9, no. 1 Supply 1, 2023.

S. Karaca, D. A. Soydan, C. B. Top, and E. U. Saritas, "Proof-of-concept simulation study: An open-sided hybrid mpi and low-field mri scanner," *International Journal on Magnetic Particle Imaging IJMPI*, vol. 10, no. 1 Supply 1, 2024.

The previous chapter has demonstrated that our system can successfully produce the required magnetic fields for LF-MRI. In this chapter, simulation studies are presented to validate the capability of our system to conduct LF-MRI. In addition, system-induced deviations are investigated.

4.1 LF-MRI Simulations

For numerical LF-MRI simulations, the Tx/Rx coils are assumed to be ideal. The magnetic field maps are imported into an in-house MRI simulator developed in MATLAB. The timing diagram of the applied pulse sequence is then subdivided into intervals, where the Bloch equations are applied to the magnetic moment vectors assigned to each grid based on the magnetic field strength at that interval. This process incorporates T_1/T_2 relaxations, rotations from RF pulses, gradient fields, and off-resonance effects. The LF-MRI signal is obtained by summing the magnetic moment vectors within the data acquisition window at each time interval. Then, the data is placed into the k-space grid corresponding to the applied pulse sequence. Finally, image reconstruction is performed via taking the inverse 2D Fourier transform of the k-space data.

The simulations are carried out within a FOV of $25 \times 25 \times 15 \text{ mm}^3$, discretized with $0.2 \times 0.2 \times 0.2 \text{ mm}^3$ grids. A spin-echo pulse sequence utilizing line-by-line Cartesian sampling is employed. The common imaging parameters across all simulations are 0.3 mm isotropic in-plane resolution, 2 mm slice thickness, and a 2D FOV of $25 \times 25 \text{ mm}^2$. Infinite TR is assumed for complete spin recovery at the beginning of each k-space line, while TE is set to 10 ms. Additionally, a phantom as illustrated in Fig. 4.1 is used in the simulations. $T_1 = 275 \text{ ms}$ and $T_2 = 80 \text{ ms}$ relaxation time constants of the phantom are assigned to mimic those of the grey matter in the LF-MRI regime [25, 34].

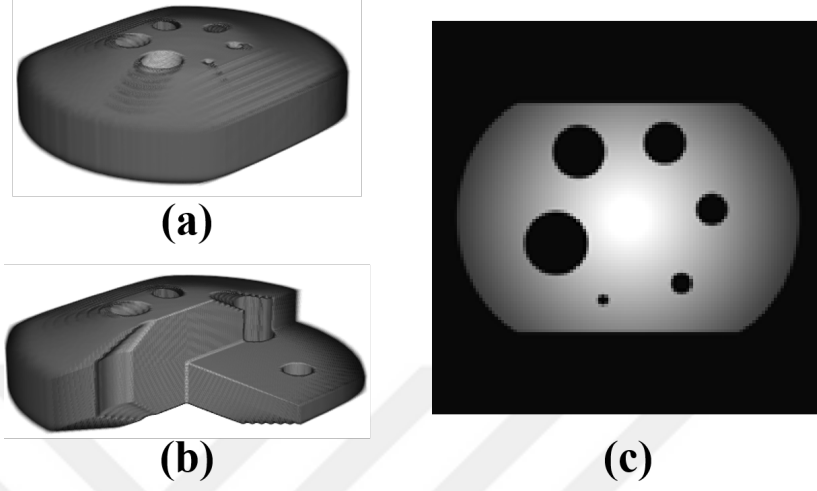


Figure 4.1: (a) The exterior and (b) the interior views of the imaging phantom used in the simulations. (c) The 2D cross-section of the axial slice in the z -direction is selected for imaging simulations.

4.1.1 Effects of Off-Resonance Level

To assess the impact of various off-resonance values through simulations, the B_0 inhomogeneity map is scaled to get a reduced off-resonance effect while maintaining the same peak value of 50 mT. The readout and RF pulse bandwidths (BWs) are selected as 100 kHz and 14 kHz, respectively. Additionally, simulations are conducted under noise-free conditions to exclusively examine the artifacts induced by off-resonance effects.

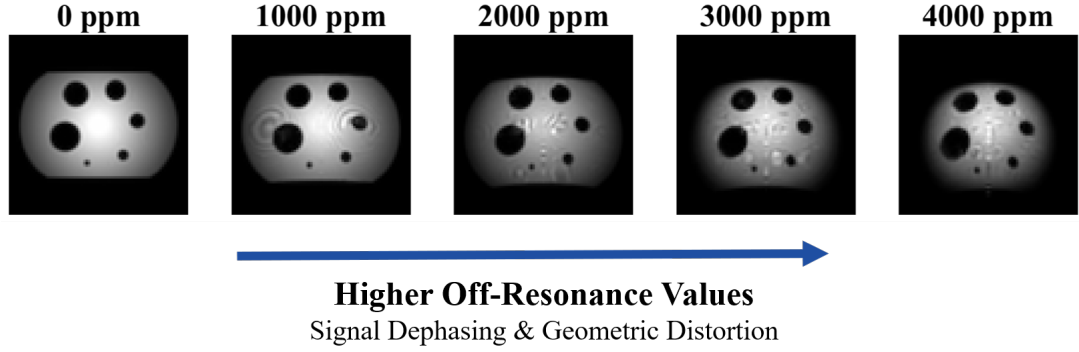


Figure 4.2: The reconstructed images for different off-resonance levels of the C_{z1} coil group. The vertical direction is designated as the frequency encoding direction, while the horizontal direction is selected as the phase encoding direction. The results show that higher off-resonance values lead to considerable dephasing and warping problems.

The results shown in Fig. 4.2 indicate that the higher off-resonance values cause significant dephasing and warping issues, leading to insufficient LF-MRI performance. This issue can be addressed by incorporating an additional shim coil into the prototype system or adjusting the pulse sequence parameters to make it more robust to the off-resonance based artifacts.

4.1.2 Effects of B_0 Field Strength

To observe the effects of B_0 field strength, simulations are carried out for B_0 field ranging between 5 and 50 mT. To demonstrate the trade-offs in choosing B_0 field strength, the effects of noise are incorporated. Accordingly, zero-mean white Gaussian noise is added to k-space data, with standard deviation set to yield 15 dB SNR at B_0 field of 20 mT. For a fair comparison, the SNR was then scaled with $B_0^{7/4}$ for different B_0 field strengths as explained in Equation (2.22). Additionally, readout and RF pulse BWs are selected as 100 kHz and 14 kHz, respectively.

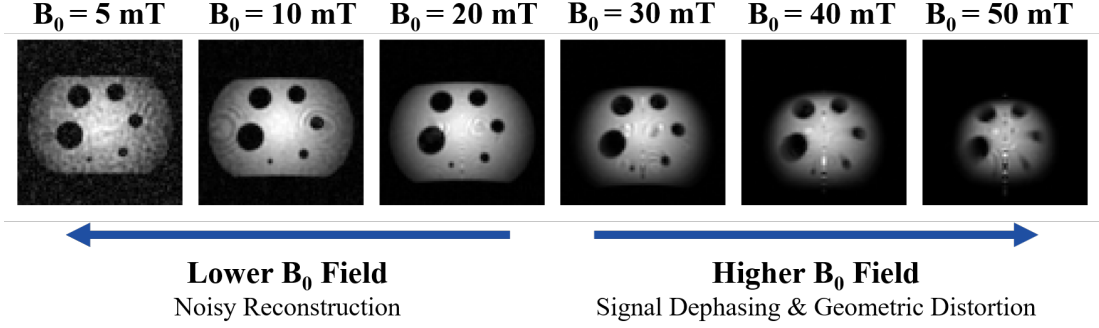


Figure 4.3: Reconstructed LF-MRI images for different B_0 field strengths. The frequency encoding direction is aligned vertically, whereas the phase encoding direction is aligned horizontally. Higher B_0 field values result in increased dephasing for the same off-resonance value, together with increased warping artifacts. Lower B_0 field values, on the other hand, have reduced SNR.

Fig. 4.3 displays the reconstructed LF-MRI images across varying B_0 field values, showing a trade-off between noise and dephasing/warping. Maintaining constant pulse sequence parameters such as readout and RF pulse bandwidths, lower B_0 field values yield noisy reconstructions, whereas higher B_0 field values result in notable signal dephasing and geometric distortions due to relative increase in off-resonance effects.

4.1.3 Effects of RF & Readout Bandwidth Values

Next, RF pulse and readout bandwidths are scaled to induce identical off-resonance effects at different B_0 field values, while keeping the remaining parameters consistent with those in the previous section. The limits of the RF pulse and readout BW used in the simulations are selected based on the experimental values in the literature [35, 36]. Additionally, noise is influenced by the readout BW. Again the standard deviation of the white Gaussian noise is set to yield 15 dB SNR at B_0 field of 20 mT and readout BW of 100 kHz. The SNR is then scaled with $B_0^{7/4} BW^{-1/2}$ for other B_0 field and readout BW values [20].

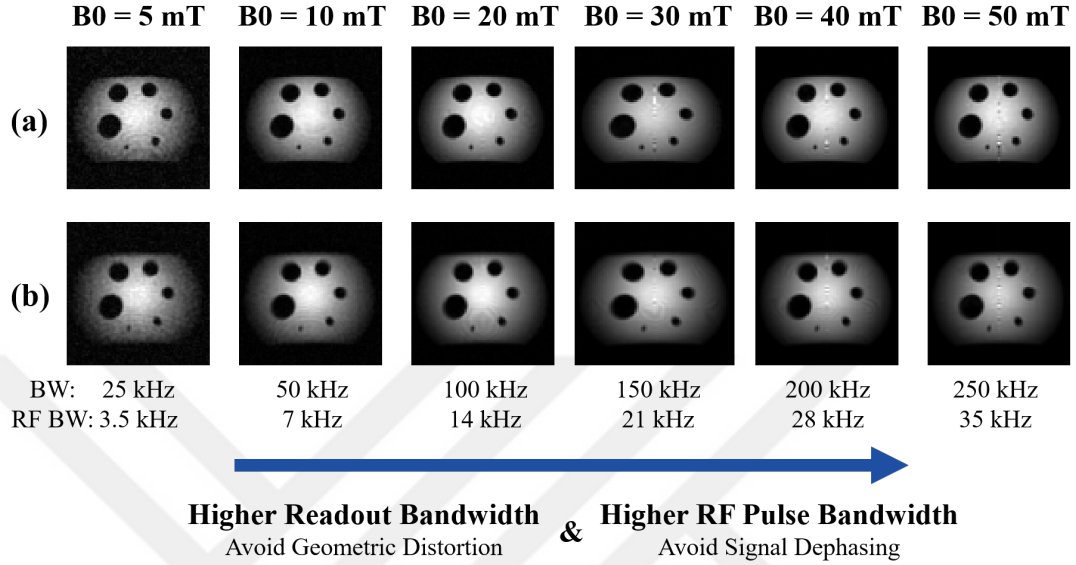


Figure 4.4: Reconstructed MRI images at different B_0 field values, in which RF pulse and readout BW are scaled to induce identical off-resonance effects at different B_0 field values. Simulation results using (a) simulated and (b) measured magnetic field maps. The vertical axis is designated for frequency encoding, while the horizontal axis is designated for phase encoding.

The reconstruction results in Fig. 4.4 show that for this scenario, SNR increases with B_0 field, and image quality is maintained even at higher B_0 field values. Increasing the RF pulse bandwidth ensures the successful excitation of spins across the FOV resulting in reduced signal loss, especially noticeable in the outer regions of the FOV, while raising the readout bandwidth reduces phase accumulation resulting from the off-resonance effect in the frequency encoding direction, thereby decreasing the warping artifacts in that direction.

The results indicate that we can successfully reconstruct images from both simulated and measured field maps. The readout and RF BW parameters are selected to reconstruct images for the simulated field maps. Given that the inhomogeneity value for the measured field maps is lower, similar parameters also lead to successfully obtained reconstructed images by reducing the artifacts due to off-resonance effects.

4.1.4 Effects of Utilizing Radial Trajectory

As described in Chapter 3, our prototype system can independently generate gradient fields in both x - and y -directions, which facilitates Cartesian sampling for LF-MRI. An alternative approach to creating gradient fields involves using a single gradient coil group that is mechanically rotated. In this configuration, MPI can be conducted using mechanically rotated FFL. However, this configuration restricts LF-MRI to radial sampling exclusively. To analyse this case, we proceed with the simulations by utilizing a radial k-space trajectory.

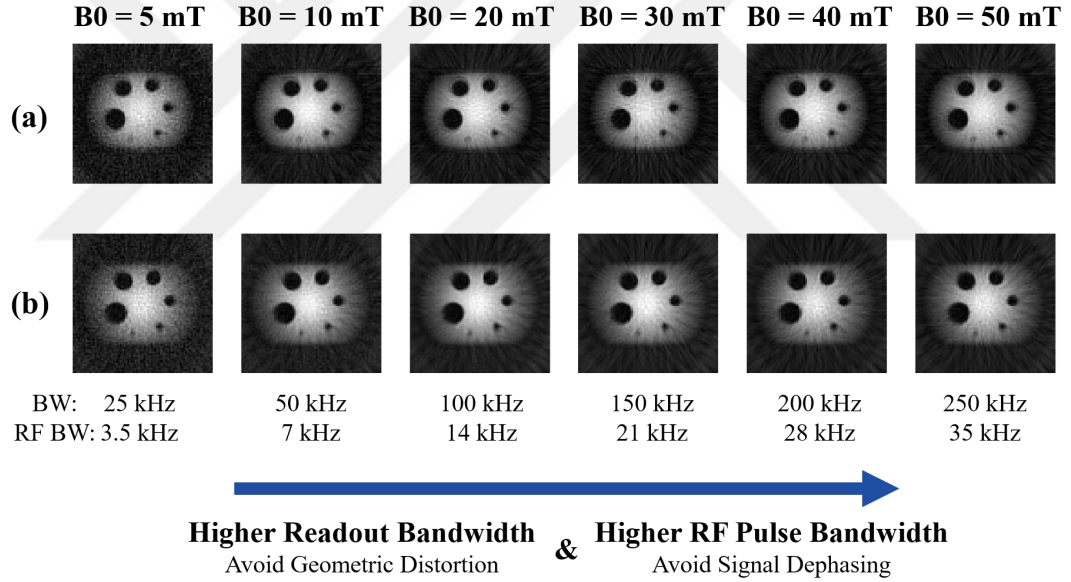


Figure 4.5: Reconstructed MRI images for radial k-space sampling at different B_0 field values, in which RF pulse and readout BW are rescaled to induce identical off-resonance effects at different B_0 field values. Simulation results for (a) simulated and (b) measured magnetic field maps.

The Fig. 4.5 demonstrates that LF-MRI can also be performed using radial sampling on the proposed hybrid system. Since the radial trajectory does not have a dedicated frequency encoding direction, warping artifacts are distributed across all directions, making them less pronounced.

4.2 Hybrid LF-MRI & MPI Simulations

4.2.1 MPI Simulation

For MPI simulations, the simulated magnetic field maps are imported into an in-house MPI simulator in MATLAB. The receive coil is assumed to be ideal. Detailed information about the MPI simulator can be found in [17]. The MPI signal is modeled according to the MPI signal model described in Chapter 2. Noise is not incorporated in these simulations, as the operating settings of the MPI system remain unchanged. For the MPI image reconstruction, we employed a system matrix-based reconstruction method utilizing the Kaczmarz algorithm.

The simulations are carried out within a FOV of $25 \times 25 \times 15 \text{ mm}^3$, discretized with $0.2 \times 0.2 \times 0.2 \text{ mm}^3$ grids. For MPI simulations, 0.5 T m^{-1} selection field is created and the FFL is rotated with 3 degree-steps. Furthermore, 6.25 mT-peak drive field at 25 kHz is applied. Additionally, the same phantom illustrated in Fig. 4.1 is used in the simulations, where the vacancies are modeled to contain MNPs to be imaged via MPI.

4.2.2 Overlaid Image

Finally, the overlaid image obtained with B_0 field of 50 mT for the current hybrid system is compared with that from an ideal hybrid system in Fig. 4.6. For LF-MRI images, the pulse sequence parameters are the same as in the images for $B_0 = 50 \text{ mT}$ shown in Figure 4.4. Additionally, the function of each coil group and corresponding field values are given in Table 4.1.

Table 4.1: Function of each coil group for MPI and LF-MRI modes for hybrid imaging. For LF-MRI gradient fields, the listed values indicate gradient limits (G_{max}) that are chosen conservatively.

Coil Group	MPI		LF-MRI	
	Purpose	Applied Field	Purpose	Applied Field
C_x	Selection Field	500 mT m ⁻¹	G_y	90 mT m ⁻¹
C_y	Selection Field	500 mT m ⁻¹	G_x	90 mT m ⁻¹
C_{z1}	Focus Field	0	B_0	50 mT
C_{z2}	Drive Field	6.25 mT	G_z	60 mT m ⁻¹

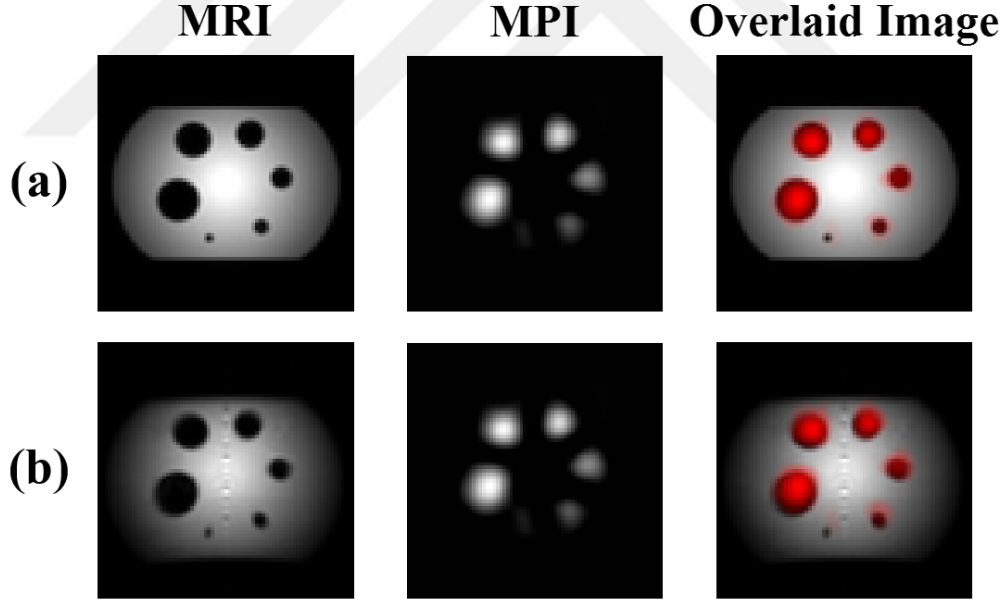


Figure 4.6: Reconstructed images for (a) ideal (i.e., with field inhomogeneities neglected) and (b) current hybrid systems (using measured field maps) for MRI mode (at $B_0 = 50$ mT, RF pulse BW = 35 kHz and readout BW = 250 kHz) and MPI modes, together with the overlaid images.

The results show that the current prototype system provides near-ideal performance for MPI. The LF-MRI image from the current system displays off-resonance-induced geometric warping, which can be fixed with unwarping methods.

Overall, the simulation study presented in this chapter indicates that the prototype hybrid MPI and LF-MRI scanner is capable of successfully performing MPI and low-field MRI with a proper selection of B_0 field strength, RF pulse duration, and bandwidths.

Chapter 5

Experimental Studies

In the previous chapters, with magnetic field characterization measurements and simulation studies, the capability of the hybrid scanner to perform LF-MRI with the addition of a Tx/Rx chain was shown. In this chapter, experimental studies demonstrating LF-MRI, MPI, and multimodal imaging performance of the system are provided.

5.1 LF-MRI Experiments

We begin the experimental studies to test the LF-MRI performance of the prototype system. For LF-MRI measurements, the C_{z2} coil group and receive coil of the MPI are removed, and the Tx/Rx chain for the LF-MRI is integrated. Note that because the C_{z2} coil group is removed, the associated slice-selective G_z gradients are disabled during imaging, leading to projection format images in LF-MRI mode.

5.1.1 Tx/Rx Chain of LF-MRI

Fig. 5.1 depicts the Tx/Rx chain employed within our configuration. A single solenoid coil (Pure Devices GmbH, Germany) serves dual purposes for transmission and signal reception, facilitated by a customized switch operating around 2 MHz (corresponding to B_0 field around 47 mT) and surrounded by an electromagnetic shield. Dividing the chain prior to the switch reveals two distinct sections: a transmit chain consisting of an RF waveform generator and RF amplifier, and a receive chain comprising a preamplifier and a data acquisition card (DAQ). To construct this chain, we employ a control unit (drive-1, Pure Devices GmbH, Germany) incorporating RF waveform generator, preamplifier, and DAQ, along with an RF amplifier (RF-200, Pure Devices GmbH, Germany), and the Tx/Rx switch (Pure Devices GmbH, Germany). This chain enables successful transmission of the RF pulse and reception of the LF-MRI signal.

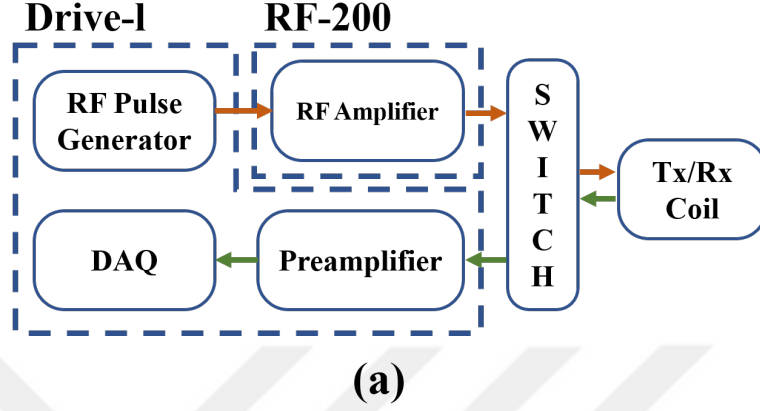


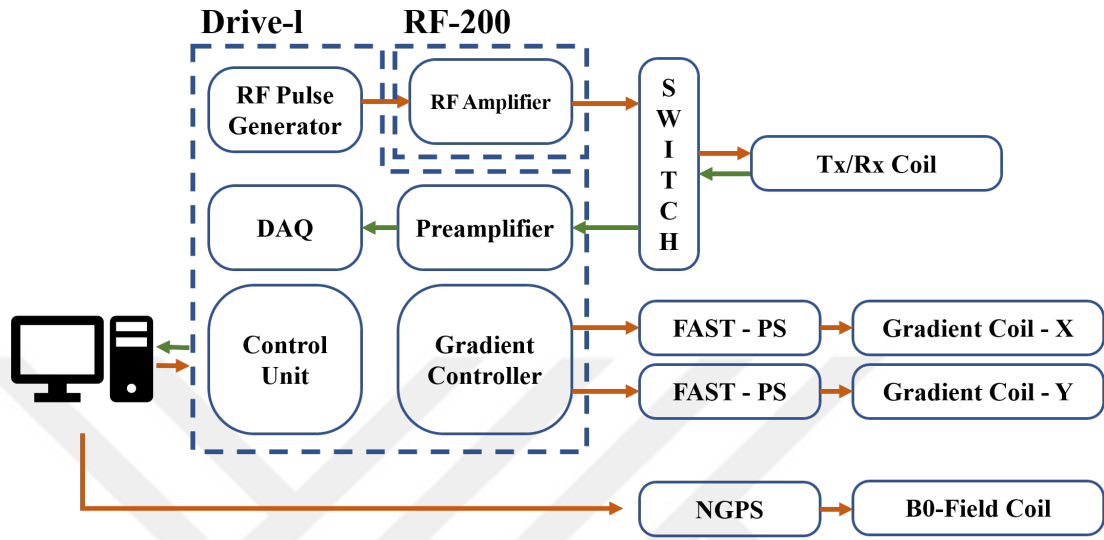
Figure 5.1: Tx/Rx chain of LF-MRI. (a) Schematic diagram and (b) a photo of the Tx/Rx chain.

5.1.2 Experimental Setup

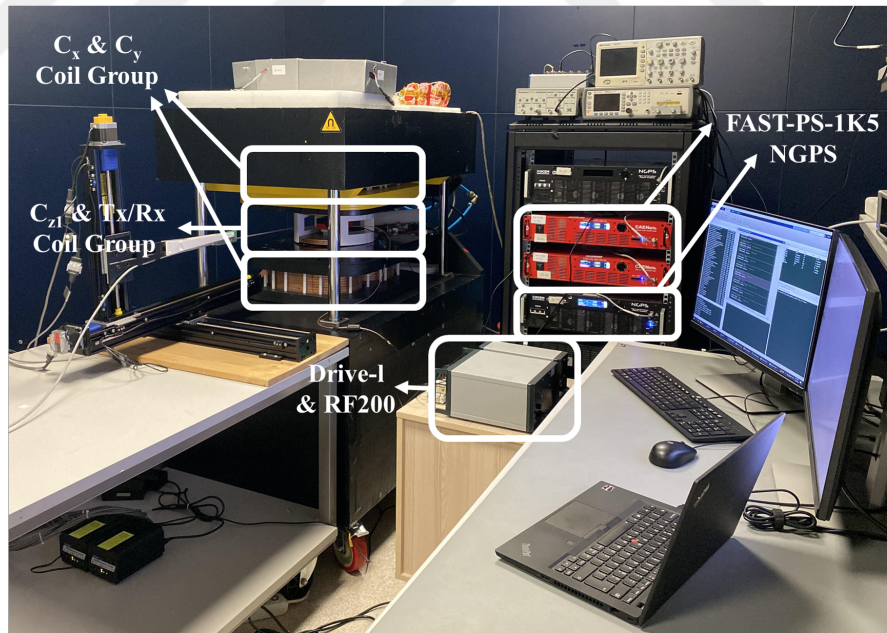
The experimental setup when the prototype hybrid scanner is operated in LF-MRI mode is shown in Fig. 5.2. Here, the Tx/Rx chain of the LF-MRI is configured as detailed in the preceding section. The timings of the RF pulses and data acquisition windows are regulated by the control unit (drive-l, Pure Devices GmbH, Germany) as defined in the corresponding pulse sequence. For the gradient coils, 1.5 kW bipolar power supplies (FAST-PS-1K5, Caen Els S.R.L., Italy) are employed due to the rationale explained in Chapter 3. The power supplies are operated in analog input mode, with respective current waveforms dictated

by the gradient control module of control unit in line with the implemented pulse sequence. The B_0 field is generated by using 10 kW power supply (NGPS, Caen Els S.R.L., Italy), with the coil current adjusted to yield a B_0 field of 50 mT. By controlling the power supply via MATLAB, the B_0 field is turned on before the pulse sequence is started. This arrangement enables MATLAB-based coding of the pulse sequences and their execution through the control unit.





(a)



(b)

Figure 5.2: Experimental setup for LF-MRI mode. (a) Schematic diagram and (b) photo of the prototype hybrid scanner operating in LF-MRI mode.

5.1.3 Phantom Preparation

For the experimental study, the phantoms are prepared following the recipes provided in [37]. The materials used in the development of the phantoms consist of 6.8 g of gelatin (gelatine 200 Bloom, food grade), 68 ml of deionized water, 29 ml of safflower oil, and 3.8 ml of dishwashing liquid.

The steps of the phantom preparation process are as follows:

1. Combine gelatin and deionized water in a glass beaker and heat the mixture to 85°C.
2. Allow the heated gelatin-water mixture to cool to 65°C.
3. Separately heat the safflower oil to 65°C.
4. Once both mixtures are at 65°C, add the dishwashing liquid, and stir the mixture with a magnetic stirrer until it cools down to 50°C.
5. Let the mixture polymerize at room temperature (approximately 25°C) for about 3.5 hours.
6. Finally, use the mixture to create phantoms in various shapes that can be employed in LF-MRI experiments.

As the material in this phantom is composed of water and oil, it is well-suited for mimicking human tissue in LF-MRI experiments. Moreover, it is quite easy to shape the phantom, which makes it very convenient for experimental use. In the subsequent sections, we will refer to this phantom as the tissue phantom.

5.1.4 Measurement of Relaxation Time Constants

The T_1 and T_2 relaxation time constants are essential in determining image contrast and tissue properties in MRI. Hence, we first measure these parameters for the prepared phantom material to understand the LF-MRI characteristics of the phantoms and determine suitable TE and TR values for the pulse sequences.

Spin-Lattice Relaxation (T_1) Time Constant: In order to determine the T_1 time constant of the phantoms, the inversion recovery method is utilized [38]. In this method, the spins are allowed to fully relax to their equilibrium magnetization along the z -direction (aligned with the B_0 field). Subsequently, a 180° RF pulse is applied to invert the magnetization of the spins to $-z$ -direction. After an inversion time of TI, a 90° RF pulse is applied (see Fig. 5.3), and the MRI signal is captured. In the subsequent TRs, this process is repeated for different inversion times. An exponential inversion recovery curve as a function of TI is fitted into the peak of the LF-MRI signals, with the time constant of the fitted exponential curve yielding the T_1 time constant.

Spin-Spin Relaxation (T_2) Time Constant: In order to determine the T_2 time constant of the phantoms, the CPMG (Carr-Purcell-Meiboom-Gill) method is utilized [38]. This method applies a 90° RF pulse to tip the spins onto the xy - plane. Following an interval of 1.5 ms, a series of 180° RF pulses are applied sequentially at intervals of 3 ms (see Fig. 5.3). As a result, signal echoes form in between subsequent 180° RF pulses, with TEs at multiples of 3 ms. Following each 180° RF pulse, the LF-MRI signal is recorded, and an exponential T_2 decay curve is fitted to the peak of the LF-MRI signals as a function of TE. The time constant of this fitted exponential curve provides the T_2 time constant.

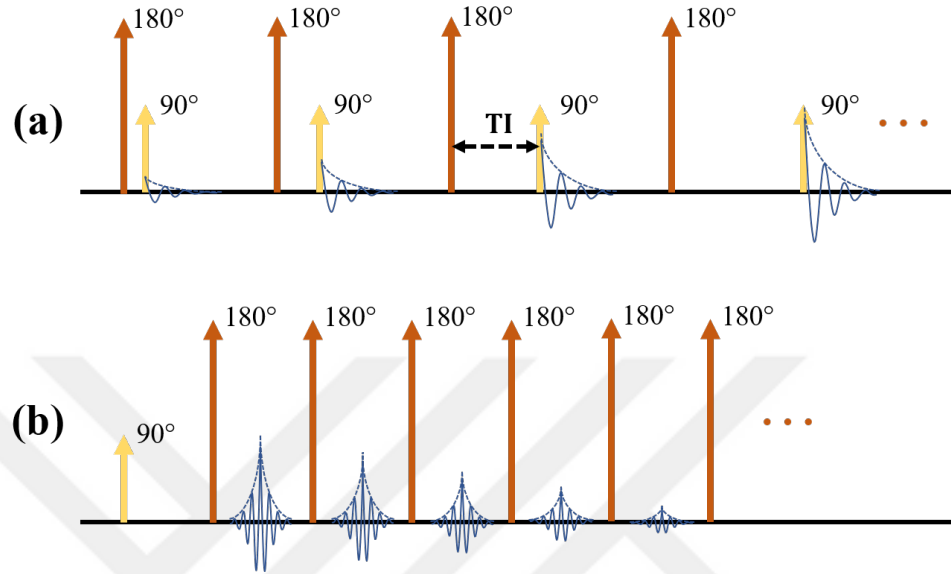


Figure 5.3: Pulse sequences used to measure T_1 and T_2 relaxation time constants. (a) Inversion recovery sequence for T_1 relaxation time measurement. (b) CPMG (Carr-Purcell-Meiboom-Gill) sequence for T_2 relaxation time measurement.

The T_1 and T_2 relaxation time measurement results of the tissue phantom and safflower oil are given in Fig. 5.4 and 5.5, respectively, and the estimated relaxation times are listed in Table 5.1.

Table 5.1: Measured values for T_1 and T_2 relaxation times for tissue phantom and safflower oil

Phantom Type	T_1 (ms)	T_2 (ms)
Tissue Phantom	583	72
Safflower Oil	87	46

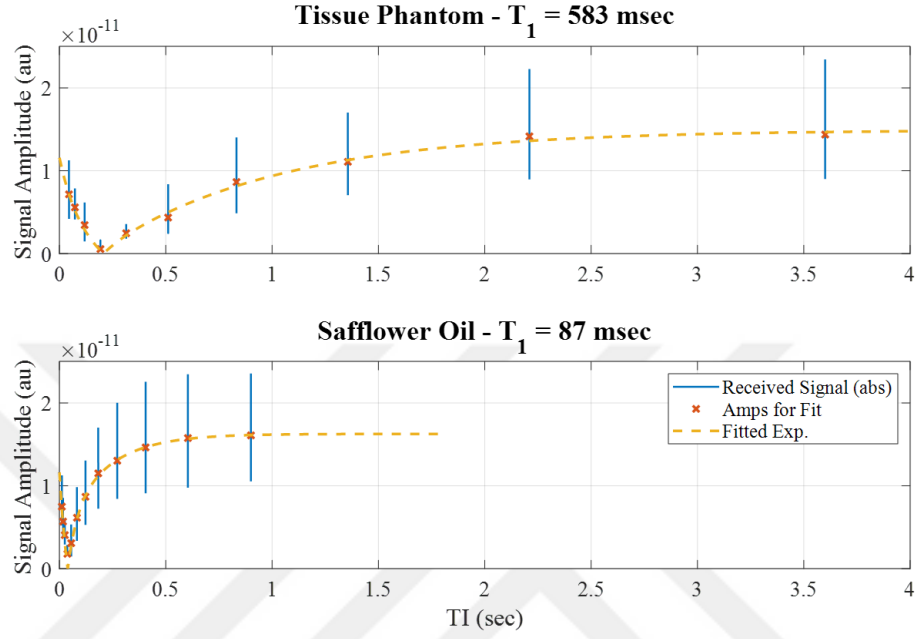


Figure 5.4: T_1 relaxation time measurement results for [Top] tissue phantom and [Bottom] safflower oil. TR is selected as 3000 ms and 500 ms, respectively.

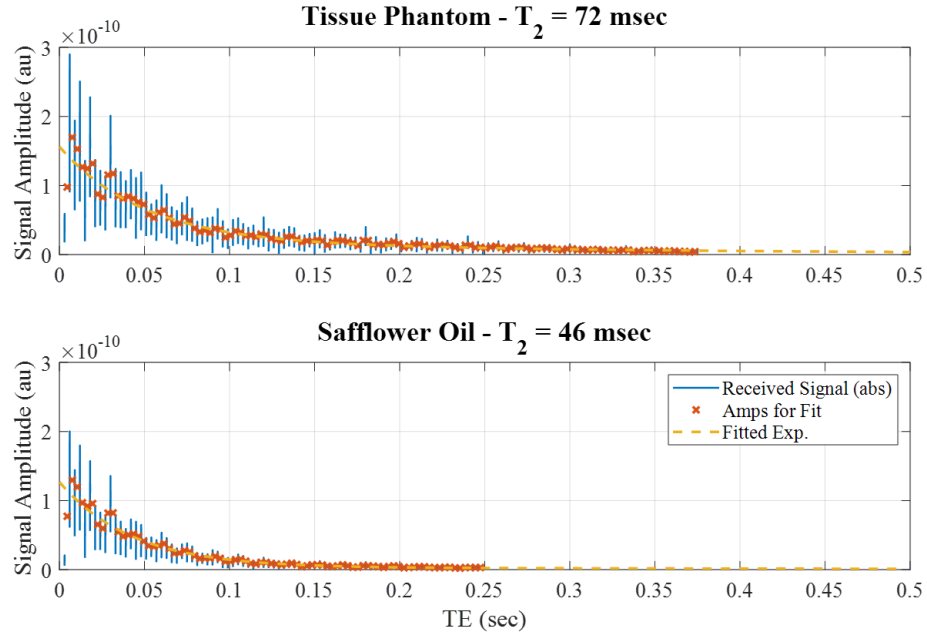


Figure 5.5: T_2 relaxation time measurement results for [Top] tissue phantom and [Bottom] safflower oil.

5.1.5 Imaging Experiments with Tissue Phantoms

After determining the T_1 and T_2 values of the phantoms, we proceed with obtaining 2D phantom images to test and verify LF-MRI performance of the system. In the following measurements, the phantoms are constructed from the same tissue phantom material, emphasizing our interest in assessing how accurately the LF-MRI images reflect the geometry of the object, rather than highlighting contrast variations. Also, the following measurements employ the same spin echo pulse sequence, with the relevant pulse sequence and imaging parameters detailed in Table 5.2.

Table 5.2: Pulse sequence and imaging parameters for phantom imaging experiments

Parameters	Value
TR (msec)	500
TE (msec)	14
FOV (mm^2)	34×32
Phase FOV	95 %
Resolution (mm^2)	0.55×1.05
Readout BW (kHz)	65
Acquisition Matrix	62×30
Image Matrix	72×72
Number of Averages	72
Scan Time (min)	18

In the imaging experiments, we first perform a prescan to accurately locate the phantom. Following this, the raw k-space data is acquired, followed by apodization and zero padding preprocessing steps. The apodization step (with 2D Gaussian filter) is utilized to smooth the images by reducing the amplitude of high-frequency elements to effectively minimize artifacts such as Gibbs ringing and truncation artifact. Then, zero-padding is applied to k-space data to increase image matrix size by filling high-frequency k-space regions with zeros. In the final step, we apply a 2D inverse Fourier transform to obtain the reconstructed image.

Four phantoms with different shapes are imaged, results of which are given as follows.

Tissue-Duo Phantom: The tissue-duo phantom has two cylindrical sections with approximate radius of 10 mm and height of 5 mm. The sections are separated by 5 mm. The imaging results for each reconstruction step are given in Fig. 5.6.

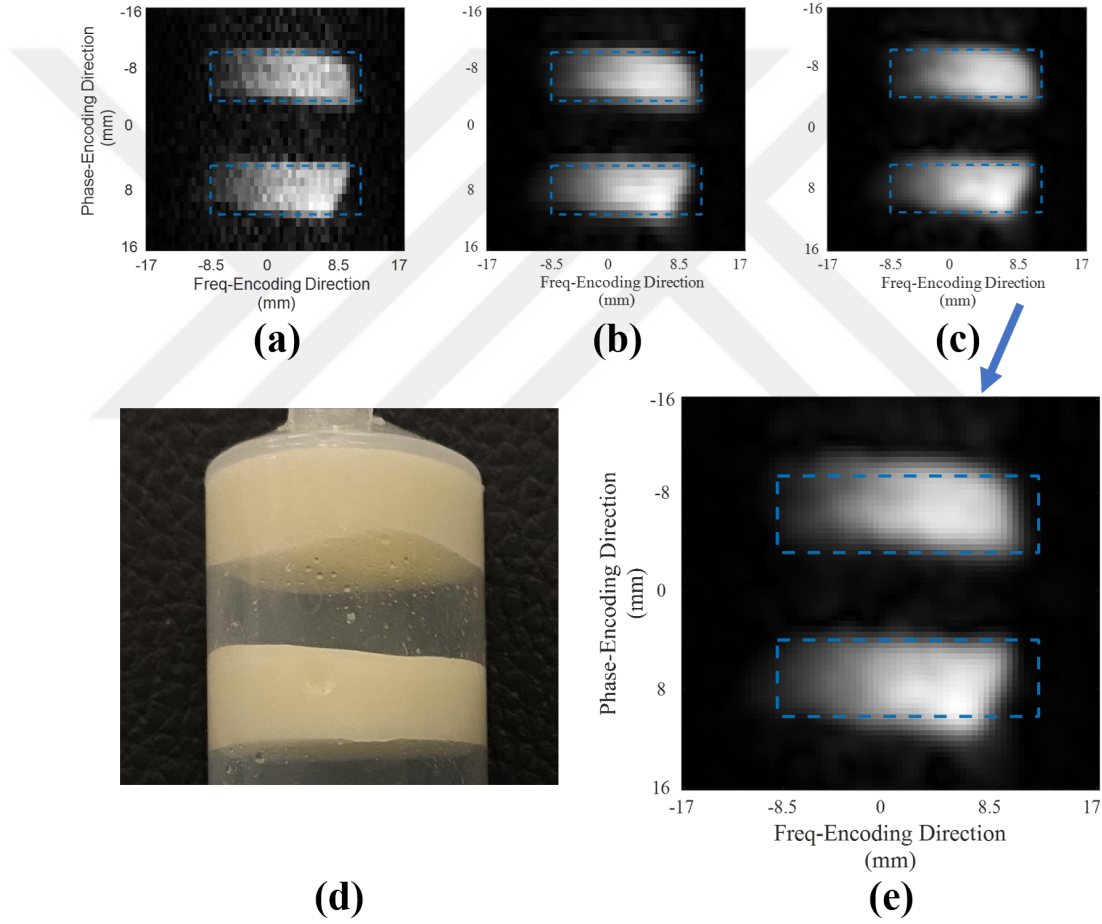


Figure 5.6: The reconstruction results of the tissue-duo phantom are as follows: (a) image reconstructed from raw k-space data, (b) with apodization applied, (c) with both apodization and zero-padding applied. (d) Photo of the tissue-duo phantom and (e) the final reconstructed MRI image. The blue dashed lines indicate the approximate shape, position, and size of the phantom.

Tissue-I Phantom: The tissue-I phantom is a rectangular phantom with dimensions of 20 mm in length and 10 mm in width. The photo and imaging result is of the phantom is given in Fig. 5.7.

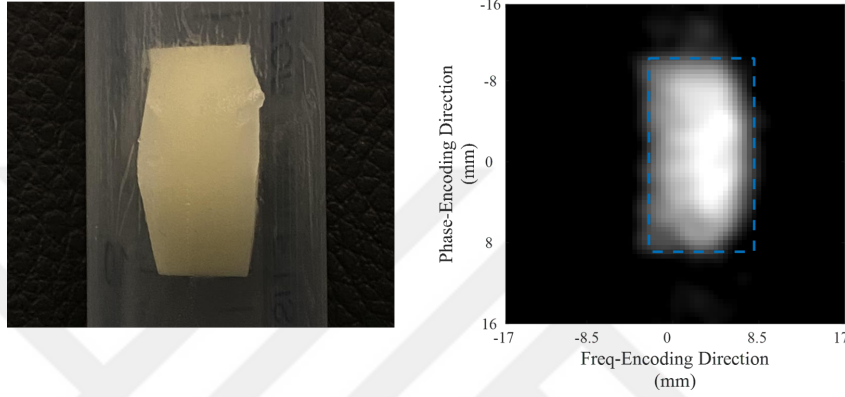


Figure 5.7: [Left] Photo of the tissue-I phantom and [Right] the final reconstructed MRI image. The blue dashed lines indicate the approximate shape, position, and size of the phantom.

Tissue-T Phantom: Tissue-T phantom involves a cylinder with a radius of 10 mm and a height of 5 mm and a rectangle with 20 mm in length and 4 mm in width, which are placed orthogonal to each other. Their projection has a T shape. The phantom photo and its reconstruction result is given in Fig 5.8.

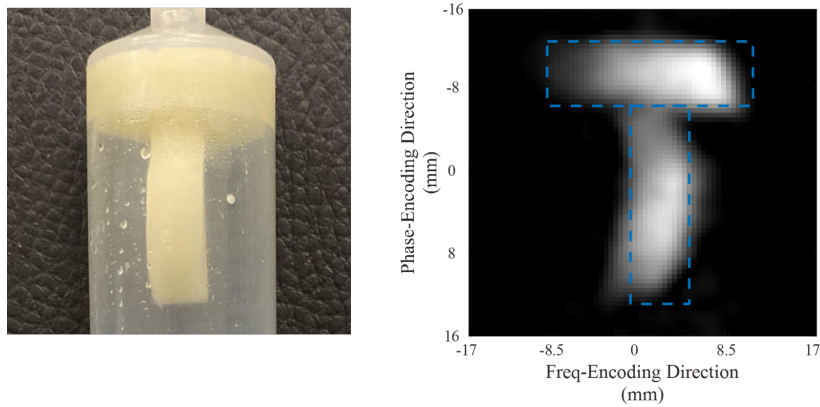


Figure 5.8: [Left] Photo of the tissue-T phantom and [Right] the reconstructed MRI image. The blue dashed lines indicate the approximate shape, position, and size of the phantom.

Tissue-O Phantom: The tissue-O phantom is a cylinder with a diameter of 20 mm and a central hole with a diameter of 6 mm. Its photo and reconstructed image is shown in Fig. 5.9.

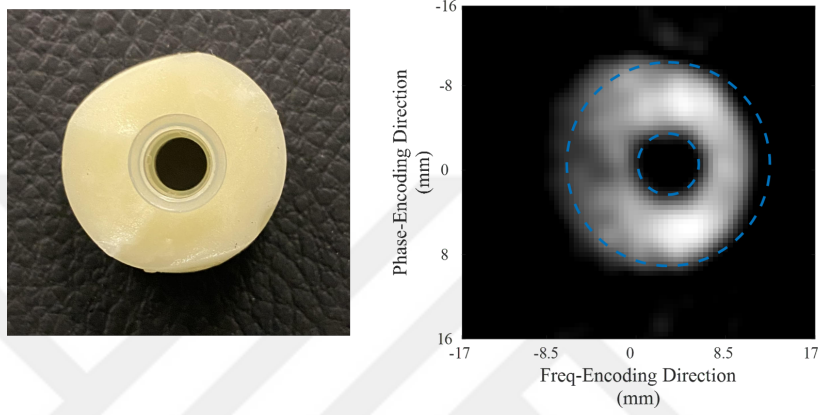


Figure 5.9: [Left] Photo and [Right] reconstructed MRI image of the tissue-O phantom. The blue dashed lines indicate the approximate shape, position, and size of the phantom.

Effects of Different Readout Bandwidths: To see the effects of readout bandwidth on the imaging performance, the tissue-O phantom is imaged at two different readout BW values of 30 kHz and 65 kHz. The resulting reconstructed images are shown in Fig. 5.10.

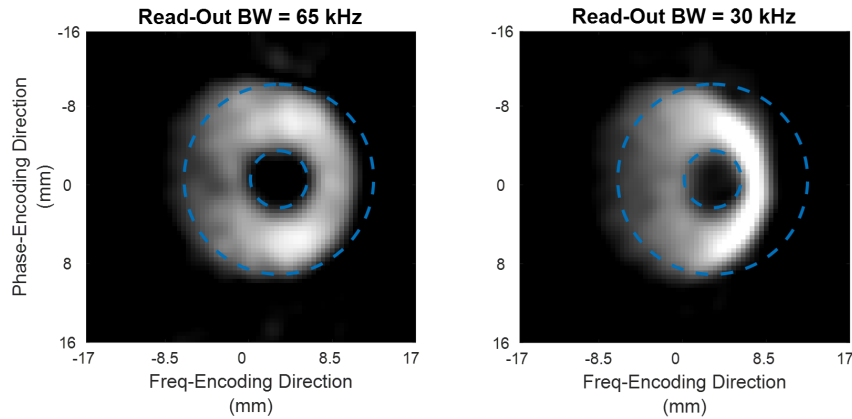


Figure 5.10: The reconstructed MRI images of tissue-O phantom with readout BW values of [Left] 65 kHz and [Right] 30 kHz.

The experimental imaging results with phantoms revealed that the geometry of the phantom can be accurately reconstructed in both the phase encoding and frequency encoding directions. However, a warping artifact caused by off-resonance effects is also noticeable in the frequency encoding direction. This artifact is more pronounced in the outer regions of the phantom where there is a greater phase accumulation due to the increased field inhomogeneity in those regions. Additionally, our experimental results revealed that the warping artifact becomes more severe with lower readout bandwidth, a finding consistent with our simulation results.

5.1.6 Imaging Experiments with Contrast Phantoms

Next, we acquire 2D MRI images of phantoms that comprise sections with different T_1 and T_2 relaxation times, to observe the contrast between these sections. The measurements utilize the same spin-echo pulse sequence, with the relevant pulse sequence and imaging parameters provided in Table 5.2.

In the experiments, the tissue-O phantom is used with an insertion of a PCR tube at its center (see Fig. 5.11). Three different phantoms are developed, using PCR tubes filled with safflower oil of 0.3 ml, SPION solution of 0.3 ml (Perimag, Micromod, Germany), or mixture of safflower oil and Perimag sample (50% Safflower oil - 50% Perimag by volume) with a total volume of 0.3 ml. The reconstruction results of these phantoms are illustrated in Fig 5.12.

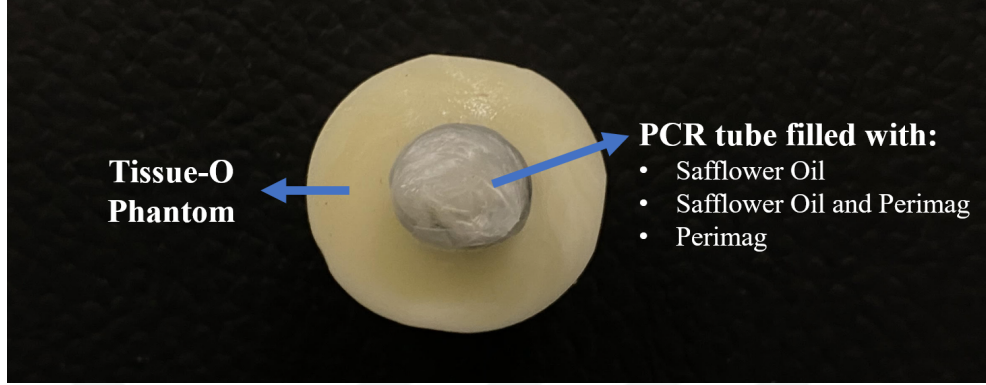


Figure 5.11: Contrast phantom design employed in imaging experiments. The outer part of the phantom consists of the tissue phantom material, with the same dimension and shape as the tissue-O phantom. At the center, a PCR tube is inserted filled with different materials to create contrast between the outer and inner parts of the phantom.

We used short TR and TE times (see Table 5.2), hence the obtained images are primarily T_1 -weighted images. The phantom with a PCR tube filled with safflower oil leads to an image whose center appears brighter (see Fig. 5.12(a)), as expected due to the lower T_1 of safflower oil. On the other hand, the center of the images appear dark for the phantoms with PCR tubes containing Perimag sample (see Fig. 5.12(b) and Fig. 5.12(c)), which is expected since the Perimag particles induce local T_2 shortening and cause negative contrast in the MRI signal.

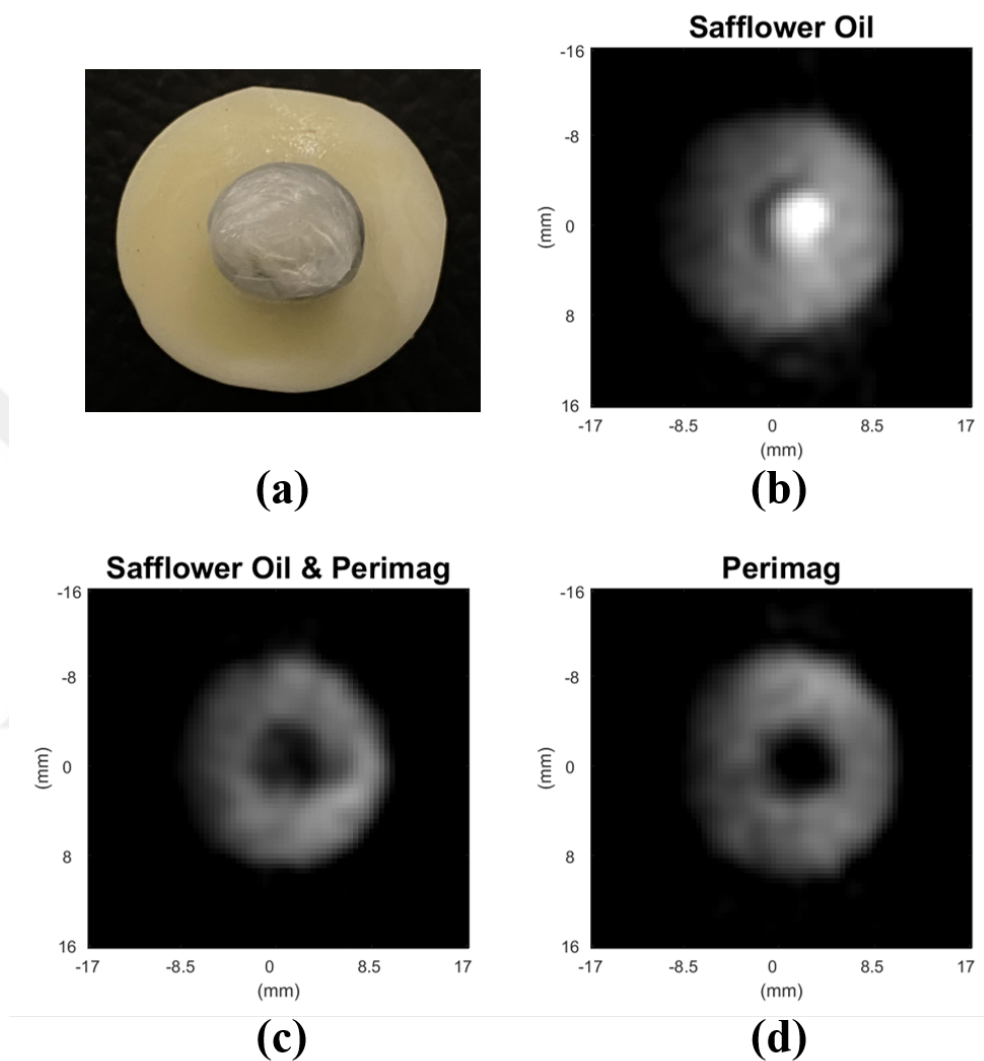


Figure 5.12: The reconstructed images of contrast phantoms. (a) Photo of the contrast phantom showing tissue-O phantom, with a PCR tube inserted at its center. MRI images for the cases when the PCR tube is filled with (b) safflower oil, (c) a mixture of safflower oil and Perimag sample, and (d) Perimag sample.

5.2 Multimodal Imaging Experiments

In this section, we present experimental results of multi-modality phantom measurements. These measurements utilize phantoms that consist of PCR tubes filled with Perimag sample, surrounded by a tissue phantom that imitates the anatomical background tissue. The objective is to image the tissue phantom with LF-MRI while capturing the distribution of Perimag sample using MPI.

5.2.1 LF-MRI Experiments

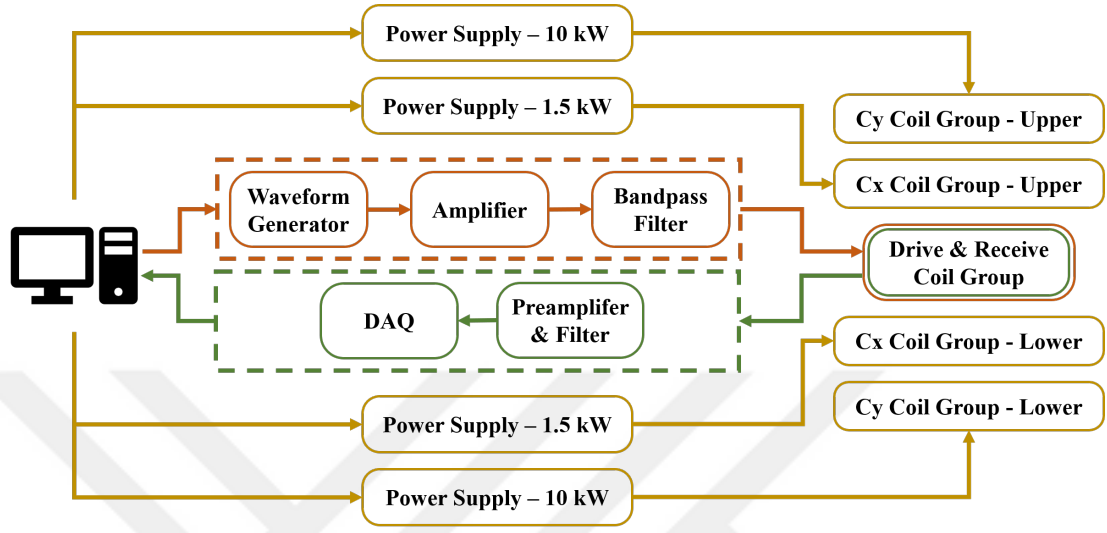
LF-MRI experiments are performed as explained in Section 5.1. The spin-echo pulse sequence is employed with the pulse sequence and imaging parameters provided in Table 5.3.

Table 5.3: Pulse sequence and imaging parameters for multimodal imaging experiments

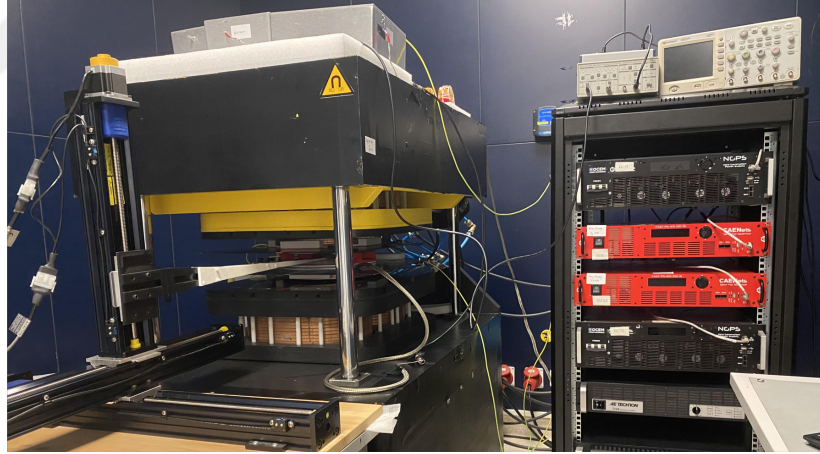
Parameters	Value
TR (msec)	500
TE (msec)	14
FOV (mm^2)	34×38
Phase FOV	112 %
Resolution (mm^2)	0.55×1.10
Readout BW (kHz)	65
Acquisition Matrix	62×35
Image Matrix	72×72
Number of Averages	72
Scan Time (min)	21

5.2.2 MPI Experiments

Experimental Setup: The experimental setup when the prototype hybrid scanner is operated in the MPI mode is illustrated in Fig. 5.13. The Tx/Rx chain of the LF-MRI is removed and C_{z2} coil group and receive coil of the MPI are integrated to the system. In order to generate the selection field, two 10 kW unipolar power supplies (NGPS, Caen Els S.R.L., Italy) are utilized to power C_y coil group, while 1.5 kW bipolar power supplies (FAST-PS-1K5, Caen Els S.R.L., Italy) are utilized to drive the C_x coil group. The desired waveform for the drive coil current is generated using a waveform generator (33500B, Keysight Technologies, CA, USA), and amplified with a power amplifier (7224, AE Techtron Inc, USA). At the amplifier output, a third order bandpass filter with notches configured at the second and third harmonics is employed to suppress the additional harmonics of the drive field. For the receive chain, the signal from the receive coil first passes through a bandstop filter to eliminate the first harmonic caused by direct coupling with the drive field. The signal is then amplified (gain = 50) and band-pass filtered (cutoffs: 10 kHz and 300 kHz) using an low-noise preamplifier (SR-560, Stanford Research Systems, MA, USA), then digitized at 2 MHz frequency using a DAQ (NI-6363 USB, National Instruments, USA) analog to digital converter module.



(a)



(b)

Figure 5.13: Experimental setup for MPI mode. (a) Schematic diagram and (b) photo of the prototype hybrid scanner operating in MPI mode.

Scanning Configuration: The currents of the C_x and C_y coil groups are adjusted to create a FFL at the $z = 0$ plane with a gradient of 0.25 T/m. The FFL is rotated from 0° to 177° with 3° increments, and imaging FOV of $20 \times 32 \text{ mm}^2$ is scanned using a 50-cycle sinusoidal drive field with a peak-to-peak amplitude of 7 mT and 24.3 kHz frequency. FFL is generated at each angle for 100 msec, and drive field waveform is applied for a 5 msec, which corresponds a

5% duty cycle to prevent the drive coil system from heating.

Image Reconstruction: The image reconstruction is performed using the system matrix reconstruction method. For system matrix measurements, SM phantom (see Fig. 5.14), filled with Perimag sample, is scanned inside a $24 \times 40 \text{ mm}^2$ FOV in 4 mm steps. The acquired signal for each position and FFL angle is transformed into frequency domain by using taking 1D Fourier transform, allowing for the selection of frequencies corresponding to the harmonics. Once the system matrix is established, phantom measurements are conducted by placing the phantom within the FOV. For Phantom-1, data is collected with an average of 10 measurements, while an average of 20 measurements is used for Phantom-2. In both the system matrix and phantom measurements, two reference (background) scans were taken: one at the start and another at the end with the sample removed from the imaging region. The averages of these reference scans are then subtracted from the acquired data.

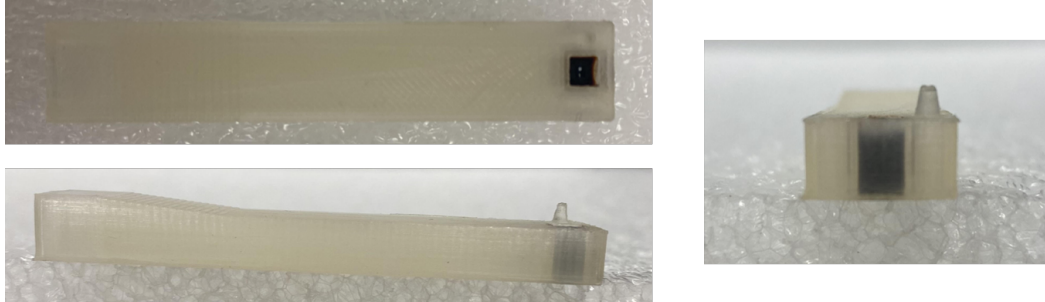


Figure 5.14: System matrix phantom. To obtain the system matrix, an undiluted MNP sample (Perimag, Micromod, Germany) of size $4 \times 4 \times 4 \text{ mm}^3$ is scanned inside the $24 \times 40 \text{ mm}^2$ FOV in 4 mm steps.

After obtaining the system matrix and phantom data, Alternating Direction Method of Multipliers (ADMM) method is utilized for the image reconstruction, in which a constrained optimization problem is formulated to minimize a linear combination of the l_1 -norm and total variation (TV) of the image as follows [18]:

$$\begin{aligned} \arg \min_{\mathbf{x}} \quad & \alpha \|\mathbf{x}\|_1 + (1 - \alpha) TV(\mathbf{x}) \\ \text{s.t.} \quad & \|\mathbf{Ax} - \mathbf{b}\|_2 < \epsilon, \end{aligned} \tag{5.1}$$

where $TV(\cdot)$ is total variation function, α is a weighting factor between l_1 -norm and TV, and ϵ is the bound on the l_2 -norm of noise. The parameters α and ϵ are determined through trial and error to achieve the best image quality. Details of the algorithm can be found in [18].

5.2.3 Multimodal Imaging Results

In the first experiment, we utilize the same contrast phantom as in the previous experiments, which includes a PCR tube filled with Perimag sample (see Fig. 5.11), called Phantom-1. The imaged phantom along with its corresponding reconstruction results for LF-MRI and MPI are presented in Fig. 5.15. Additionally, an overlaid image is obtained by merging the LF-MRI and MPI reconstruction results (see Fig. 5.15), where the MPI image is displayed in red color.

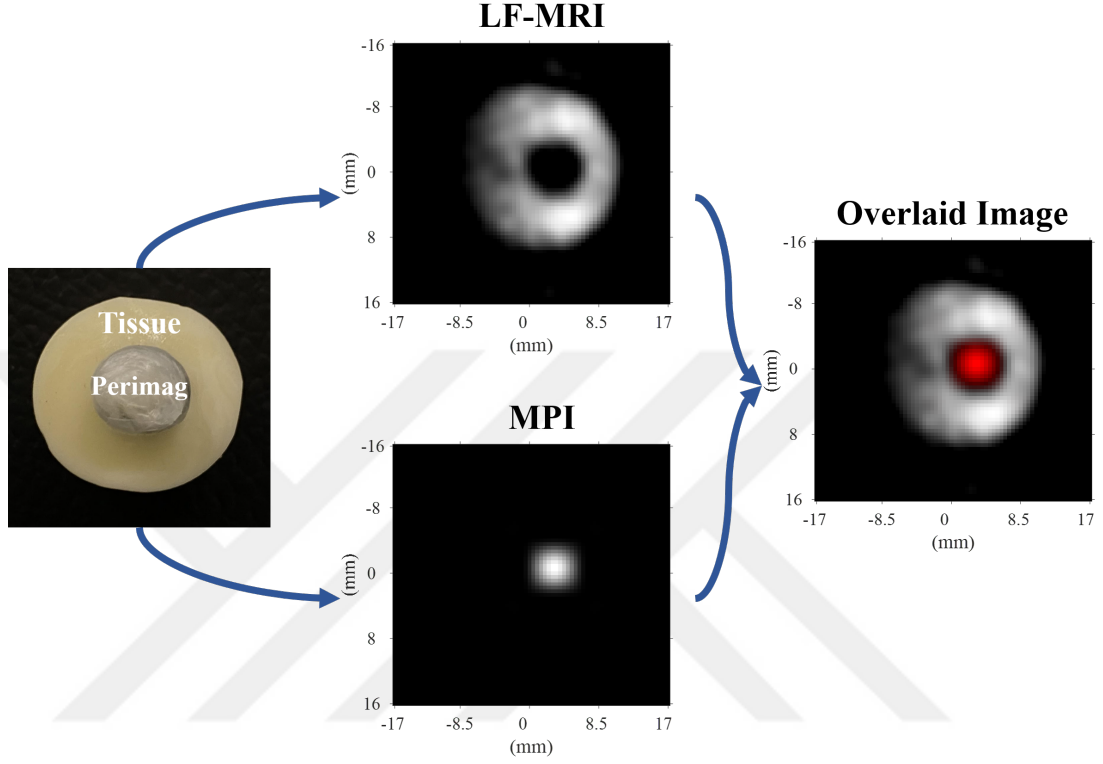


Figure 5.15: The multimodal imaging phantom consists of two parts: tissue phantom material and Perimag sample. The LF-MRI image effectively captures the tissue phantom, while the MPI image displays Perimag section of the phantom. Finally, the overlaid image combines the tissue phantom visualization from the LF-MRI image with the Perimag sample details from the MPI image.

For the second experiment, we employ a wider tissue phantom with maximum dimensions of $28 \text{ mm} \times 20 \text{ mm}$ that contains two 5 mm diameter PCR tubes filled with Perimag samples, called as Phantom-2. The Phantom-2 along with its corresponding reconstruction results for LF-MRI and MPI are presented in Fig. 5.16. Additionally, overlaid image is obtained by combining the LF-MRI and MPI reconstruction results (see Fig. 5.16).

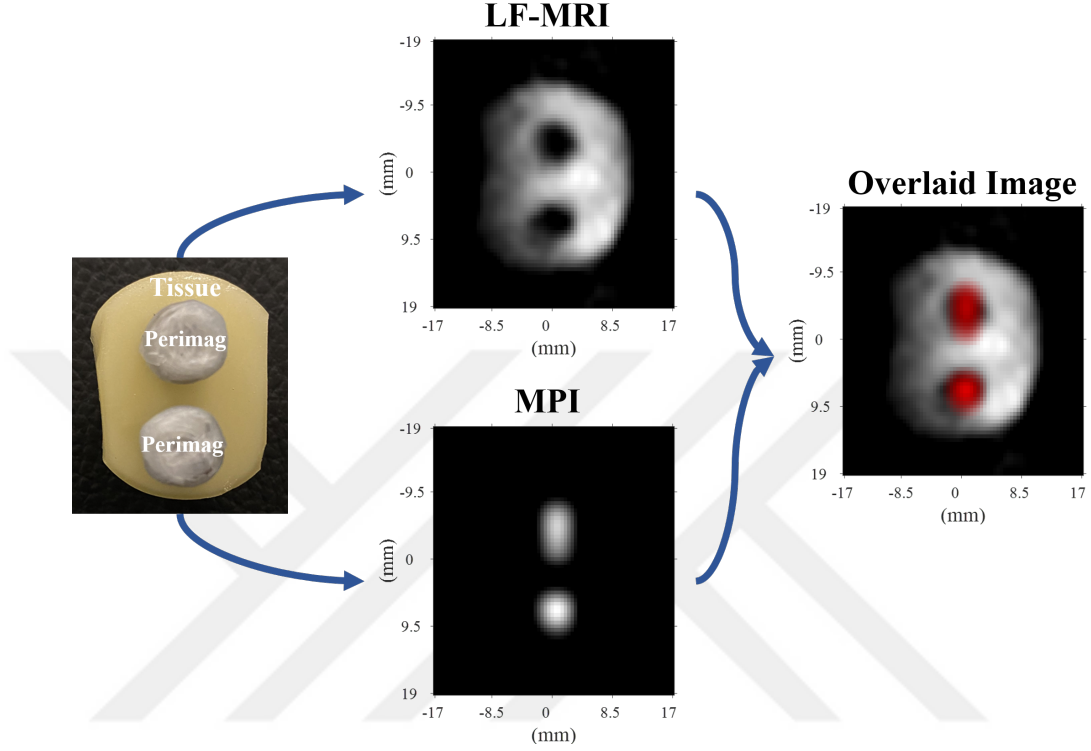


Figure 5.16: [Left] The phantom design utilized in multimodal imaging experiments is composed of the tissue phantom material and contains two PCR tubes inserted within it. These PCR tubes are filled with Perimag samples. [Middle] LF-MRI and MPI images for the phantom, and [Right] the overlaid image. The LF-MRI image effectively captures the tissue phantom, yet warping artifact remains in the frequency encoding direction. On the other hand, the MPI image distinctly displays the two dots representing the Perimag section of the phantom. Consequently, we have the overlaid image, in which the detailed representation of the distribution of the Perimag sample is provided via MPI, while the structure of the tissue phantom is provided via LF-MRI.

5.2.4 Discussion

In our multimodality imaging experiments, we utilized two phantoms comprising both tissue phantom and Perimag samples. The phantoms were imaged using both MPI and LF-MRI. The MPI scan provided the distribution of the Perimag

samples. However, since the tissue phantom does not generate any MPI signal, it is not visible in the MPI image. On the other hand, the LF-MRI mode effectively captured the structure of the tissue phantoms. As a result, we obtained an overlaid image that presents a comprehensive view: the distribution of the Perimag sample was provided through MPI, while the structure of the tissue phantom was obtained by LF-MRI. These findings highlight the capability of performing each imaging technique effectively with our prototype system.



Chapter 6

Conclusion

This thesis introduced a novel preclinical-size hybrid MPI-LF MRI system, in which the distribution of the MNPs is imaged with high contrast and sensitivity via MPI while providing anatomical information through LF-MRI. The MPI performance of the system was validated through simulation studies and experimental works. First, we conducted feasibility studies for LF-MRI by analyzing the magnetic fields of the system to determine their suitability for LF-MRI applications. The results showed that the magnetic field properties were comparable with existing literature, confirming that the system is suitable for LF-MRI. Following this assessment, we developed an MRI simulator to investigate system-induced deviations, revealing that adjusting the B_0 field strength and pulse sequence parameters, such as readout and RF BWs, is crucial for achieving high quality LF-MRI images. Subsequently, the Tx/Rx chain of the LF-MRI (the only missing component in the prototype MPI system that the hybrid system builds on), was integrated into the system, and LF-MRI performance was evaluated experimentally. The experiments indicated that the reconstructed images successfully captured the shapes of the phantoms and the contrast differences among various materials. Finally, a multimodal phantom was created, allowing to perform both MPI and LF-MRI. In the resultant images, the phantom parts designed to mimic human tissue were imaged using LF-MRI, while the SPION distributions were visualized via MPI. In conclusion, this research demonstrates, through both

simulations and experiments, the capability of the proposed hybrid scanner to successfully perform MPI and LF-MRI.

The coil configuration of the proposed hybrid system follows an open-sided design, except for the Tx/Rx coil of the MRI, where a solenoid coil is utilized for the experimental studies. This coil can be replaced with a surface coil [19], enabling the development of an open-sided hybrid system.

The system can also be enhanced with further studies, including:

1. **Electronic switching between the modalities:** Currently, we physically swap between the C_{z2} coil group and receive coil of MPI and the Tx/Rx coil of LF-MRI to transition between modalities. Integrating these coil groups within the system together would allow for electronic switching between the MPI and LF-MRI modes.
2. **Application of slice-selective gradient field for LF-MRI:** Because the dimensions of the Tx/Rx coil of LF-MRI is not compatible with the C_{z2} coil group, a slice-selective gradient field is not applied, leading to projection format LF-MRI images. Note that projection format imaging may be sufficient for providing an anatomical references for the acquired MPI images. Implementing G_z gradient field using C_{z2} coil group would expand the imaging capabilities of LF-MRI to 2D slice imaging and 3D volumetric imaging format.
3. **Improving the homogeneity of the B_0 field:** The current system exhibits an inhomogeneity level of approximately 2000 ppm for a circular FOV with a diameter of 20 mm. By adding a B_0 shim coil or redesigning the C_{z1} coil group, B_0 field homogeneity can be improved to reduce the warping artifacts and the signal loss due to dephasing. Additionally, this improvement would allow for an expansion of the FOV in conjunction with the implementation of a larger bore Tx/Rx coil for LF-MRI.

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