

EFFECTS OF SCANNING AND RECONSTRUCTION PARAMETERS ON IMAGE QUALITY IN MAGNETIC PARTICLE IMAGING

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By
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Effects of Scanning and Reconstruction Parameters on Image Quality
in Magnetic Particle Imaging

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January 2018

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

EFFECTS OF SCANNING AND RECONSTRUCTION PARAMETERS ON IMAGE QUALITY IN MAGNETIC PARTICLE IMAGING

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M.S. in Electrical and Electronics Engineering

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Magnetic particle imaging (MPI) is a novel medical imaging modality, based on the magnetization of the superparamagnetic iron oxide nanoparticles. In MPI, an external magnetic field called the drive field is applied to excite the nanoparticles. The link between the image quality and the drive field parameters is complex, as nanoparticle behavior changes with the drive field parameters. In addition, the maximum applicable drive field strength is limited by human safety restrictions. Recent studies have shown that the resolution improves at low drive field amplitudes and SNR enhances as drive field frequency increases. Other studies have confirmed that scanning at frequencies as high as 150 kHz is feasible for human-size MPI scanners. However, how the image quality is affected by drive field parameters, especially for high frequencies around 150 kHz, was not investigated. This thesis investigates the effects of the drive field parameters on the image quality in MPI with relaxometer experiments. The effects of the safety limits are also explored across different drive field frequencies via simulations. The results provide important insight in determining the optimal drive field parameters for safe MPI scanners. This thesis also introduces a new method for improving the image quality in MPI. MPI images can suffer from asymmetric hazing and irregular trending artifacts when nanoparticle response is delayed due to relaxation effects. This thesis proposes a new method based on averaging of relaxation effects from negative and positive half-cycles of the MPI signal, combined with a Savitzky-Golay detrending filter. Both experimental and simulation results demonstrate a significant improvement in image quality.

Keywords: Magnetic Particle Imaging, Drive Field Parameters, Image Reconstruction, Magnetic Field Safety Limits.

ÖZET

TARAMA VE GERİÇATIM PARAMETRELERİNİN MANYETİK PARÇACIK GÖRÜNTÜLEMEDE GÖRÜNTÜ KALİTESİNE ETKİLERİ

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Manyetik parçacık görüntüleme (MPG), süperparamanyetik demir oksit nanoparçacıkların mıknatıslanmasına dayanan yeni bir tıbbi görüntüleme yöntemidir. Nanoparçacıkların uyarılması için eksitasyon alanı adı verilen bir manyetik alan uygulanır. Görüntü kalitesi ve eksitasyon parametreleri arasındaki bağ karmaşıktır; çünkü nanoparçacık davranışı eksitasyon parametreleri ile değişir. Ek olarak, eksitasyon şiddeti, insan boyutundaki MPG tarayıcıları için güvenlik kısıtlamaları ile sınırlıdır. Son çalışmalar, düşük eksitasyon genliklerinde çözünürlüğün arttığını göstermiştir ve eksitasyon frekansı arttıkça SGO artar. Diğer çalışmalar 150 kHz'e kadar yüksek frekanslarda taramanın insan boyutundaki MPG tarayıcıları için mümkün olduğunu doğrulamıştır. Öte yandan, görüntü kalitesinin eksitasyon parametreleriyle nasıl etkilendiği, özellikle 150 kHz civarındaki yüksek frekanslar için araştırılmamıştır. Bu tezde, relaksometre deneyleri ile eksitasyon parametrelerinin görüntü kalitesi üzerindeki etkileri araştırılmıştır. Güvenlik sınırlarının etkileri de farklı eksitasyon frekansları için benzetimlerle incelenmiştir. Sonuçlar, güvenli MPG tarayıcıları için en uygun eksitasyon parametrelerini belirlemede önemli bilgiler sağlar. Bu tez, görüntü kalitesini artırmak için yeni bir geriçatım tekniği de sunmaktadır. MPG görüntüleri, relaksasyon etkileri nedeniyle asimetrik bulanıklık ve düzensiz tırmanma artifaktlarından muzdariptir. Bu tez, Savitzky-Golay filtreleme ile, MPG sinyalinin negatif ve pozitif yarım periyotlarının relaksasyon etkilerinin ortalamasına dayanan yeni bir yöntem önermektedir. Deney ve benzetim sonuçları görüntü kalitesinde önemli bir iyileşme göstermektedir.

Anahtar sözcükler: Manyetik Parçacık Görüntüleme, Eksitasyon Parametreleri, Görüntü Geriçatımı, Manyetik Alan Güvenlik Sınırları.

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Contents

1	Introduction	1
1.1	Related Work	2
1.2	Motivation and Contribution	3
1.3	Organization of Thesis	4
2	Overview of Magnetic Particle Imaging	6
2.1	Fundamentals of MPI	6
2.1.1	Signal Generation and Acquisition	6
2.1.2	Image Reconstruction	11
2.2	Magnetic Fields and Hardware Requirements	13
2.2.1	Drive Field	13
2.2.2	Receive Coil and Receive Chain	13
2.2.3	Additional Fields or Robot Movement	14
2.3	Relaxation Effect	14

2.4	Safety Concerns	16
2.4.1	Specific Absorption Rate (SAR)	17
2.4.2	Peripheral Nerve Stimulation (PNS)	18
3	Effects of Drive Field on Image Quality	20
3.1	Experimental Setup and Methodology	20
3.1.1	Relaxometer Setup	20
3.1.2	Relaxometer Measurements	24
3.1.3	Point Spread Function (PSF) Formation	25
3.2	Relaxometer Results	25
3.3	Simulation Results	31
3.3.1	Nanoparticle Diameter Estimation	31
3.3.2	Simulations Based on Relaxometer Results	31
4	Effects of Reconstruction Parameters	34
4.1	Averaging of Negative and Positive Half-Cycles	36
4.2	Detrending using Savitzky-Golay Filter	36
4.2.1	Simulation Results	37
4.3	Combining Averaging and Detrending	39
4.3.1	Experimental Results	42

5	Effects of Safety Limits on Image Quality	44
5.1	Simulation Parameters	44
5.1.1	Nanoparticle Diameter Estimation	45
5.1.2	Simulation Results	46
6	Conclusion	53
A	Derivation of Particle Diameter Estimation Formula	60

List of Figures

2.1	Schematic of the direct feedthrough problem.	7
2.2	Magnetization of the SPIONs when an external magnetic field is applied can be modeled via the Langevin function. To acquire signal from the nanoparticles, their magnetization has to be in the dynamic region.	8
2.3	Permanent magnet configuration for generating selection field magnets are in Maxwell configuration.	9
2.4	Magnetization of the SPIONs can be described by a Langevin function as in Figure 2.2. Its derivative gives the PSF of the MPI system. Full width at half maximum (FWHM) of the Langevin function, i.e., resolution of a native MPI system, is approximately 4.16. [1]	10
2.5	The resolution of the MPI images improves as the gradient strength and the nanoparticle size increase [1].	12
2.6	3-section gradiometer type receive coil is demonstrated in relation with the drive coil and the sample. Red arrows indicate the direction of the windings for the sections of the receive coil.	14
2.7	The effect of the relaxation phenomena on the MPI images [2] The direction of blurring changes with the scanning direction	15

2.8	Magnetostimulation limit for the drive field in MPI up to 150 kHz is plotted for the human torso [3].	19
3.1	Relaxometer setup.	21
3.2	(a) Impedance matching circuit for 10 kHz drive field frequency (b) Impedance matching circuit for 25 kHz drive field frequency (c) Impedance matching circuit for 148.5 kHz drive field frequency	23
3.3	(a) Drive coil (b) gradiometer type receive coil, (c) nanoparticle sample. When the relaxometer setup is operating, the receive coil is placed inside the drive coil and the nanoparticle sample is placed inside the receive coil.	24
3.4	Flowchart of the relaxometer setup	24
3.5	PSFs were formed by using all available odd harmonics, under 2 drive field strengths, 5 mT and 10 mT. The PSFs which were formed by using the negative half-cycle and the positive half-cycle are shown separately.	26
3.6	PSFs were formed by using all the available odd harmonics, under 3 drive field strengths, 5 mT, 7 mT, and 10 mT. The PSFs that were formed from the positive half-cycle are shown. FWHM values for these PSFs are given in Table 3.1.	26
3.7	PSFs were formed by using the odd harmonics up to 6th, under 2 drive field strengths, 5 mT and 10 mT. The PSFs that were formed by using the negative half-cycle and the positive half-cycle are shown separately.	27
3.8	PSFs were formed by using only the odd harmonics up to the 6th harmonic, under 3 drive field strengths, 5 mT, 7mT and 10 mT. The PSFs, which were formed from the positive half-cycle are shown. FWHM values for these PSFs are given in Table 3.2. . . .	28

3.9	Decay of the frequency components in dB.	30
3.10	2D resolution phantom with dimensions 1 cm x 15.3 cm. Line sources are of 1 mm width and they are separated by 3 mm, 5 mm, and 7 mm from their centers.	32
3.11	2D MPI images at 10 kHz, 25 kHz, and 148.5 kHz drive field frequency and at 10 mT drive field strength.	33
4.1	Simulated MPI images of the resolution phantom. For the ideal case, the relaxation effect was ignored. MPI images with the relaxation effect, obtained from the positive half-cycle (POS) and the negative half-cycle (NEG) are shown. Comparison of the centerlines is given at the bottom. Trending and asymmetric hazing artifacts are observed for POS and NEG images.	35
4.2	FWHM of the detrended MPI images for different frame lengths in Savitzky-Golay (SG) filters. The change in the FWHM of the MPI image was simulated for different overlap percentages of pFOVs and for different drive field amplitudes. Here, frame length=0 denotes the case when detrending was not applied.	38
4.3	Standard x-space reconstruction compared with possible combinations of averaging and detrending techniques, for SNR=100. The effects of detrending was tested for negative, positive, and averaged images. In addition, the ordering of the operations were investigated. The detrended results are provided in the right column.	40
4.4	Standard x-space reconstruction compared with possible combinations of averaging and detrending techniques, for SNR=2. The effects of detrending was tested for negative, positive, and averaged images. In addition, the ordering of the operations were investigated. The detrended results are provided in the right column.	41

4.5	PSNR values of the images under different noise levels.	42
4.6	(a) The MPI Scanner developed in our lab. (b) The standard x-space reconstructed MPI images from negative and positive half-cycles.	43
4.7	Standard x-space reconstruction compared with possible combinations of averaging and detrending techniques for the experimental data. The effects of detrending was tested for negative, positive, and averaged images. In addition, the ordering of the operations were investigated. The detrended results are provided in the right column.	43
5.1	Estimated particle distributions for Resovist and UW33 SPIONs .	46
5.2	2D simulation results for (a) the resolution phantom at 25 kHz. The results (b) at a high drive field strength of 30 mT and (c) at the safety limit of 7.6 mT.	47
5.3	Centerlines for the simulated 2D images. (a) Comparison of images at a high drive field strength 30 mT and the safety limit of 7.6 mT at 25 kHz. (b) Comparison of images at the safety limits at two different frequencies, 4.5 kHz and 25 kHz. For reference, the without relaxation effects is also shown. (8 cm of 12 cm).	48
5.4	1D simulation results of the resolution phantom. (a) Comparison at 25 kHz for Resovist. (b) Comparison at safety limits for Resovist. (c) Comparison at 25 kHz for UW33. (d) Comparison at safety limits for UW33. (e) Comparison at 25 kHz for Resovist at low SNR. (f) Comparison at safety limits for Resovist at low SNR.	49
5.5	2D simulation of the resolution phantom with Resovist at safety limits for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz. . .	51

5.6	2D simulation of the resolution phantom with UW33 at safety limits for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz. . .	51
5.7	2D simulation of the resolution phantom with Resovist at 30 mT for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz.	52
5.8	2D simulation of the resolution phantom with UW33 at 30 mT for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz.	52

List of Tables

3.1	FWHM of the PSFs in Figure 3.5 and Figure 3.6 in [mT]	25
3.2	FWHM of the PSFs in Figure 3.7 and Figure 3.8 in [mT]	28
3.3	Relaxation and effective particle diameter estimations derived from relaxometer experiment results at 7 mT:	31
3.4	Relaxation and effective particle diameter estimations derived from relaxometer experiment results at 10 mT:	32
5.1	Relaxation time constants for Resovist SPIONs at 4.5 kHz and 25 kHz, at magnetostimulation safety limits and an additional test field	45
5.2	Relaxation time constants for UW33 SPIONs at 4.5 kHz and 25 kHz, at magnetostimulation safety limits and an additional test field	45

Chapter 1

Introduction

Magnetic particle imaging (MPI), first introduced in 2005, is a novel imaging modality that detects and localizes the spatial distribution of the superparamagnetic iron oxide nanoparticles (SPIONs) [4]. MPI is a very promising tomographic imaging modality with the advantages of high sensitivity, high temporal resolution, and background signal suppression. It is expected that, the sensitivity of MPI may exceed that of Magnetic Resonance Imaging (MRI) by several orders [5, 6, 7]. Contrary to Computed Tomography (CT) or X-Ray, MPI is free of ionizing radiation; and contrary to Positron Emission Tomography (PET) or Single Photon Emission Computed Tomography (SPECT), MPI is free of radioactivity. SPIONs are clinically approved non-toxic tracer materials. Unlike gadolinium and iodine based tracers that are being used as contrast agents in MRI and X-Ray, iron oxide nanoparticles are safe for patients that suffer from chronic kidney disease (CKD).

Application areas of MPI include, but are not restricted to, cardiovascular imaging and intervention, neurovascular medicine, inflammation, metabolic research, cancer diagnosis, brain injury detection, perfusion imaging, and in vivo tracking of magnetically labeled cells [8, 9, 10, 11].

1.1 Related Work

MPI is a rather new tomographic imaging modality. In 2005, MPI was proposed for the first time [4]. In 2009, first real-time 3D in-vivo MPI images were shown [12]. There have been extensive contributions to MPI since its first introduction, as MPI is still in a rapid development phase.

Initially, MPI has evolved around the tracers that were already in use and proven to be safe for clinical use. Image quality and resolution in MPI are highly dependent on nanoparticle properties. Hence, there has been extensive effort in tailoring tracer materials, so that they are bio-compatible and they provide a better fit to MPI. It was shown that with the tailored iron oxide tracers, the image quality of MPI can be significantly improved [13].

Although nanoparticle properties are important in determining the image quality in MPI, the image reconstruction process is also very crucial. There are two main reconstruction methods in MPI: system matrix (harmonic-space) reconstruction and x-space reconstruction. In the system matrix approach, an extensive calibration scan is needed prior to the imaging process. For this calibration, a point-source phantom is placed at every possible pixel location in the field-of-view (FOV) and the measurements from each pixel location are saved as a matrix. This matrix is composed of frequency response of a point-source phantom in each and every location. Then, the constructed system matrix is used to reconstruct the image via solving an inverse problem. In the x-space approach, a calibration process is not required. The image is reconstructed by velocity compensation followed by a gridding step [14]. This method is faster and computationally less expensive than the system-matrix reconstruction, as storage of a huge matrix and solution of an inversion problem are not required in the x-space approach. In this thesis, the x-space reconstruction method was considered.

While a human MPI scanner does not exist yet, human preclinical experiments are being conducted on phantoms or on small animals. Scaling the preclinical

MPI scanners to human-size requires the investigation of both the feasibility of the scanner of that size and the human safety limits on the applied external magnetic fields. In the recent studies, the specific absorption rate (SAR) and magnetostimulation were investigated for the alternating magnetic fields in the kHz-range that are relevant to MPI. As a brief summary, tissue heating in 10 kHz-100 kHz drive field frequency range was simulated for the different tissue types in the human body and it is expected that tissue heating will not be hazardous at 25 kHz, which is the frequency that MPI commonly operates at [15]. In a different work, the PNS and SAR limits in 24 kHz-162 kHz drive field frequency range were investigated experimentally and it was concluded that the SAR limits are not limiting, and increasing the drive field frequency in order to speed up the MPI scanner is possible in building a clinical MPI scanner [16]. SAR limits in MPI were investigated based on MRI safety standards and it was also verified that operating at a drive field frequency of 150 kHz is safe in a clinical MPI scanner [17].

1.2 Motivation and Contribution

MPI is a rapidly developing medical imaging modality, with numerous challenges that are waiting to be resolved. Even though imaging at 25 kHz drive field frequency is quite popular, there have not been enough studies on finding the optimal drive field frequency for obtaining high quality images in MPI. Therefore image quality at various drive field frequencies and drive field amplitudes was analyzed in this study.

In this thesis, the drive field parameters of MPI were investigated with the goal of determining the optimal scanning parameters for MPI. The effects of drive field frequency and amplitude on the MPI image quality were analyzed both experimentally and via simulations. In a recent work, it was concluded that operating at 150 kHz in clinical MPI is feasible from the safety aspects [17]. Since signal-to-noise-ratio (SNR) and imaging speed increase with increasing drive field frequency, applying a higher drive field frequency, around 150 kHz, in clinical

MPI scanners was proposed [16, 17]. As 25 kHz is currently more popular in MPI, the frequency range around 150 kHz has not yet been studied for image quality. Therefore, the effects of operating at 150 kHz drive field frequency were investigated in terms of the resulting image quality.

One of the most popular MPI image reconstruction schemes called x-space MPI reconstruction produces artifacts, especially when the relaxation behavior of the nanoparticles becomes significant. These artifacts appear as asymmetric background haze and irregular trending in the MPI images. This thesis proposes an improvement on the x-space reconstruction based on averaging positive and negative half-cycles of the MPI signal, combined with a Savitzky-Golay detrending filter. Via experimental imaging results and simulations, it is shown that the proposed method provides significant improvement over the x-space reconstruction. The performance of the technique was evaluated under different noise levels.

There is currently no clinical MPI scanner and the ultimate goal is to scale MPI scanner to human sizes. It is known that, MPI is limited by magnetostimulation and SAR limits, but the effects of the safety limits on the image quality were not investigated. This thesis investigates the effects of human safety limits on the image quality in MPI. This analysis is critical for MPI, considering that the ultimate goal of MPI is to transition from preclinical scanner to clinical scanners.

1.3 Organization of Thesis

This thesis is composed of 6 chapters: The main objective of this work, the motivation for the problem, and the related works are presented in Chapter 1. Chapter 2 is dedicated to the theoretical background of MPI. Chapter 3 covers the methodology, setup and simulation parameters, and the results for determining the effects of scanning parameters on the image quality in MPI. Chapter 4 presents the improved x-space reconstruction technique, together with simulation and experimental imaging results. Chapter 5 is dedicated to the simulation analysis

for determining the effects of the safety limits on image quality in MPI. Chapter 6 concludes this thesis with overall inference and future work. Supplementary information is provided in the Appendix.



Chapter 2

Overview of Magnetic Particle Imaging

In this section, the signal generation, acquisition and image formation for magnetic particle imaging (MPI) are covered. Secondly, the hardware requirements and the required magnetic fields are explained. Then, the relaxation phenomenon is discussed. Finally, the main safety considerations for the applied magnetic fields are covered.

2.1 Fundamentals of MPI

In this part, how the signal is generated and received, and how the MPI image is formed are explained from x-space reconstruction approach.

2.1.1 Signal Generation and Acquisition

MPI exploits the nonlinear response of the SPIONs. The nanoparticles are excited by an externally applied alternating magnetic field, amplitude of which is in the

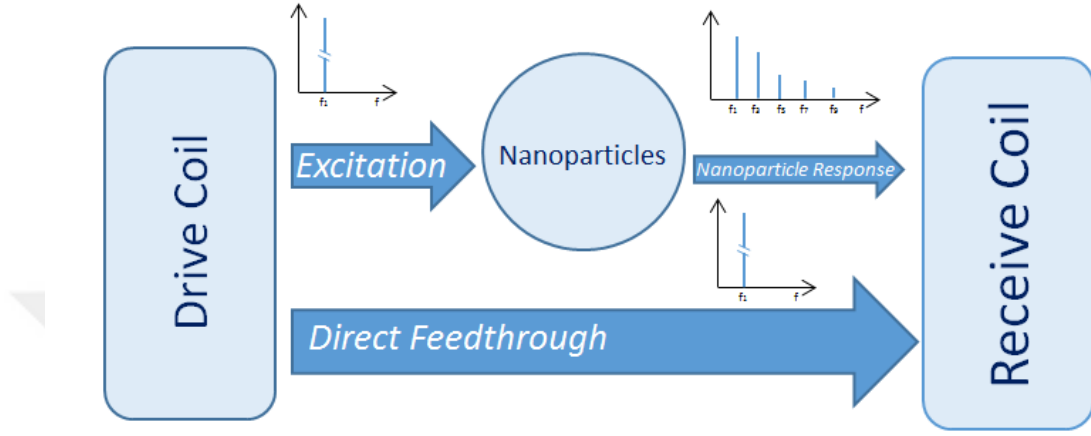


Figure 2.1: Schematic of the direct feedthrough problem.

range of 5 mT to 50 mT. This alternating magnetic field is called the drive field and is typically a sinusoid, though it is possible to excite the nanoparticles with a triangular waveform or with any other oscillating arbitrary waveform [1, 18, 19]. In MPI, the excitation of the nanoparticles and the reception of the signal occur simultaneously. As a result, excitation field interferes with the received signal. The direct feedthrough problem is represented in Figure 2.1. Suppose we apply a sinusoid magnetic field to nanoparticles, then the received nanoparticle signal would have a frequency component at the fundamental frequency, as well as at its harmonics due to the nonlinear response of the nanoparticles. As compared to the nanoparticle signal, interference of the excitation signal is millions-fold higher [20]. The interference at the fundamental frequency could be overcome by utilizing a high-pass filter or a notch-filter. For the excitation waveforms other than a sinusoid, isolating the receive signal from the excitation signal becomes problematic. Therefore, sinusoidal waveform is the most common waveform of choice for the drive field. The loss of the fundamental frequency component leads to a DC loss in the final MPI images, which was shown to be recoverable [20, 21].

Magnetization of the nanoparticles is linear under low excitation fields. Under higher external magnetic field, nanoparticles' magnetization saturates (Figure 2.2). Signal can only be obtained from the nanoparticles in the dynamic region.

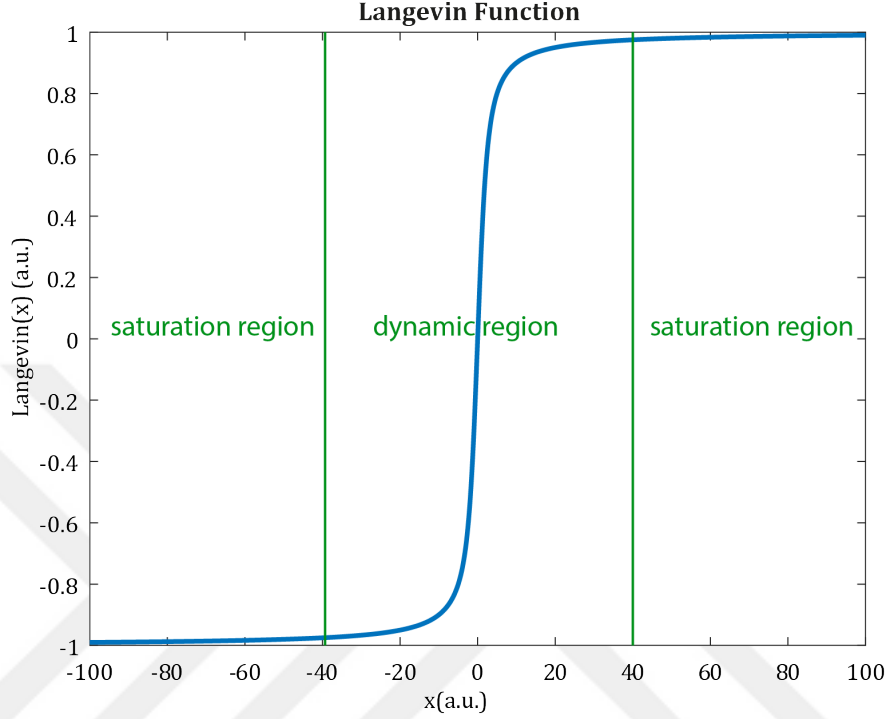


Figure 2.2: Magnetization of the SPIONs when an external magnetic field is applied can be modeled via the Langevin function. To acquire signal from the nanoparticles, their magnetization has to be in the dynamic region.

This magnetization behavior of the nanoparticles can be modeled with the Langevin function, $\mathcal{L}(\cdot)$, as given in Equation 2.1 [1]:

$$M(H) = m\rho\mathcal{L}(kH) \quad (2.1)$$

Here, $M(H)$ is the magnetization of the nanoparticles, $k[m/A]$ is a property of the nanoparticles, $\rho[particle/m^3]$ is the density of the nanoparticles, $m[Am^2]$ is the magnetic moment of the nanoparticles, and H is the external field.

Since signal reception is performed via inductive coils, the voltage created is closely related to the derivative of the total magnetization of the nanoparticles (Equation 2.2) [1].

In an MPI system, a strong inhomogeneous static magnetic field is applied to saturate nanoparticles everywhere except a field-free region (FFR) or field-free point (FFP). Selection field determines the resolution of the MPI scanner.

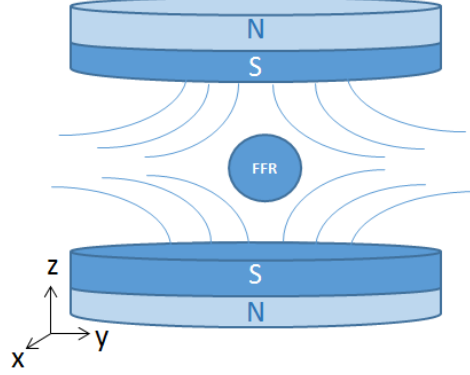


Figure 2.3: Permanent magnet configuration for generating selection field magnets are in Maxwell configuration.

Resolution improves with higher selection field gradients. Typically, a selection field gradient strength is in 1 T/m- 5 T/m range. Selection field can be created by either electromagnetic coils or permanent magnets. Electromagnetic coils consume energy but field strength can be adjusted. Permanent magnets do not consume energy, however field strength is a fixed value. When permanent magnets are used, they are positioned as in Fig 2.3. In constructing the MPI scanner in our lab, permanent magnets were used.

$$s_{ideal}(t) = B_1 m \rho(x) * \dot{\mathcal{L}}[kGx] |_{x=x_s(t)} kG \dot{x}_s(t) \quad (2.2)$$

Here, $B_1 [T/A]$ is the receive coil sensitivity, $m [Am^2]$ is the magnetic moment of nanoparticles, $x_s(t) [x]$ is the time-dependent position of the field-free region (FFR) , and $G [T/m/\mu_0]$ is selection field gradient strength .

In Equation 2.2, $\dot{\mathcal{L}}[kGx]$ is the derivative of the Langevin function and as shown in the next section, it corresponds to the point spread function (PSF) , $h(x)$, of the MPI system. The PSF is defined as in Equation 2.3 (Figure 2.4):

$$h(x) = \dot{\mathcal{L}}[kGx] = \frac{1}{(kGx)^2} - \frac{1}{\sinh^2(kGx)} \quad (2.3)$$

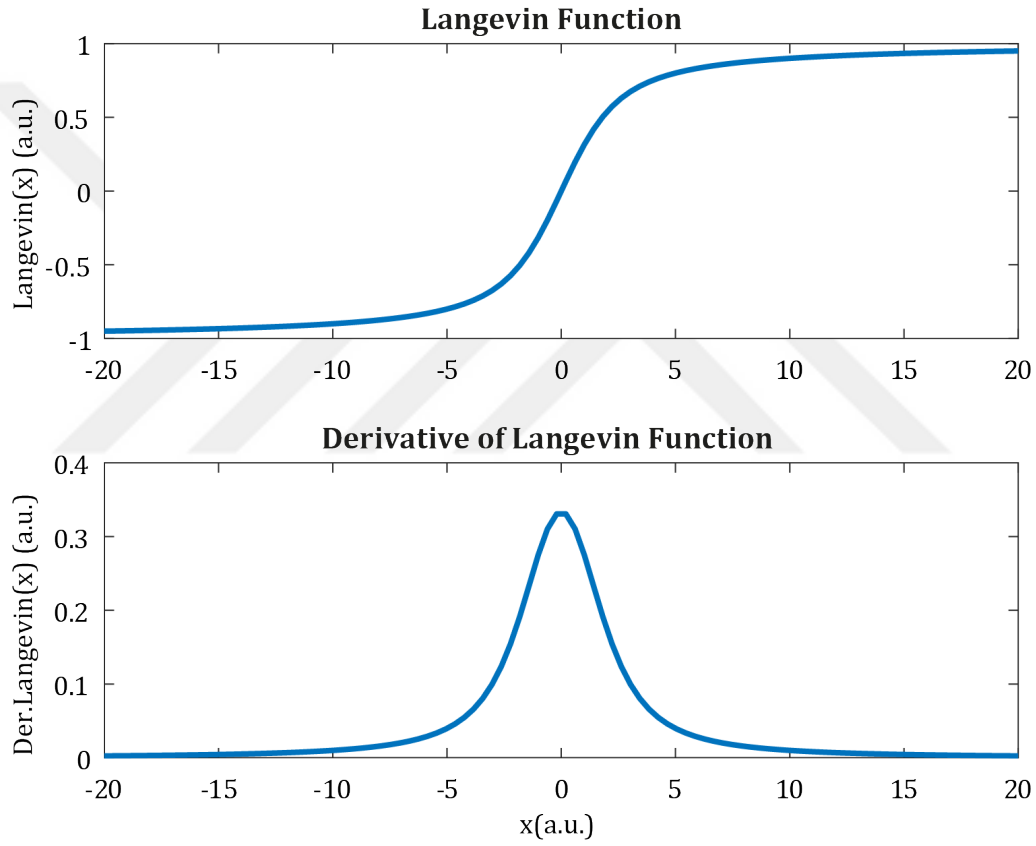


Figure 2.4: Magnetization of the SPIONs can be described by a Langevin function as in Figure 2.2. Its derivative gives the PSF of the MPI system. Full width at half maximum (FWHM) of the Langevin function, i.e., resolution of a native MPI system, is approximately 4.16. [1]

2.1.2 Image Reconstruction

MPI image can be formulated as the original nanoparticle distribution convolved with the PSF of the MPI system, as given in Equation 2.4:

$$IMG(x) = \hat{\rho}(x) = \rho(x) * h(x) \quad (2.4)$$

Then, the signal equation can be reformulated as in Equation 2.5 in terms of the MPI image, $\hat{\rho}(x)$:

$$s_{ideal}(t) = C \hat{\rho}(x) \dot{x}_s(t) \quad (2.5)$$

Here, $C = B_1 m k G$ is a constant.

MPI image can be obtained from the received signal by dividing out the velocity, $\dot{x}_s(t)$, and the constant terms [1]:

$$IMG(x_s(t)) = \hat{\rho}(x_s(t)) = \frac{s_{ideal}(t)}{C \dot{x}_s(t)} \quad (2.6)$$

From Equation 2.4, the MPI image depends on $h(x)$, which is a function of kGx . Therefore, the resolution of the MPI image depends on the properties of the SPIONs and the strength of the selection field gradient. Higher selection field gradient and larger nanoparticle diameters imply better resolution in the MPI images. The influence of the gradient strength and the core diameter of the nanoparticles on the resolution of the MPI images is shown in Figure 2.5

The signal equations and the image equations that were introduced above were for 1D MPI images to provide a better understanding of an MPI system. The equations for 3D MPI signal and image equation can also be expressed in a similar fashion [22].

In MPI, the field of view (FOV) depends on the drive field amplitude. Because of the safety restrictions on the drive field amplitude (see Section 2.4 Safety Concerns), it is not possible to scan the whole imaging area at once. Instead of this, partial FOVs (pFOVs) are imaged and then they are combined together to form the final MPI image. Due to the filtering of the fundamental frequency, the

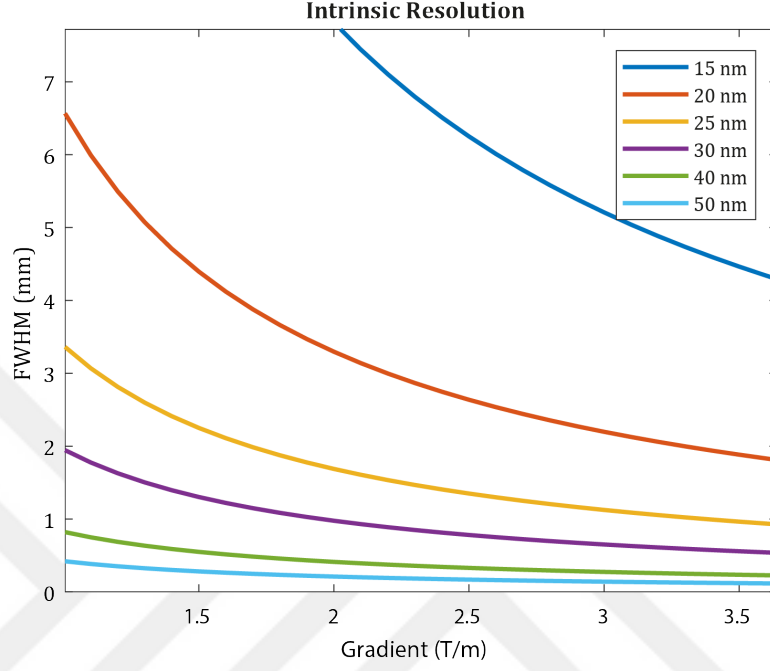


Figure 2.5: The resolution of the MPI images improves as the gradient strength and the nanoparticle size increase [1].

DC component of each pFOV image is lost. However, stitching pFOVs to form the final image is still possible using the continuity and smoothness of the MPI images [23]. There are still attempts to avoid the artifacts which result from the stitching of the overlapping pFOVs. There were various techniques to reconstruct the images from overlapping pFOVs to obtain native MPI images. This problem and alternative solutions are addressed in Chapter 4.

Resolution of the obtained images can be further improved by deconvolution techniques. However, PSF of the system is large and deconvolution techniques have potential to introduce new artifacts. Therefore, the main objective is to improve the native MPI images.

2.2 Magnetic Fields and Hardware Requirements

2.2.1 Drive Field

Drive field (excitation field) is a homogeneous, oscillating magnetic field that excites the nanoparticles. This field is in 1 kHz - 150 kHz frequency range. Typically, frequencies around 25 kHz are utilized in current MPI scanners. The amplitude of the excitation field determines the size of the FOV. By applying higher drive field amplitudes, scanning a larger region in an MPI system is possible. However, drive field amplitude is restricted by safety limits. Drive field frequency determines the imaging speed. Assuming a sinusoidal waveform, the drive field can be formulated as in Equation 2.7:

$$H_d(t) = H_p \cos(2\pi f_d t) \quad (2.7)$$

2.2.2 Receive Coil and Receive Chain

By Faraday's Law of Induction, voltage is induced in the received coils when a time-varying magnetic field is generated by the drive coils. The receive coil is placed the closest to the bore of the MPI scanner. There may be one receive coil or several receive coils depending on the function and the design of the MPI system.

Receive coils in our lab are gradiometer type coils that have 3 sections. The direction of the winding in the middle section is opposite to those in the first and the third sections. The aim in using a gradiometer type receive coil is to minimize the direct feedthrough voltage on the receive coil when no SPIONs are inside the receive coil under an alternating magnetic field. A gradiometer-type receive coil that is positioned inside a drive coil is illustrated in Figure 2.6.

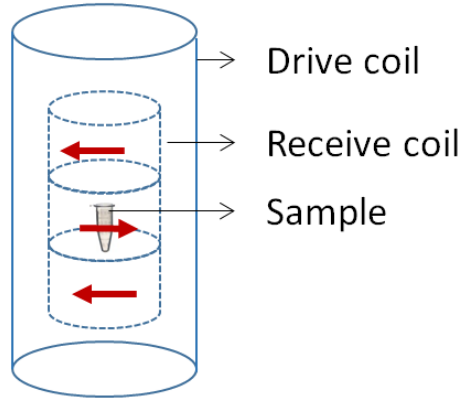


Figure 2.6: 3-section gradiometer type receive coil is demonstrated in relation with the drive coil and the sample. Red arrows indicate the direction of the windings for the sections of the receive coil.

2.2.3 Additional Fields or Robot Movement

FFR can be shifted in a trajectory to cover the whole imaging region. This can be achieved by using additional slowly-varying magnetic fields, called 'focus fields'. For each dimension a pair of focus coils are needed. Another approach is to have a FFR at a fixed position and instead of shifting FFR, shifting an imaging phantom to be imaged. The MPI system in our lab follows the second approach. It benefits from mechanical robots that can shift the imaged object in 3 dimensions.

It is important to note that, different MPI scanner topologies can be implemented for different applications of MPI. Here, the most common MPI topology was discussed to introduce the basics of MPI.

2.3 Relaxation Effect

When an alternating magnetic field is applied to the nanoparticles, the nanoparticles try to align their magnetization with the applied magnetic field. However, the nanoparticles respond to the alternating magnetic field with a delay.

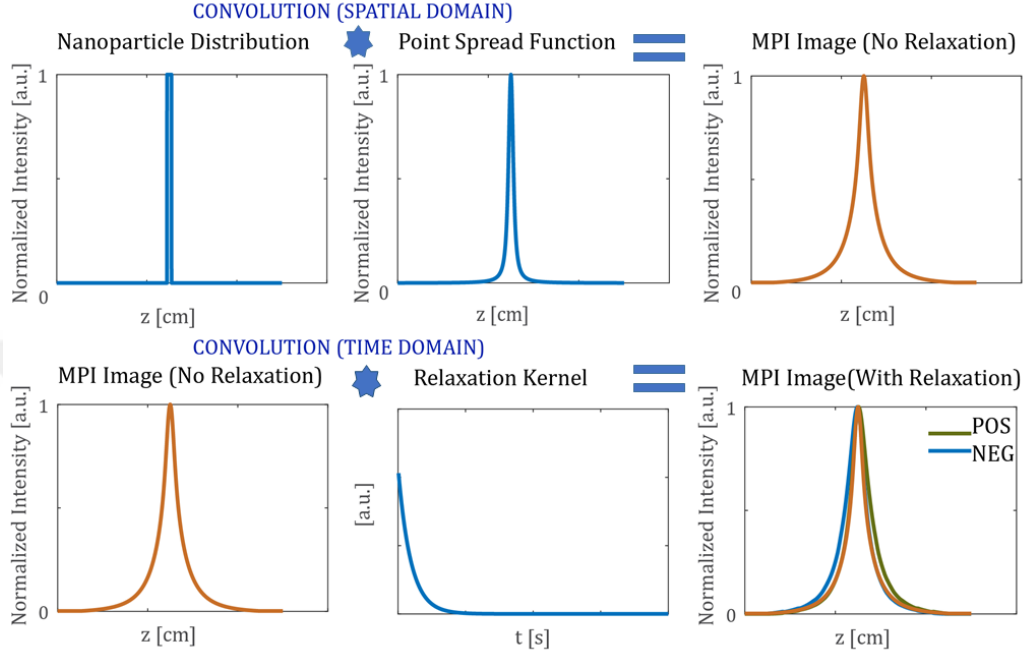


Figure 2.7: The effect of the relaxation phenomena on the MPI images [2] The direction of blurring changes with the scanning direction

The delayed response of the nanoparticles causes blurring in the final MPI images (Figure 2.7). This blurring effect can be modeled as a convolution of the ideal MPI signal with an exponential function defined by a relaxation time constant (Equation 2.8)[24] :

$$sdiab(t) = s(t) * r(t) \quad (2.8)$$

$$\text{where, } r(t) = \frac{1}{\tau} \exp(-t/\tau) u(t)$$

Here, $u(t)$ is the Heaviside step function and τ is the relaxation time constant.

This delayed response can be explained by two mechanisms: Néel relaxation and Brownian relaxation. Both mechanisms are effective in determining the overall relaxation effect of the nanoparticles.

In Néel relaxation mechanism, the nanoparticles try to align their magnetization with the magnetic field internally. Relaxation time constant due

to Néel Mechanism can be expressed as in Equation 2.9 [25]:

$$\tau_N = \tau_{N0} \exp \left(\frac{k_C V_C}{k_B T} \right) \quad (2.9)$$

Here, k_C [Joule/ m^3] is the crystalline anisotropy constant, V_C [m^3] is the volume of the magnetic core, k_B [Joule/K] is Boltzmann's constant and T [K] is the temperature, τ_{N0} is constant.

In Brownian relaxation mechanism, nanoparticles try to align their magnetization by physical rotation. Therefore, Brownian motion is highly affected by the medium of the nanoparticles. The relaxation time constant for the Brownian mechanism is formulated as in Equation 2.10 [25]:

$$\tau_B = \frac{3\eta V_H}{k_B T} \quad (2.10)$$

Here, η is viscosity, V_H is hydrodynamic volume.

The overall relaxation time constant can be obtained as:

$$\frac{1}{\tau} = \frac{1}{\tau_B} + \frac{1}{\tau_N} \quad (2.11)$$

It is evident from Equation 2.9 and Equation 2.10 that the relaxation time constant highly depends on the nanoparticle diameter, temperature, and viscosity of the medium.

2.4 Safety Concerns

Currently, a human-size clinical MPI scanner does not exist. Studies are being carried out to scale MPI scanners to human-size. Time-varying magnetic fields in MPI raise two main safety issues: specific absorption rate (SAR) and peripheral nerve stimulation (PNS).

2.4.1 Specific Absorption Rate (SAR)

Power absorbed by the human body or tissues is a well-known problem, that needs to be taken into account in design parameters and scanning parameters.

Time-varying magnetic fields cause tissue heating. The drive field is the main source of SAR tissue heating. According to International Electrotechnical Commission (IEC), $1^{\circ}C$ temperature rise in tissues is permitted. Accordingly, the SAR limit is restricted by $4W/kg$ in 6 minutes and $8W/kg$ in 10s for the whole body [17]. The local SAR limit, which is the heating limit for 10g of tissue, is restricted by $20W/kg$ in 6 minutes and $40W/kg$ in 10s [17].

From Faraday's Law of induction, the induced electric field due to a sinusoidal drive field that is applied to a cylinder of radius r is given in 2.12 :

$$E(t) = 2\pi r f B_p \cos(2\pi f t) \quad (2.12)$$

Here, $E(t)$ is the induced electric field. The SAR limit depends on the electric field strength, the electrical conductivity and the mass density of the body, and can be expressed as in Equation 2.13 [26]:

$$SAR = \frac{1}{\rho} \sigma E^2 \quad (2.13)$$

In a more general form, it can be expressed as a function of volume-of-interest, as given in Equation 2.14 [15]:

$$SAR(V) = \frac{1}{M} \int \sigma(V) ||E(V)||^2 dV \quad (2.14)$$

Here, M is the mass, V is the volume, σ electrical conductivity, ρ is the mass density.

Electrical conductivity increases with frequency [15]. SAR limit is proportional to the square of the electric field strength and the electric field strength increases

with linearly frequency, which implies that the SAR limit is proportional to f^2 . Therefore, at higher drive field frequencies, SAR is more pronounced. Recent studies on SAR in MPI scanners show that, imaging at 150 kHz with drive field strengths 5.5 mT in longitudinal direction and 2.2 mT in sagittal direction is possible without exceeding SAR limits [16].

2.4.2 Peripheral Nerve Stimulation (PNS)

Time-varying magnetic fields also cause peripheral nerve stimulation (PNS), also known as magnetostimulation. Drive field is the main source of magnetostimulation in MPI. Fundamental Law of Magnetostimulation states that, the threshold for magnetic field strength decreases as the frequency of the time-varying field increases, as formulated in Equation 2.15 [27], [16]:

$$B_{th}(f) = B_{min} \left(1 + \frac{f_{chron}}{f} \right) \quad (2.15)$$

Here, f_{chron} is the chronaxie frequency and B_{min} is the minimum magnetic field required to cause magnetostimulation.

A recent work showed experimentally that the PNS limits decrease with increasing frequency and this limit is inversely proportional to the body part size [3]. Magnetostimulation limits vary with drive field frequency, drive field amplitude, pulse duration, and duty cycle [3, 28, 29].

In a recent work, magnetostimulation limit for the human torso in MPI was formulated as in Equation 2.16 [3]:

$$B_{th}(f) = \Delta B_{min} \left(1 + \frac{1}{2\tau_c f} \right) \quad (2.16)$$

Here, τ_c is the chronaxie time constant which determines the rate of decay of the function and ΔB_{min} is the minimum change in the magnetic field required to

cause magnetostimulation and is extrapolated to be $289 \mu s$ and is $14.3 mT_{p-p}$ for the human torso [3].

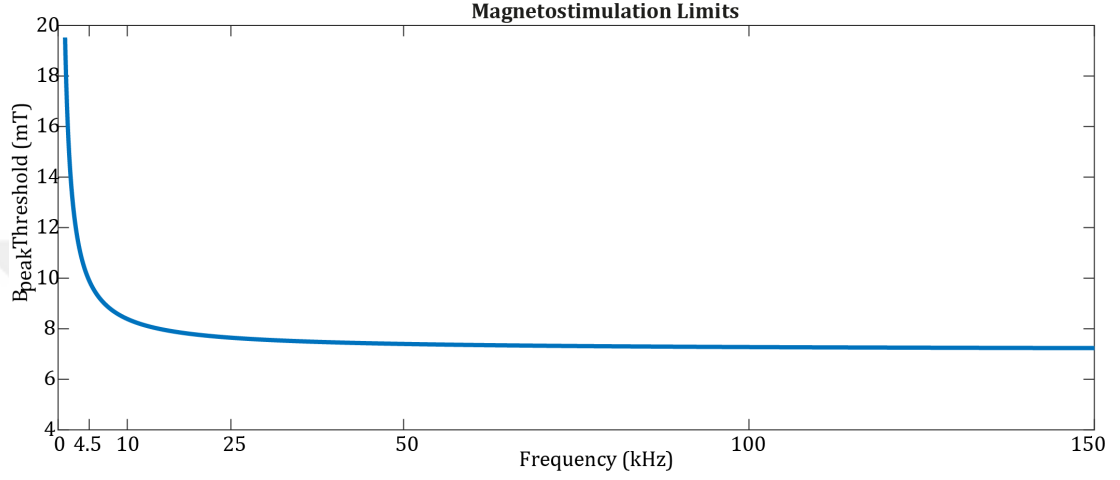


Figure 2.8: Magnetostimulation limit for the drive field in MPI up to 150 kHz is plotted for the human torso [3].

Chapter 3

Effects of Drive Field on Image Quality

This chapter is based on “Effects of Drive Field Parameters in Magnetic Particle Imaging: A Relaxometer Study”, E. Bozkurt, M. Utkur, Y. Muslu, E.U. Saritas, presented at the 21st National Biomedical Engineering Meeting (BIYOMUT), November 2017, Istanbul, Turkey.

3.1 Experimental Setup and Methodology

3.1.1 Relaxometer Setup

Our in-house relaxometer setup, also known as a magnetic particle spectrometer, was used in the experiments for determining the effects of drive field parameters on image quality. A relaxometer works in similar principle with an MPI scanner. A relaxometer is a device that can acquire nanoparticles’ temporal response to an alternating magnetic field. In contrast to an MPI scanner, a relaxometer can neither localize the nanoparticle distribution nor provide any spatial information. Rather, it is used in nanoparticle characterization.

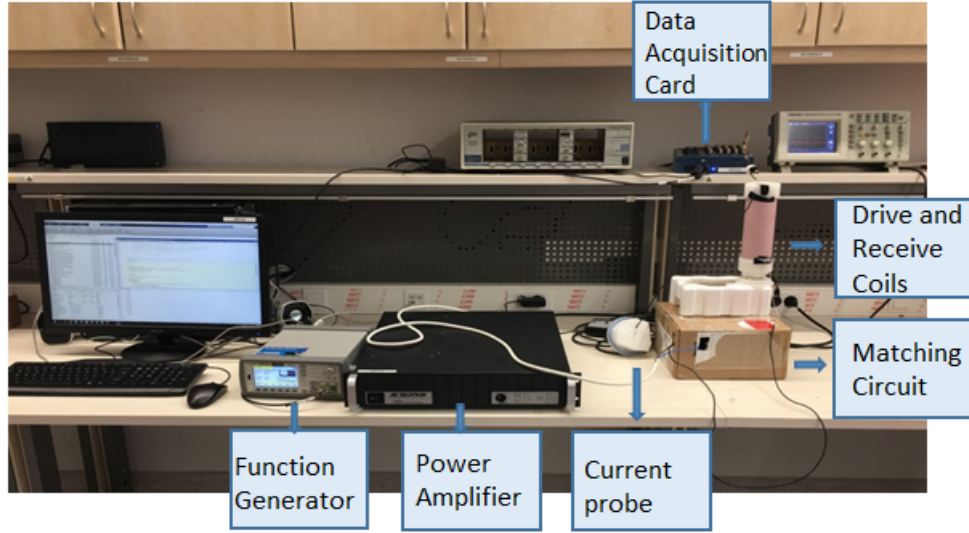


Figure 3.1: Relaxometer setup.

Even though a relaxometer cannot provide any spatial information about the nanoparticles' position, a PSF can be obtained from the received signal. Since PSF includes the information about the resolution of the image, we can estimate the resolution if we had used an MPI scanner to image that nanoparticle distribution at that drive field parameters. Therefore, a relaxometer is useful in providing insight about the nanoparticle response and the quality of the final MPI images.

Our in-house relaxometer setup consists of a data acquisition card (NI USB-6363), power amplifier (AE Techron 7224), Rogowski current probe (Power Electronic Measurements Ltd, UK), function generator (Stanford Research Systems DS345), matching circuit, drive coil, and receive coil. The relaxometer setup and the whole system are controlled with a PC (32 GB RAM, 3.60 GHz, Intel Core i7). The signal transmission and signal reception commands and the post-processing phase are performed via MATLAB (Mathworks, Natick, MA). A pictorial depiction of the relaxometer setup is given in Figure 3.1.

The system needs to be calibrated first. The system is calibrated to a target

drive field amplitude by measuring the current applied to the drive coil, via the Rogowski current probe. The sensitivity of the drive coil is known to be 0.97 mT/A, hence the drive field amplitude can be calculated directly from the measured current.

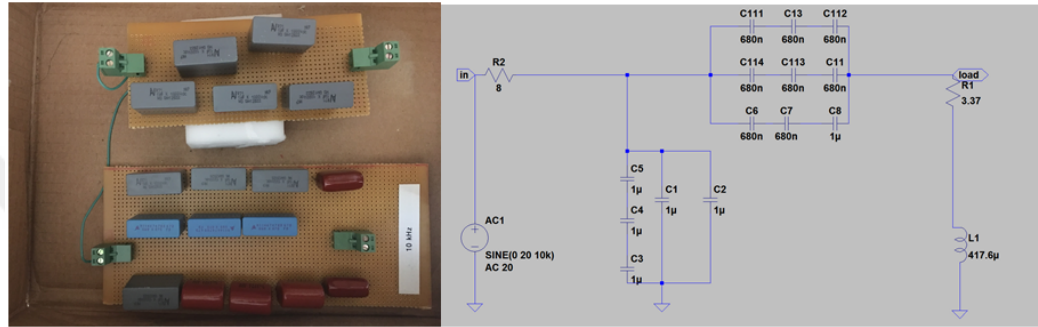
After the calibration step, signal generation is initiated with MATLAB. The signal, which is sent to the data acquisition card, is amplified using the power amplifier. A sinusoidal signal is used in the experiments and an impedance matching circuit is utilized to maximize the power delivered to the drive coil. For each drive field frequency, a different capacitive network was used for resonant impedance matching (see Figure 3.2). These circuits were designed to endure high voltages, ranging up to 2 kV.

An oscillating magnetic field is generated inside the drive coil, which can be described as in Equation 3.1:

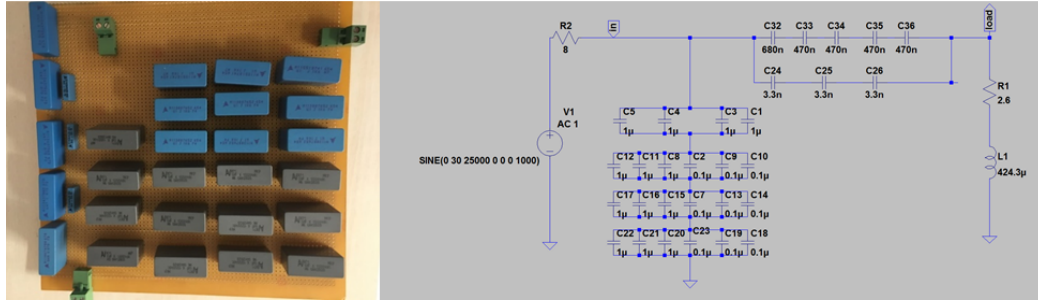
$$B_d(t) = B_p \cdot \sin(2\pi f_d t) \quad (3.1)$$

Here, B_p denotes the amplitude of the applied magnetic field and f_d denotes the drive field frequency. The receive coil is placed co-axially inside the drive coil such that they are isocentric (Figure 3.3(a), 3.3(b)). 89 mmol Fe/L undiluted Nanomag-MIP (Micromod Partikeltechnologie GmbH, Rostock) is used as the nanoparticle sample (Figure 3.3(c)).

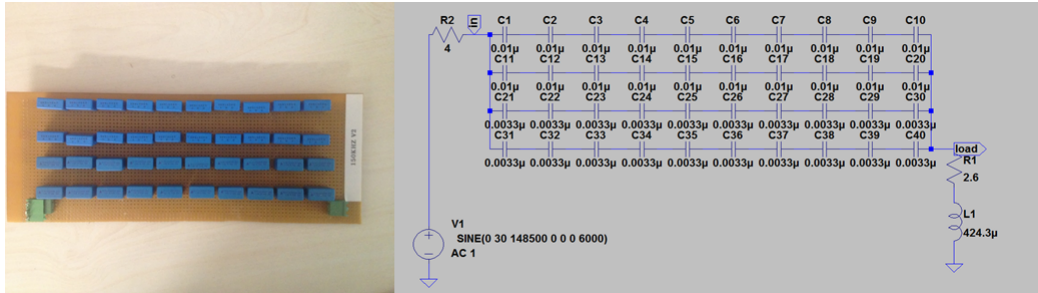
A voltage is induced in the receive coil as a result of the nanoparticles' response to the alternating magnetic field. This signal is transferred to the PC via the data acquisition card, with 2 Megasample / second sampling rate. A flowchart of the relaxometer processes is given in Figure 3.4.



(a)



(b)



(c)

Figure 3.2: (a) Impedance matching circuit for 10 kHz drive field frequency (b) Impedance matching circuit for 25 kHz drive field frequency (c) Impedance matching circuit for 148.5 kHz drive field frequency

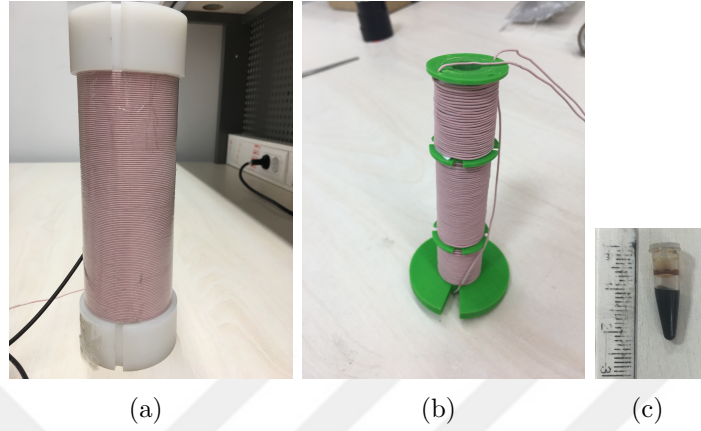


Figure 3.3: (a) Drive coil (b) gradiometer type receive coil, (c) nanoparticle sample. When the relaxometer setup is operating, the receive coil is placed inside the drive coil and the nanoparticle sample is placed inside the receive coil.

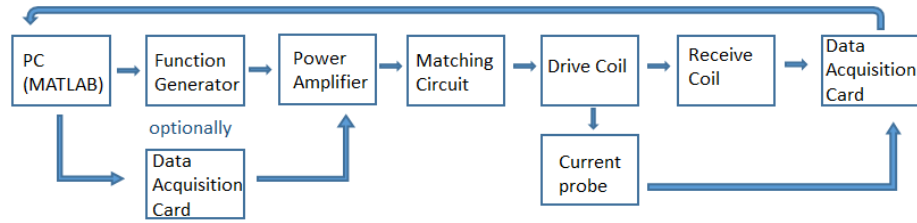


Figure 3.4: Flowchart of the relaxometer setup

3.1.2 Relaxometer Measurements

Measurements were conducted at various drive field frequencies (10 kHz, 25 kHz, 148.5 kHz) and at various excitation field amplitudes (minimum at 4 mT and maximum at 15 mT). At these excitation frequencies, drive field amplitudes are expected to not exceed 7 mT for human-size MPI scanners [3]. Hence, the parameters that were chosen in relaxometer measurements are relevant to realistic human-size MPI scanner parameters.

To avoid background interferences, a measurement without the nanoparticle sample was performed and this signal was subtracted from the signal that was received from the nanoparticles. Autocorrelations of the signals were calculated before subtraction to avoid potential phase shifts between the signals. The regions

of the signal with irregular amplitudes were discarded and only the regions with constant signal amplitude were used in the post-processing phase.

3.1.3 Point Spread Function (PSF) Formation

In a relaxometer experiment, the PSFs are obtained by dividing the signal by the velocity of the drive field. It is possible to obtain two separate PSFs: one from the half cycle where the drive field velocity is positive, and one from where the drive field velocity is negative. Here, these two PSFs are referred to as “positive PSF” and “negative PSF”.

3.2 Relaxometer Results

The measurements were performed at 3 different drive field frequencies, namely, 10 kHz, 25 kHz, and 148.5 kHz, as described in the previous section. The applied drive field strength varied between 4 mT and 15 mT. In this section, results for the drive field strengths of 5 mT, 7 mT, and 10 mT are presented.

Table 3.1: FWHM of the PSFs in Figure 3.5 and Figure 3.6 in [mT]

	Excitation Field Amplitude		
Frequency	5 mT	7 mT	10 mT
10 kHz	2.51	3.06	3.74
25 kHz	2.41	2.99	3.61
148.5 kHz	3.18	4.78	6.14

The effects of the drive field frequency on the PSF are presented for 5 mT and 10 mT drive field amplitudes. The PSFs that were formed with all available frequency components under 5 mT and 10 mT drive field strengths and at 10 kHz, 25 kHz, and 148.5 kHz drive field frequencies are provided in Figure 3.5. The PSFs are wider at 148.5 kHz as compared to other frequencies, under both 5 mT and 10 mT drive field strengths. The numerical comparison of the full width

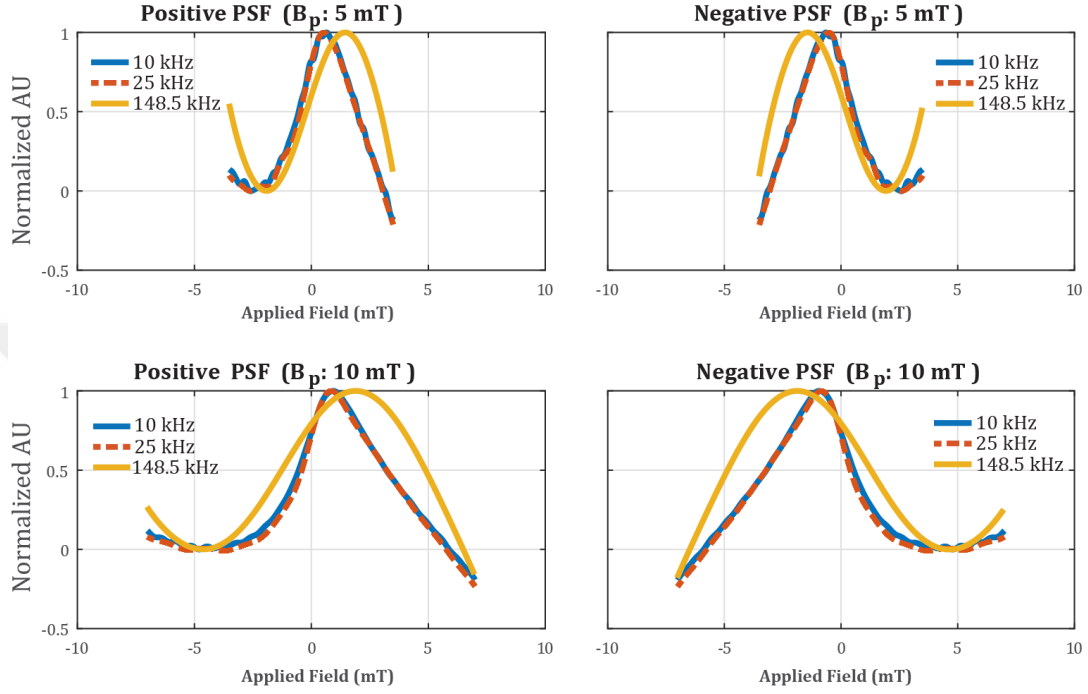


Figure 3.5: PSFs were formed by using all available odd harmonics, under 2 drive field strengths, 5 mT and 10 mT. The PSFs which were formed by using the negative half-cycle and the positive half-cycle are shown separately.

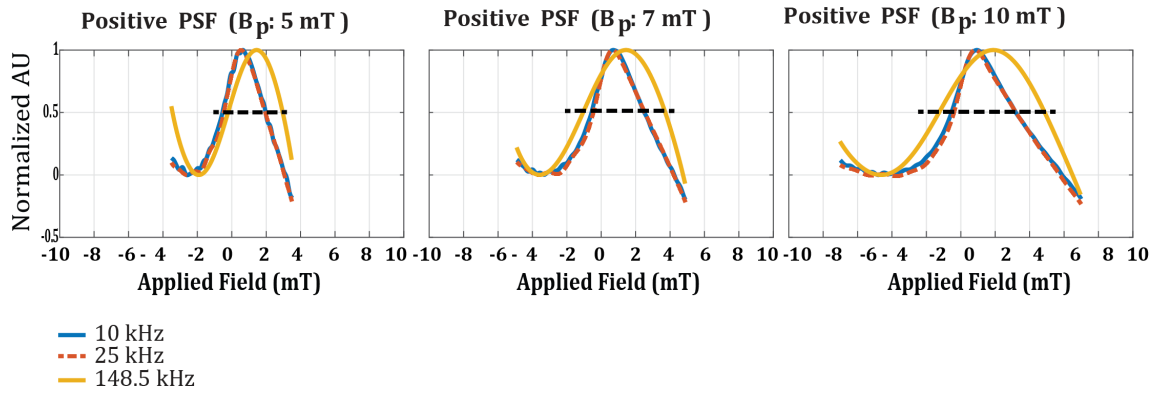


Figure 3.6: PSFs were formed by using all the available odd harmonics, under 3 drive field strengths, 5 mT, 7 mT, and 10 mT. The PSFs that were formed from the positive half-cycle are shown. FWHM values for these PSFs are given in Table 3.1.

at half maximum (FWHM) values for the PSFs (Figure 3.6) are provided in Table 3.1, which were obtained under 5 mT, 7 mT, and 10 mT drive field strengths. It can also be seen from Table 3.1 that the results at 10 kHz are close to those at 25 kHz, but the narrowest PSFs were achieved at 25 kHz under all three drive field strengths.

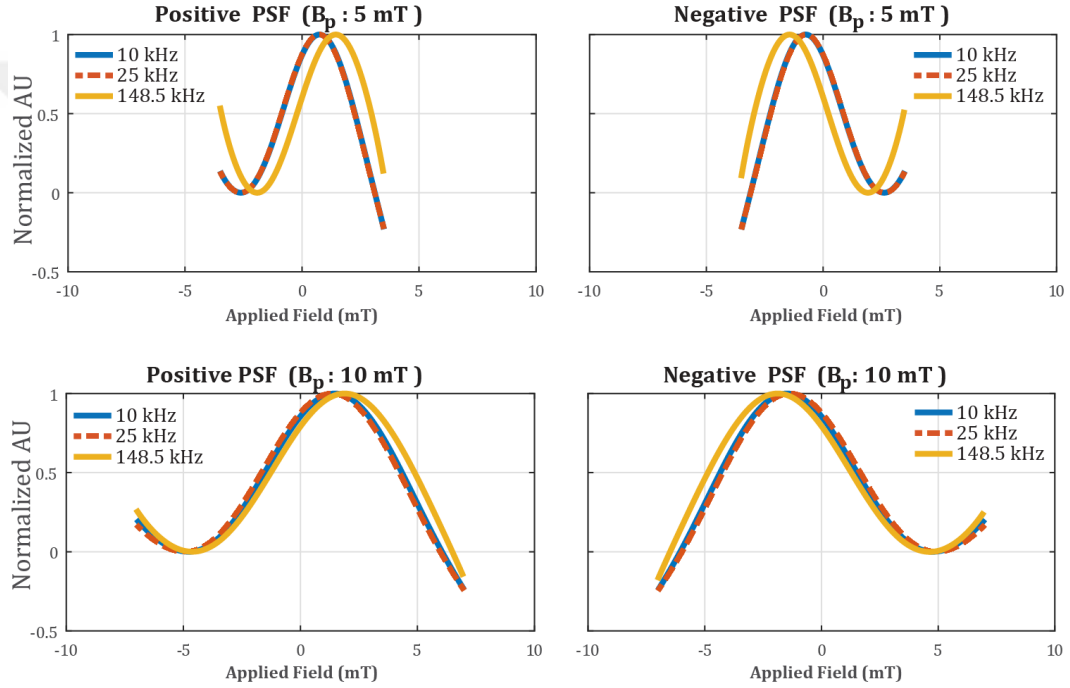


Figure 3.7: PSFs were formed by using the odd harmonics up to 6th, under 2 drive field strengths, 5 mT and 10 mT. The PSFs that were formed by using the negative half-cycle and the positive half-cycle are shown separately.

Sampling rate of the data acquisition card was 2 Megasamples/s. Therefore, only the harmonics up to 6th could be acquired for 148.5 kHz. It was necessary to do a fair comparison, in addition to the results shown in Figure 3.5 and Figure 3.6. To have a fair comparison and to see the effects of the number of harmonics used in forming the PSFs, only the 3rd and the 5th harmonics of the signals were used for all frequencies. The corresponding PSFs are shown for 5 mT and 10 mT drive field strengths in Figure 3.7. Since fewer frequency components were used at 10 kHz and 25 kHz, the PSFs widened compared to the previous case. The PSFs obtained at different frequencies look more similar to each other. However,

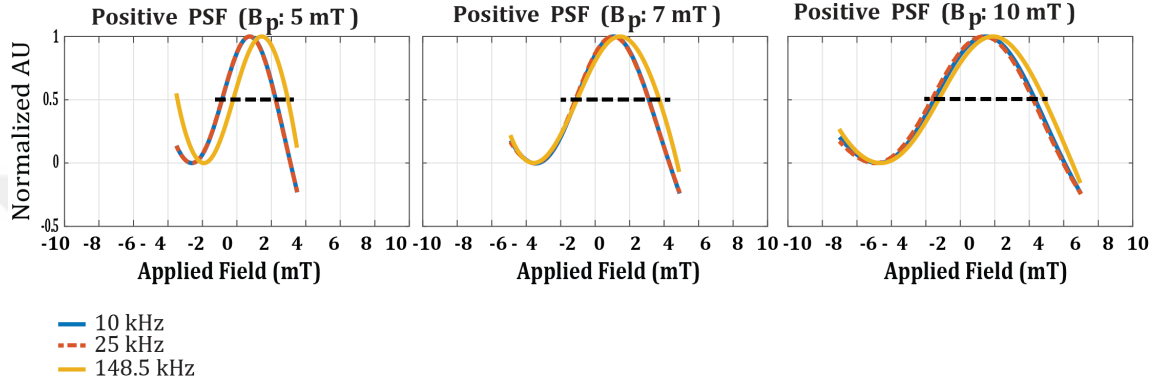


Figure 3.8: PSFs were formed by using only the odd harmonics up to the 6th harmonic, under 3 drive field strengths, 5 mT, 7mT and 10 mT. The PSFs, which were formed from the positive half-cycle are shown. FWHM values for these PSFs are given in Table 3.2.

Table 3.2: FWHM of the PSFs in Figure 3.7 and Figure 3.8 in [mT]

	Excitation Field Amplitude		
Frequency	5 mT	7 mT	10 mT
10 kHz	3.12	4.21	5.87
25 kHz	3.12	4.25	5.89
148.5 kHz	3.18	4.78	6.14

it was observed that, at 148.5 kHz, the FWHM values of the PSFs (Figure 3.8) are still greater than those at 10 kHz and 25 kHz as given in Table 3.2.

The signals that were obtained from the relaxometer experiments were also analyzed in the frequency domain and the decay of the harmonic components are given in Figure 3.9. When the rates of decay of the harmonic components are compared for all three frequencies, it can be seen that, the harmonic components of the signal at 148.5 kHz decay much faster than those at 10 kHz or 25 kHz. Harmonic components decay the slowest at 25 kHz for both drive field amplitudes, which explains why the PSFs at 25 kHz have better resolution (i.e., smaller FWHM values) than the PSFs at 10 kHz or 148.5 kHz under the same drive field amplitudes. The nanoparticles are unable to follow the change in magnetic field at high drive field frequencies, which can be the reason for the poor resolution at 148.5 kHz. Based on these experimental results, the resolution of the MPI images will be better at 25 kHz, compared to 10 kHz or 148.5 kHz.

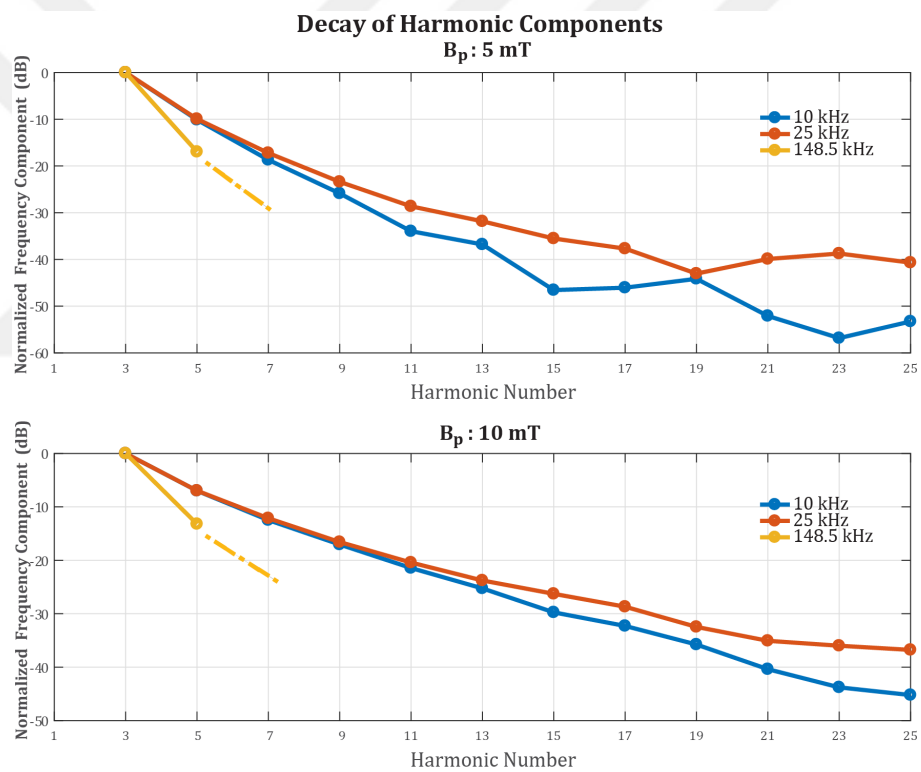


Figure 3.9: Decay of the frequency components in dB.

3.3 Simulation Results

3.3.1 Nanoparticle Diameter Estimation

The relaxation time constants were estimated based on a technique developed in a recent work [30] and the PSFs were deconvolved with Wiener deconvolution with the relaxation kernels (see Chapter 2) and native PSFs were obtained. FWHM values of these native PSFs were denoted as $FWHM_B$. Using these $FWHM_B$ values, effective nanoparticle diameters were derived from Equation 3.2, which is based on a recent work [1] (see Appendix A) :

$$d = \left(\frac{4.16 \cdot 6 \cdot k_B \cdot T \cdot \mu_0}{0.6 \cdot \pi \cdot FWHM_B} \right)^{1/3} \quad (3.2)$$

Effective nanoparticle diameters were estimated at 7 mT and 10 mT drive field strengths, according to Equation 3.2 and the experimental $FWHM_B$ values for 10 kHz, 25 kHz, and 148.5 kHz in Table 3.3 and Table 3.4, respectively. Relaxation time constant estimations were also provided, which were included in the simulation parameters.

Table 3.3: Relaxation and effective particle diameter estimations derived from relaxometer experiment results at 7 mT:

Frequency(kHz)	tau(μ sec)	effective diameter (nm)
10 kHz	4.34	25.59
25 kHz	1.87	26.67
148.5 kHz	0.75	23.01

3.3.2 Simulations Based on Relaxometer Results

To verify the experimental results, 2D simulations were performed at 10 kHz, 25 kHz, and 148.5 kHz drive field frequencies, with a custom MPI simulation toolbox developed in MATLAB.

Table 3.4: Relaxation and effective particle diameter estimations derived from relaxometer experiment results at 10 mT:

Frequency(kHz)	tau(μ sec)	effective diameter (nm)
10 kHz	4.42	23.45
25 kHz	1.85	24.98
148.5 kHz	0.42	21.45

The 2D resolution phantom is made up of 6 line sources of 1 mm width, separated by 3 mm, 5 mm, and 7 mm from their centers, respectively. FOV is 1 cm x 15.3 cm as shown in Figure 3.10. This resolution phantom is utilized in simulations at 10 mT drive field amplitude. The 2D simulation results at 10 mT drive field amplitude are shown in Figure 3.11.

10 kHz and 25 kHz images are very similar, but the images at 25 kHz are slightly better, which is in good agreement with the experimental results.



Figure 3.10: 2D resolution phantom with dimensions 1 cm x 15.3 cm. Line sources are of 1 mm width and they are separated by 3 mm, 5 mm, and 7 mm from their centers.

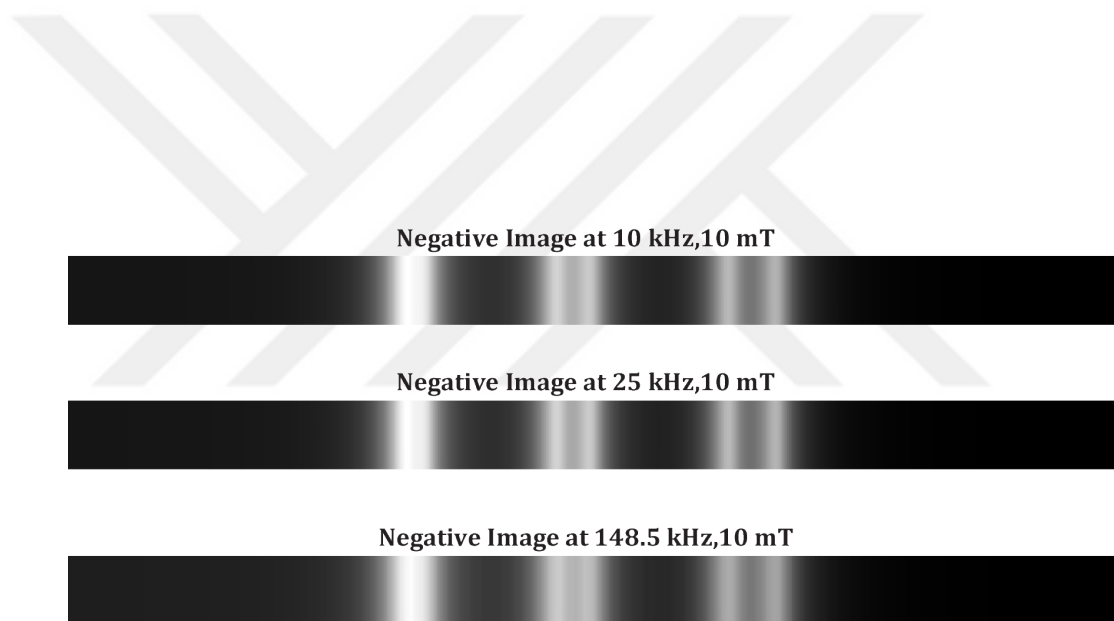


Figure 3.11: 2D MPI images at 10 kHz, 25 kHz, and 148.5 kHz drive field frequency and at 10 mT drive field strength.

Chapter 4

Effects of Reconstruction Parameters

The post-processing and reconstruction of the images are equally important as choosing the optimal scanning parameters in MPI. This section describes novel improvements on the x-space image reconstruction technique to increase the quality of MPI images.

Due to safety limitations, it is not possible to cover the whole imaging area at once. Hence, smaller sections of the imaging area are covered as partial FOVs (pFOVs) and then they are stitched together. Due to the contamination of the first harmonic by the direct feedthrough problem, the fundamental frequency is filtered out. Filtering out the fundamental frequency results in DC loss for each pFOV image [20]. However, by using the smoothness and positivity properties of the MPI images, this loss is recoverable (see Chapter 2). Here, a simple and conventional method is to combine the overlapping pFOVs starting from one end to the other end of the image, in a line-by-line fashion. Stitching of pFOVs starting from one end, however, may lead to an accumulation of errors at the other end. These errors appear as irregular trending artifacts or asymmetric hazing in the final MPI images (Figure 4.1). These artifacts are more pronounced when the relaxation time constant gets large. To demonstrate this problem, a simulation

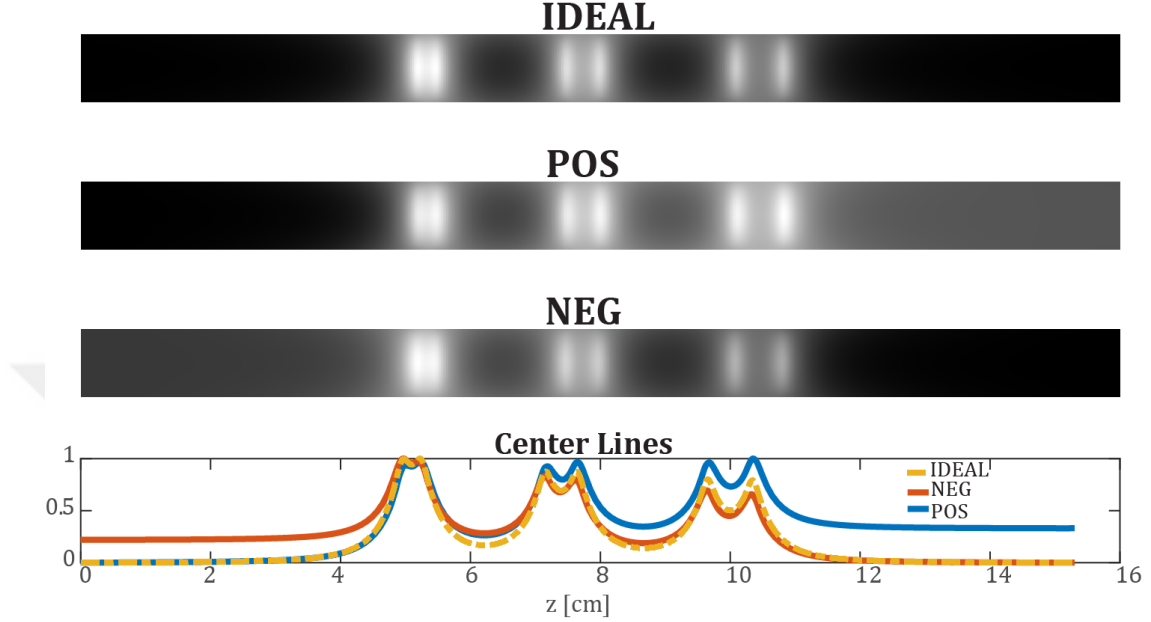


Figure 4.1: Simulated MPI images of the resolution phantom. For the ideal case, the relaxation effect was ignored. MPI images with the relaxation effect, obtained from the positive half-cycle (POS) and the negative half-cycle (NEG) are shown. Comparison of the centerlines is given at the bottom. Trending and asymmetric hazing artifacts are observed for POS and NEG images.

result is given in Figure 4.1. In this simulation, a resolution phantom of 1 cm x 15.3 cm was used. The drive field frequency was 148.5 kHz and drive field strength was 7 mT. The relaxation time constant was $0.4 \mu s$. The selection field gradient was $[-7, 3.5, 3.5]$ T/m. The overlap between the neighboring pFOVs was chosen as 80%. Acquisition of 3 lines was simulated, with an acquisition time of 20 ms.

For the “IDEAL” image in Figure 4.1, the nanoparticles were assumed to respond to the alternating magnetic field instantaneously, i.e., the relaxation effect was ignored. In the MPI images that were simulated including the relaxation effect and which were obtained from the positive half-cycle (POS) and the negative half-cycle (NEG), an asymmetric hazing depending on the scanning direction can be observed.

The following sections propose two different techniques to overcome the trending and hazing problems: averaging and detrending.

4.1 Averaging of Negative and Positive Half-Cycles

In standard x-space reconstruction, MPI images that are formed from negative and positive half-cycles are utilized as stand-alone images, or averaged after the reconstruction. Averaging negative and positive pFOVS before stitching the pFOVs can improve image quality. This improvement stems from the fact that the drive field speed drops to zero at the edges of pFOVs, which leads to the trending artifacts when combining the pFOVs. This is particularly true when the nanoparticle relaxation effects are significant. Averaging the positive and negative pFOVs before applying x-space reconstruction compensates for this problem at the edges of the pFOVs and thereby reduces the severity of these artifacts. The other advantage of this method is, it is computationally less complex and faster; because x-space reconstruction is applied only once. If the POS and NEG images are averaged after the reconstruction, however, the reconstruction would need to be applied twice.

4.2 Detrending using Savitzky-Golay Filter

Savitzky-Golay filters are low-pass filters that are mostly used for smoothing purposes [31],[32]. Yet, they are also commonly used for background subtraction for removing trending effects in the data due to variations in the background signal [33]. They can smooth out noisy data without distorting the signal; hence these filters are helpful in increasing the SNR. To apply Savitzky-Golay filters, the data has to be slowly varying, and the adjacent data points have to be related. Savitzky-Golay filters are commonly used in detrending functional Magnetic Resonance Imaging (fMRI) data and electrocardiogram (ECG) data [34]. As the MPI images also show slow variations, this thesis proposes using

Savitzky-Golay filters for removing the trending and hazing artifacts shown in Figure 4.1.

One disadvantage of the Savitzky-Golay filter is, the parameters have to be determined visually [32] . Therefore, the Savitzky-Golay filter parameters were first analyzed to see their effects on the MPI images.

4.2.1 Simulation Results

Simulations were carried out on a point-source phantom and the PSFs were obtained. The effects of this detrending method on the resolution of the image was quantified using the FWHM metric. The change in resolution was compared when different filter frame lengths were used under 7 mT and 10 mT drive field amplitudes and different overlap percentages of pFOVs. The results are shown in Figure 4.2. Here, the goal was to detrend the MPI images without causing an increase in FWHM resolution.

As seen in Figure 4.2, it is possible to detrend the MPI images with minimal distortions. There were 400 samples/pFOV at 7 mT and 572 samples/pFOV at 10 mT. Based on Figure 4.2, frame lengths around 1/4th of the number of the samples per pFOV is suitable. In this thesis, 2nd order Savitzky-Golay filters were used. However, no significant difference was observed when the filter order was reduced to 1 or increased to 3.

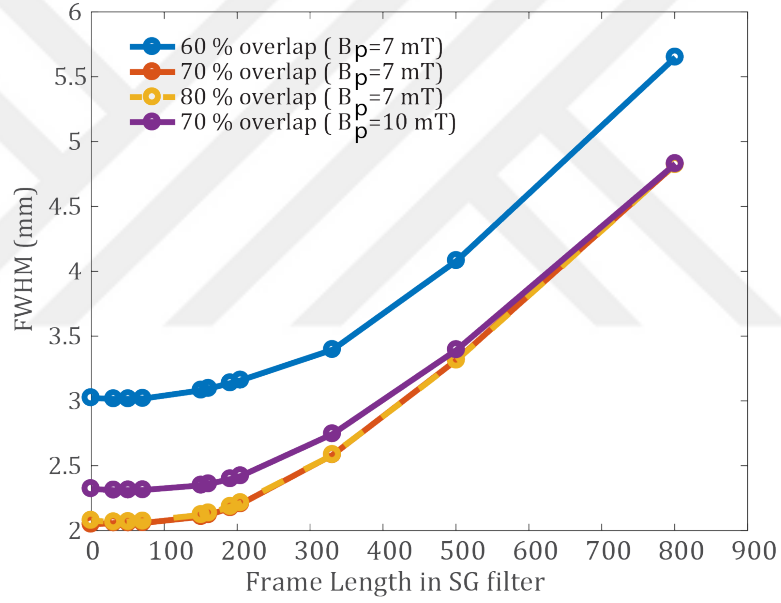


Figure 4.2: FWHM of the detrended MPI images for different frame lengths in Savitzky-Golay (SG) filters. The change in the FWHM of the MPI image was simulated for different overlap percentages of pFOVs and for different drive field amplitudes. Here, frame length=0 denotes the case when detrending was not applied.

4.3 Combining Averaging and Detrending

MPI images with standard x-space reconstruction were compared with possible combinations of averaging and detrending techniques. The results are shown for SNR=100 and SNR=2 cases in Figure 4.3 and Figure 4.4, respectively. These simulations were performed at a drive field frequency of 25 kHz and drive field amplitude of 7 mT. The effective particle diameter was 26.67 nm, based on the estimations given in Section 3.3.1. The relaxation time constant was chosen as 3 μs . Overlap percentage between the neighboring pFOVs was 80%. 10 lines were acquired.

The following images were compared:

- 1) POS: x-space reconstructed image from the positive half-cycle of the MPI signal.
- 2) NEG: x-space reconstructed image from the negative half-cycle of the MPI signal.
- 3) AVE + RECON: averaging of positive and negative half-cycles of the MPI signal, followed by x-space reconstruction.
- 4) RECON + AVE: x-space reconstruction of images from positive and negative half-cycles of the MPI signal, followed by averaging.
- 5) POS + DET: x-space reconstructed image from the positive half-cycle of the MPI signal, followed by detrending.
- 6) NEG + DET: x-space reconstructed image from the negative half-cycle of the MPI signal, followed by detrending.
- 7) AVE + RECON + DET: averaging of positive and negative half-cycles of the MPI signal, followed by x-space reconstruction and then detrending.
- 8) RECON + AVE + DET: x-space reconstruction of images from positive and negative half-cycles of the MPI signal, followed by averaging and then detrending.
- 9) RECON + DET + AVE: x-space reconstruction of images from positive and negative half-cycles of the MPI signal, followed by detrending of each reconstructed image separately. The detrended images are then averaged.

It can be seen in Figure 4.3 that the image quality was the highest for AVE

+ RECON +DET and RECON + AVE + DET. Then next best technique was RECON + DET + AVE. These three techniques successfully remove the trending and hazing artifacts seen in NEG and POS images. At SNR=2 (Figure 4.4) , due to the increased noise, trending artifacts showed a more irregular structure in POS and NEG images. The techniques that combined averaging and detrending successfully overcame a majority of the techniques revealed similar results as in SNR=100. Accordingly, AVE + RECON + DET and RECON + DET + AVE performed the best, followed by RECON + DET + AVE.

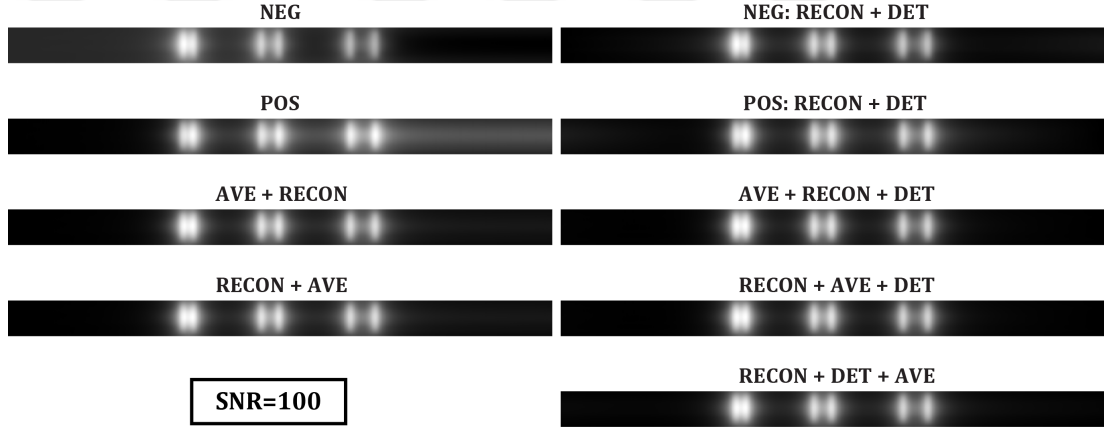


Figure 4.3: Standard x-space reconstruction compared with possible combinations of averaging and detrending techniques, for SNR=100. The effects of detrending was tested for negative, positive, and averaged images. In addition, the ordering of the operations were investigated. The detrended results are provided in the right column.

Next, the performances of the methods were tested under 7 different noise levels, ranging between SNR=2 and SNR=100. At each SNR level, Monte Carlo simulations were performed with 10 repetitions. The resulting image qualities were compared quantitatively using the peak signal-to-noise ratio (PSNR) [dB] metric, given as follows:

$$PSNR = 10 \cdot \log_{10} \left(\frac{MAX_{MPI_{ideal}}^2}{MSE} \right) \quad (4.1)$$

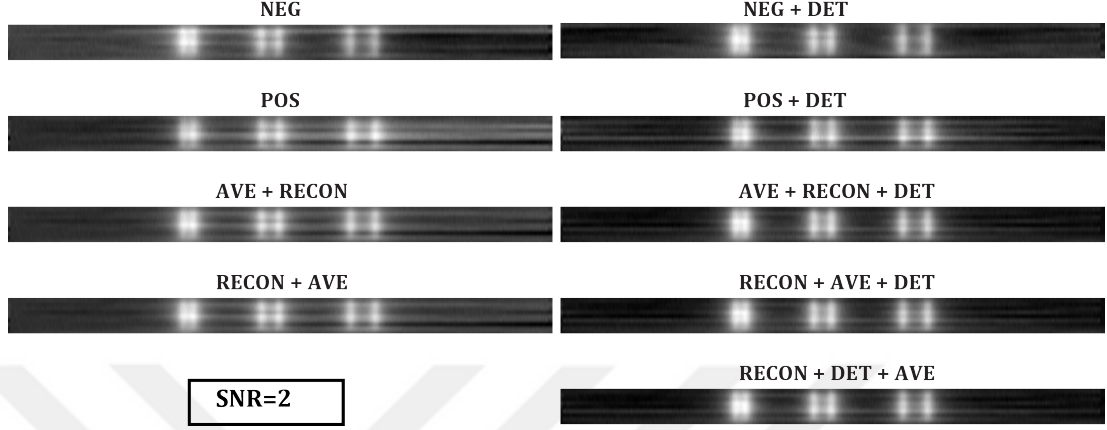


Figure 4.4: Standard x-space reconstruction compared with possible combinations of averaging and detrending techniques, for SNR=2. The effects of detrending was tested for negative, positive, and averaged images. In addition, the ordering of the operations were investigated. The detrended results are provided in the right column.

Here, Mean Squared Error (MSE) is

$$MSE = \frac{1}{m n} \sum_{i=0}^{m-1} \sum_{j=0}^{n-1} [MPI_{ideal}(i, j) - MPI_{new}(i, j)]^2 \quad (4.2)$$

Here, $MAX_{MPI_{ideal}}$ is the maximum signal intensity of the reference MPI image, MPI_{ideal} . MPI_{new} denotes the obtained MPI image, that is compared to the ideal image. m is the number of rows of the images, n is the number of columns of the images. In PSNR calculations, the obtained images were compared with the ideal MPI image, in which there is no noise and nanoparticles were assumed to respond to the alternating magnetic field instantly (i.e., no relaxation effects), but all other parameters were the same. The PSNR comparison of the images are given in Figure 4.5. The plotted lines denote the average over 10 repeated simulations at each SNR level for each technique.

The highest PSNR values were reached for AVE + RECON + DET and RECON + AVE + DET. The next best technique was RECON + DET + AVE. The lowest PSNR values were obtained from standard x-space reconstructed POS and NEG images. These results indicate that both averaging and detrending significantly improve image quality. To achieve better results, detrending should

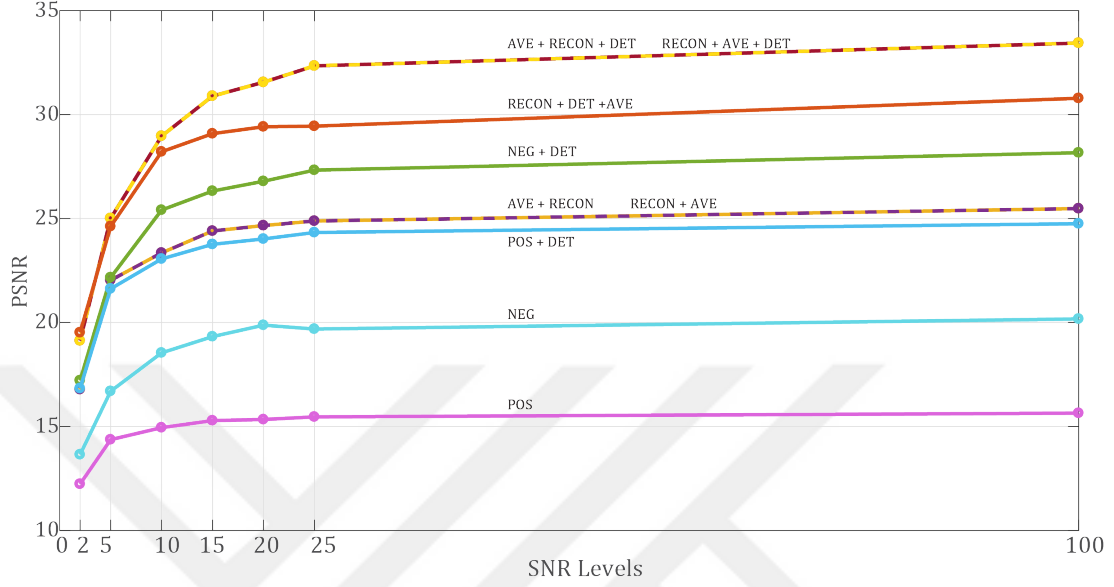


Figure 4.5: PSNR values of the images under different noise levels.

be applied at the last step.

4.3.1 Experimental Results

These methods were also compared using the experimental data from our in-house MPI scanner. An imaging phantom containing 3 tubes was scanned with our MPI scanner. The phantom size was 0.8 cm x 9.5 cm. It was scanned at a drive field frequency of 9.7 kHz and drive field strength of 15 mT. The selection field gradient was $G = [-4.8, 2.4, 2.4]$ T/m. The overlap percentage of the neighboring pFOVs was 85%. Harmonic components up to the 6th harmonic were used in the image reconstruction. 9 lines were acquired.

As seen in Figure 4.7, the experimental results are consistent with simulation results. Combining averaging and detrending significantly improved the image quality when compared to the standard x-space reconstruction. The best image quality was achieved for AVE + RECON + DET and RECON + AVE + DET. The third best technique was RECON + DET + AVE.



Figure 4.6: (a) The MPI Scanner developed in our lab. (b) The standard x-space reconstructed MPI images from negative and positive half-cycles.

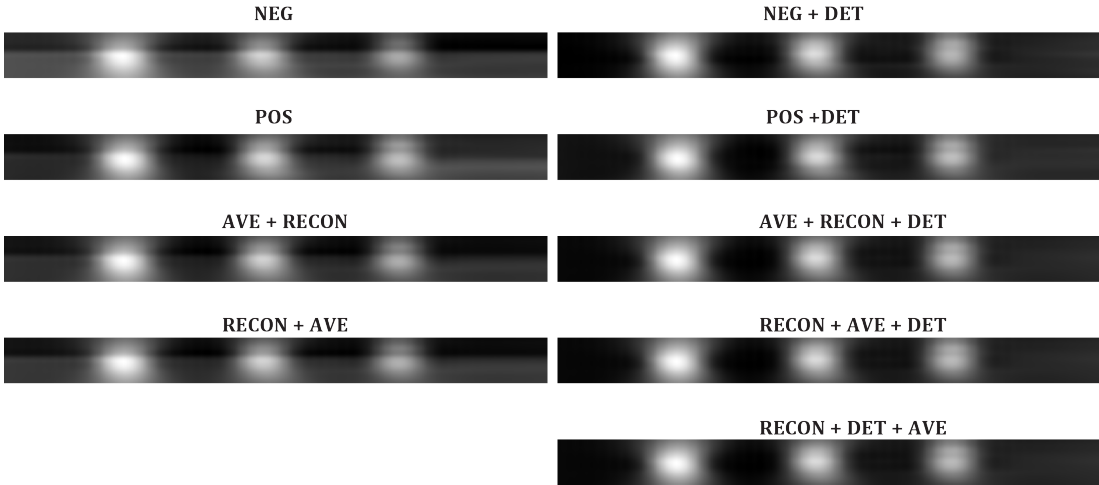


Figure 4.7: Standard x-space reconstruction compared with possible combinations of averaging and detrending techniques for the experimental data. The effects of detrending was tested for negative, positive, and averaged images. In addition, the ordering of the operations were investigated. The detrended results are provided in the right column.

Chapter 5

Effects of Safety Limits on Image Quality

This section is based on “Effects of Safety Limits on Image Quality in MPI”.E. Bozkurt, O.B. Demirel, D. Sarica, Y. Muslu, E.U. Saritas, the 6th International Workshop on Magnetic Particle Imaging (IWMPI), March 2016, Lübeck, Germany.

5.1 Simulation Parameters

In this section, the effects of safety limits on the MPI image quality was analyzed with simulations. Simulations were performed at 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz under 5 mT to 30 mT drive field strengths. At these frequencies, the drive field strength is restricted by the magnetostimulation limits, hence the magnetostimulation limits on drive field strengths for the human torso were considered in the simulations.

To visualize a more realistic scenario, the relaxation effect was also taken into consideration. The relaxation effect was modeled as a convolution of

nanoparticles' Langevin response with an exponential function defined by a relaxation time constant [24] (see Chapter 2.3). The relaxation time constants were based on a recent experimental work [2]. The maximum allowable drive field strengths for the human torso and an additional test field strength. The corresponding relaxation time constants for two different types of SPIONs, Resovist and UW33 are also listed in the Table 5.1 and 5.2 [2].

Table 5.1: Relaxation time constants for Resovist SPIONs at 4.5 kHz and 25 kHz, at magnetostimulation safety limits and an additional test field

Frequency (kHz)	Safety Limit		Additional Test Field	
	Bpeak (mT)	τ (sec)	Bpeak (mT)	τ (sec)
4.5	9.9	6.2	30	3.9
25	7.6	1.2	30	0.92

Table 5.2: Relaxation time constants for UW33 SPIONs at 4.5 kHz and 25 kHz, at magnetostimulation safety limits and an additional test field

Frequency (kHz)	Safety Limit		Additional Test Field	
	Bpeak (mT)	τ (sec)	Bpeak (mT)	τ (sec)
4.5	9.9	2.8	30	1.6
25	7.6	0.56	30	0.43

Selection field gradient strength was taken as $G=[3.5, -7, 3.5]$ T/m. Overlap ratio of the pFOVs along the z-direction was 60%. To have a fair comparison at different frequencies, the total scan-time was kept constant, 60 ms for all images. Additive White Gaussian noise was also kept uniform across all simulations.

5.1.1 Nanoparticle Diameter Estimation

In the simulations, the nanoparticle size can be modeled as a log-normal distribution [35]. Resovist and UW33 were estimated to be log-normally distributed, $17.2 \text{ nm} \pm 4 \text{ nm}$ and $20 \text{ nm} \pm 2 \text{ nm}$, respectively (Fig 5.1). These estimations were based on resolution measurements from a previous work

[2]. Accordingly, a point source phantom was simulated and its resolution was fitted to the resolution given in [2], to achieve more realistic results.

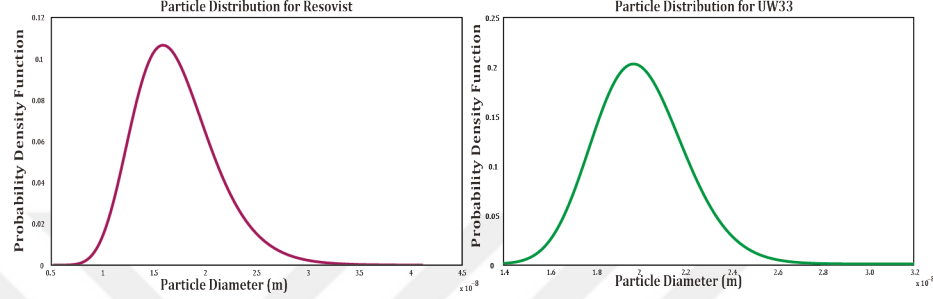


Figure 5.1: Estimated particle distributions for Resovist and UW33 SPIONs

5.1.2 Simulation Results

The MPI images of a resolution phantom simulated at 25 kHz at the safety limit of 7.6 mT and at a higher drive field strength of 30 mT are shown in Figure 5.2. The 2D resolution phantom was made up of 6 line sources of 1 mm width. They were separated by 2 mm, 4 mm, and 6 mm from their centers, respectively. FOV was 2 cm x 12 cm. The centerline images of the 2D MPI images from Figure 5.2 are shown in Figure 5.3 (a), together with the centerline for an image where relaxation effects are ignored. Figure 5.3 (b) shows the centerline for images simulated at the safety limits at 25 kHz and 4.5 kHz.

In Figure 5.4, the centerline images are shown for a variety of different cases. Here, a 2D resolution phantom was used, containing 6 line sources of 1 mm width. They were separated by 3 mm, 5 mm, and 7 mm from their centers, respectively. FOV was 1 cm x 15.3 cm. The images were simulated at 25 kHz and at safety limits for different types of nanoparticles: Resovist and UW33. The simulations for Resovist were carried out at low signal levels also, the results of which are provided at the bottom row of Figure 5.4.

These simulation results have confirmed that the resolution of the MPI images improves at lower drive field amplitudes (Figure 5.3 (a), Figure 5.2, Figure 5.4),

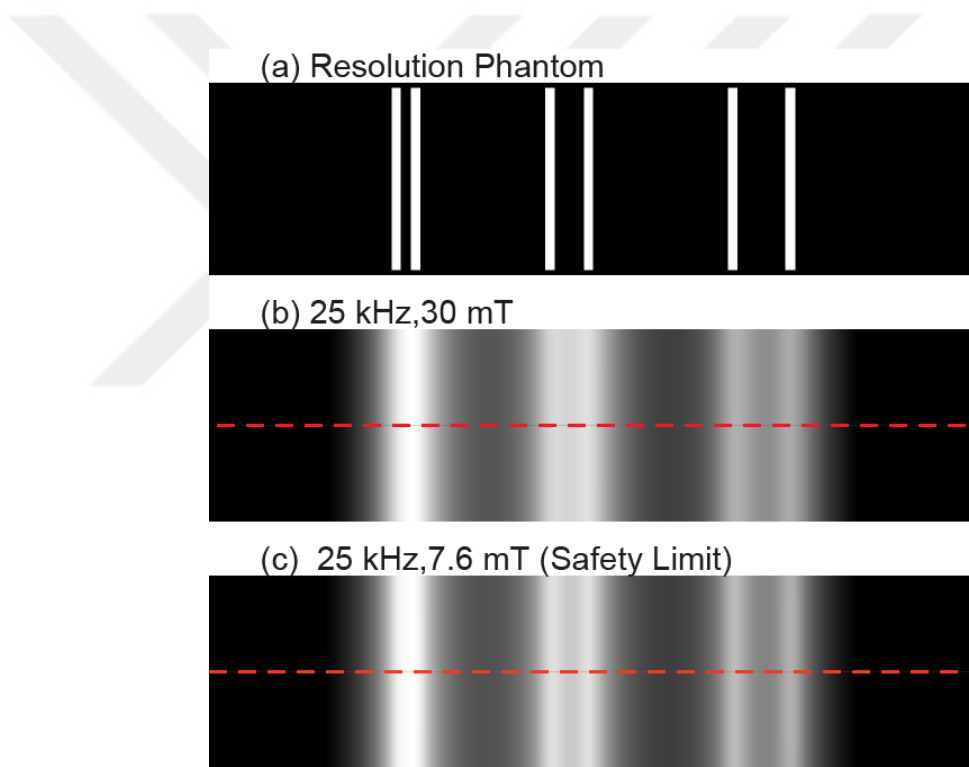


Figure 5.2: 2D simulation results for (a) the resolution phantom at 25 kHz. The results (b) at a high drive field strength of 30 mT and (c) at the safety limit of 7.6 mT.

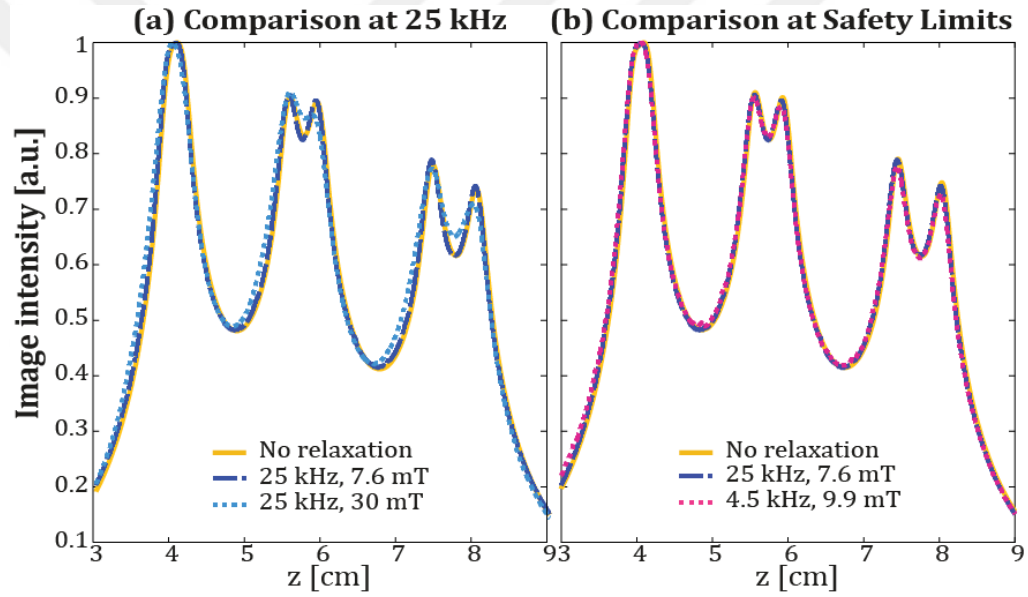


Figure 5.3: Centerlines for the simulated 2D images. (a) Comparison of images at a high drive field strength 30 mT and the safety limit of 7.6 mT at 25 kHz. (b) Comparison of images at the safety limits at two different frequencies, 4.5 kHz and 25 kHz. For reference, the without relaxation effects is also shown. (8 cm of 12 cm).

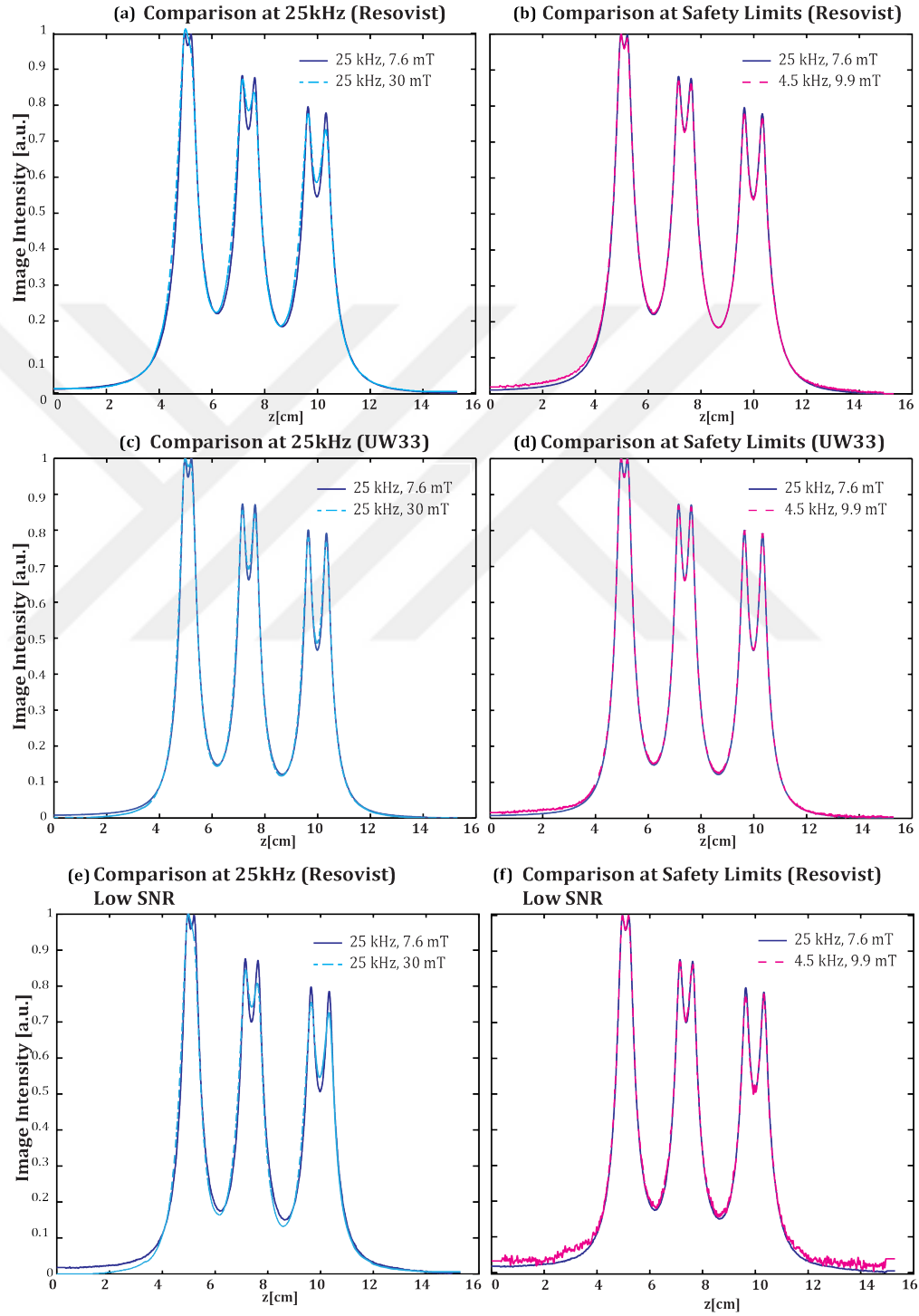


Figure 5.4: 1D simulation results of the resolution phantom. (a) Comparison at 25 kHz for Resovist. (b) Comparison at safety limits for Resovist. (c) Comparison at 25 kHz for UW33. (d) Comparison at safety limits for UW33. (e) Comparison at 25 kHz for Resovist at low SNR. (f) Comparison at safety limits for Resovist at low SNR.

and this result is consistent with the existing literature [2]. Interestingly, as long as we stay at the safety limits, scanning at different drive field frequencies has no direct impact on the resolution of the MPI images. However, the greater the frequency, the higher the SNR. Therefore, at 4.5 kHz, artifacts are visible due to the lower signal level at that frequency (Figure 5.4 (f)).

Safety limit simulations were extended to include 9.3 kHz and 12.2 kHz, in addition to 4.5 kHz and 25 kHz to verify the results for the other frequencies in this interval for Resovist and UW33. Simulated MPI images at the safety limits and at the additional test field of 30 mT are given in Figure 5.5, Figure 5.6, Figure 5.7 and Figure 5.8 at frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz and 25 kHz for two different types of nanoparticles: Resovist and UW33. It is seen that, at the safety limits, the image resolution is better, compared to the images simulated at test field, for both nanoparticle types. These results are in agreement with the previous simulation results given in Figure 5.2, Figure 5.3 and in Figure 5.4. The simulation results at the frequencies 9.3 kHz and 12.2 kHz show the same trend with the previous results for 4.5 kHz and 25 kHz.

When these results are combined with the results in Chapter 3, one can conclude that in 4 kHz-25 kHz range, the resolution remains comparable at the safety limits. In contrast, the resolution deteriorates at higher frequencies around 150 kHz, potentially due to the nanoparticles not being able to follow the rapid changes in the drive field.

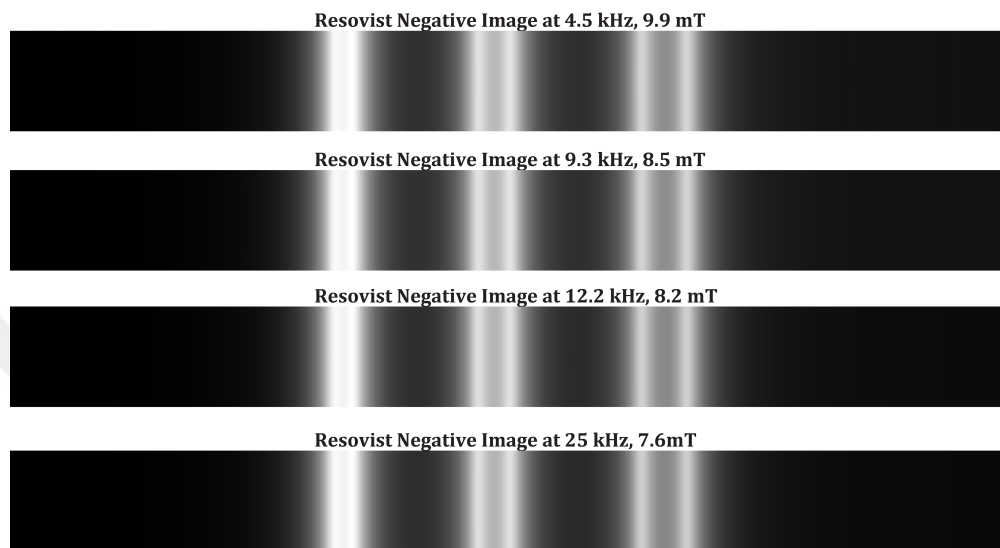


Figure 5.5: 2D simulation of the resolution phantom with Resovist at safety limits for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz.

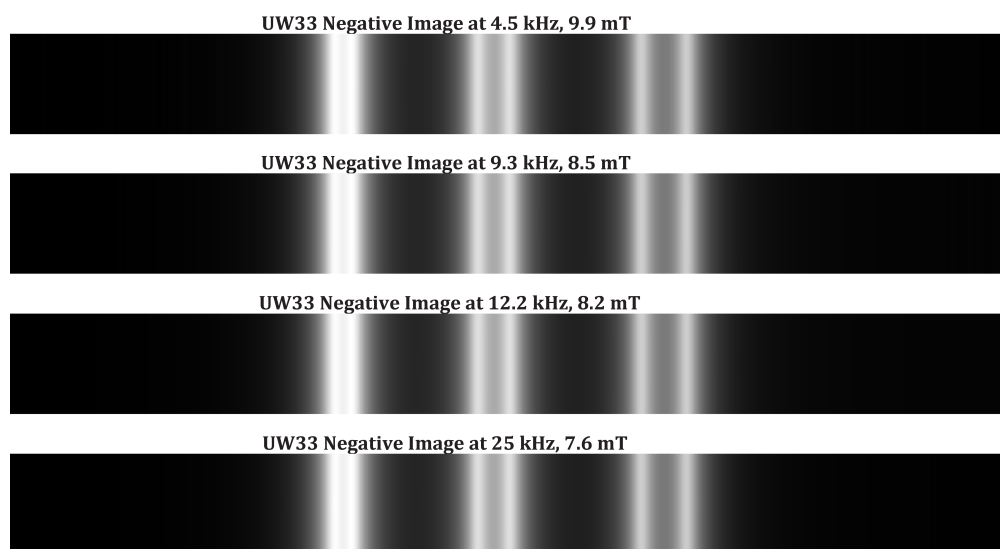


Figure 5.6: 2D simulation of the resolution phantom with UW33 at safety limits for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz.

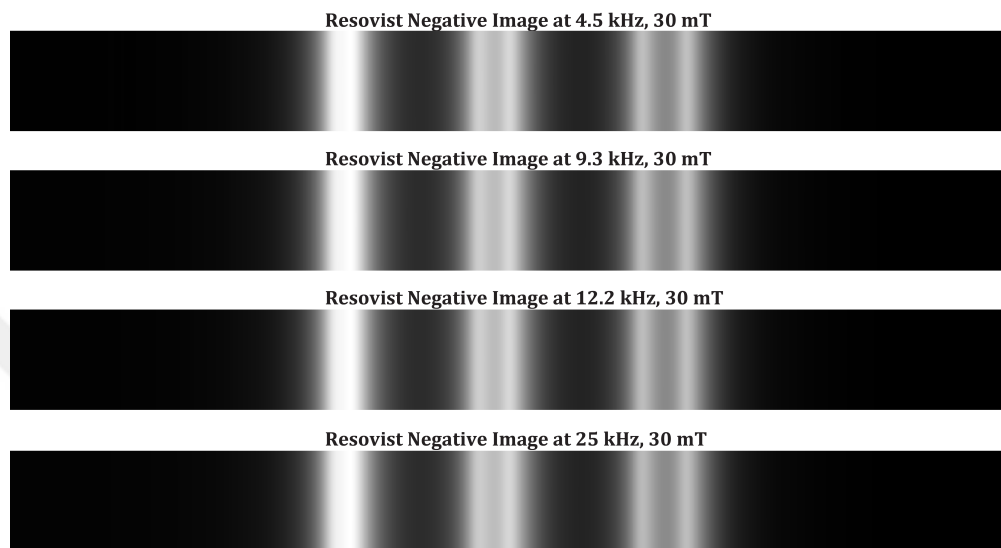


Figure 5.7: 2D simulation of the resolution phantom with Resovist at 30 mT for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz.

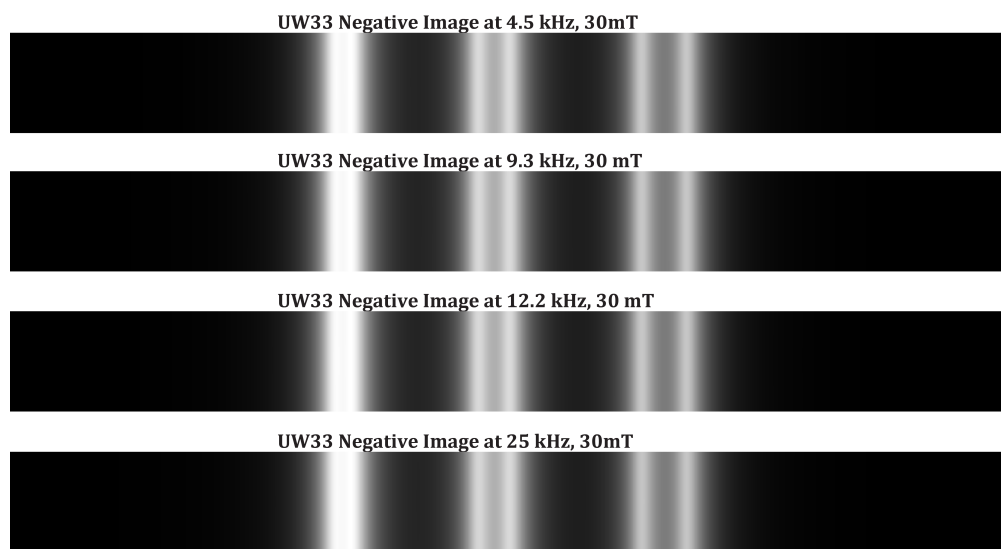


Figure 5.8: 2D simulation of the resolution phantom with UW33 at 30 mT for frequencies 4.5 kHz, 9.3 kHz, 12.2 kHz, and 25 kHz.

Chapter 6

Conclusion

In this thesis, the effects of the drive field strength and the drive field frequency on the MPI image quality were investigated to determine the optimal scanning parameters for clinical MPI scanners. Accordingly, the PSFs at 25 kHz were narrower than the PSFs at 10 kHz and 148.5 kHz. This implies that the MPI images will have higher resolution if they are acquired at 25 kHz, as opposed to 10 kHz or 148.5 kHz. The PSFs that were obtained at 10 kHz and 25 kHz are close to each other in terms of resolution, however, the SNR is higher at 25 kHz. In addition, 10 kHz is in the human hearing range, whereas 25 kHz is not. Therefore, considering the comfort of the patients, this can be another reason for the choice of 25 kHz as the operating frequency for clinical MPI scanners. At higher drive field frequencies around 150 kHz, however, the resolution of the MPI images deteriorates, hence the image quality worsens. This may be due to the SPIONs not being able to follow such fast changing magnetic fields. The analysis of the frequency components demonstrated that the decay rate is faster at 148.5 kHz. So, there is a correlation between the decay of the frequency components and the image resolution.

Another aim of this thesis was to increase the quality of the MPI images with improvements in image reconstruction and post-processing. To solve the relaxation-induced hazing / trending problem in MPI images, averaging and

detrending methods were applied. Averaging before the reconstruction and averaging after the reconstruction were analyzed separately, and the results were further enhanced with the application of a Savitzky-Golay filter. The results on the simulated and experimental MPI images demonstrated that artifacts are significantly reduced and the overall image quality is improved with the proposed method.

Effects of the safety limits on the MPI images were also investigated via simulations. The results showed that the resolution of the MPI image is not affected as long as we stay at the safety limits in 5 kHz-25 kHz range. However, the SNR increases as the drive field frequency increases, implying that frequencies around 25 kHz are more preferable. It was also confirmed that applying higher drive field strengths does not improve image quality.

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Appendix A

Derivation of Particle Diameter Estimation Formula

Based on the work [1], the FWHM of $\mathcal{L}(\cdot)$ function, in other words, the native resolution of MPI is $kH = 4.16$. Starting from this point, the derivation of the particle diameter estimation formula in Chapter 3 as follows, based on a recent work [1]:

$$\begin{aligned} kH &= 4.16 \\ 4.16 &= \frac{k}{\mu_0} FWHM_B \Rightarrow FWHM_B = \frac{4.16 \cdot \mu_0}{k} \\ k &= \frac{\mu_0 \cdot m}{k_B \cdot T} \Rightarrow FWHM_B = \frac{4.16 \cdot k_B \cdot T}{m} \\ m &= \frac{M_{sat} \cdot \pi \cdot d^3}{6} \Rightarrow FWHM_B = \frac{4.16 \cdot 6 \cdot k_B \cdot T}{M_{sat} \cdot \pi \cdot d^3} \\ M_{sat} &= \frac{0.6 \cdot T}{\mu_0} \Rightarrow FWHM_B = \frac{(4.16) \cdot 6 \cdot k_B \cdot T \cdot \mu_0}{0.6 \cdot \pi \cdot d^3} \end{aligned} \tag{A.1}$$

Then the effective core diameter, d is:

$$d = \left(\frac{(4.16) \cdot 6 \cdot k_B \cdot T \cdot \mu_0}{0.6 \cdot \pi \cdot FWHM_B} \right)^{1/3} \tag{A.2}$$

Nomenclature

Acronyms

CKD Chronic Kidney Disease, page 1

CT Computed Tomography , page 1

ECG Electrocardiogram , page 36

FFP Field Free Point , page 8

FFR Field Free Region , page 8

fMRI Functional Magnetic Resonance Imaging , page 36

FOV Field of View , page 2

FOV Field of View , page 11

FWHM Full Width at Half Maximum , page 27

IEC International Electrotechnical Comission , page 17

MPI Magnetic Particle Imaging , page 1

MRI Magnetic Resonance Imaging , page 1

MSE Mean Squared Error

PET Positron Emission Tomography , page 1

pFOV Partial Field of View , page 11

PNS Peripheral Nerve Stimulation , page 16

PSF Point Spread Function , page 9

PSNR Peak Signal to Noise Ratio

SAR Specific Absorption Rate , page 16

SAR Specific Absorption Rate, page 3

SNR Signal to Noise Ratio

SPECT Single Photon Emission Computed Tomography , page 1

SPION Superparamagnetic Iron Oxide Nanoparticles , page 1

Symbols

ρ	Density of nanoparticles along x , page 8	$particle/m^3$
G	Selection field gradient strength , page 9	$T/m/\mu_0$
k	Nanoparticle property , page 8	m/A
m	Magnetic moment of nanoparticles , page 8	Am^2
m	Magnetic moment of nanoparticles , page 9	Am^2
x_s	Time-dependent position of FFR , page 9	m
B_1	Receive coil inhomogeneity , page 9	T/A
η	Viscosity , page 16	$Joule/m^3$
$\mathcal{L}(\cdot)$	Langevin function , page 9	
σ	Electrical conductivity , page 17	ohm^{-1}
τ	Relaxation time constant , page 15	s
$E(t)$	Induced electric field , page 17	V/m
k_B	Volume of the magnetic core , page 16	$Joule/K$

k_C	Crystalline anisotropy constant , page 16	$Joule/m^3$
$M(H)$	Magnetization of nanoparticles , page 8	kA/m
T	Temperature , page 16	K
V_C	Volume of the magnetic core , page 16	m^3
V_H	Hydrodynamic volume , page 16	m^3