ANALYSIS OF CARTESIAN AND PROJECTION (K,T)-SPACE SAMPLING PATTERNS WHEN USING THE PARTIALLY SEPARABLE FUNCTIONS MODEL FOR CARDIAC PERFUSION MR IMAGING

BY

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THESIS

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ABSTRACT

Cardiac perfusion MRI aims to analyze perfusion characteristics of the heart through the injection of a contrast agent. In clinical practice, cardiac perfusion imaging is used to diagnose ischemic myocardial tissue, coronary artery disease, and, to a lesser extent, myocardial infarctions. To diagnose these tissues and diseases, real-time ECG triggered cardiac imaging techniques (fast $T_1$-weighted gradient echo, echo planar, or steady-state free precession sequences) are typically used to capture the quick wash-in and wash-out of the contrast agent. An alternative approach for real-time MRI based on the partially separable functions (PSF) model has been shown to provide reconstructions of dynamic sequences with good spatial and temporal resolutions without the need for ECG triggering. Although previous studies have demonstrated good results using the PSF model, a detailed analysis on the effect of the choice of sampling pattern has yet to be performed. Consequently, this thesis aims to analyze the ability of various Cartesian and projection sampling trajectories to characterize perfusion characteristics of the heart when the perfusion is spatially inhomogeneous using the PSF dynamic imaging method. Ten total sampling patterns (five Cartesian and five projection) were analyzed. Overall, the Cartesian sampling patterns provided better reconstructions in terms of image quality, image sequence NRMSE, and relative error of the quantitative perfusion parameters. Also, the Cartesian sampling patterns provided a more accurate reconstruction of the smallest simulated perfusion defect in the myocardium. However, the best sampling pattern performer for the other size defects varied. Also, projection sampling patterns showed a superior robustness to noise compared to Cartesian sampling patterns.
To my mother, for her unabated love and support. To my father, for his guidance and support.
ACKNOWLEDGMENTS

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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>DFT</td>
<td>Discrete Fourier transform</td>
</tr>
<tr>
<td>DIME</td>
<td>Dynamic imaging by model estimation</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>FOV</td>
<td>Field of view</td>
</tr>
<tr>
<td>MR</td>
<td>Magnetic resonance</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>NRMSE</td>
<td>Normalized root mean square error</td>
</tr>
<tr>
<td>PET</td>
<td>Positron emission tomography</td>
</tr>
<tr>
<td>PSF</td>
<td>Partially separable functions</td>
</tr>
<tr>
<td>SI</td>
<td>Signal intensity</td>
</tr>
<tr>
<td>SNR</td>
<td>Signal-to-noise ratio</td>
</tr>
<tr>
<td>SPECT</td>
<td>Single photon emission computed tomography</td>
</tr>
<tr>
<td>SSFP</td>
<td>Steady-state free precession</td>
</tr>
<tr>
<td>SVD</td>
<td>Singular value decomposition</td>
</tr>
<tr>
<td>TSS</td>
<td>Time-sequential sampling</td>
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</tbody>
</table>
CHAPTER 1

INTRODUCTION

1.1 Introduction to Cardiac Perfusion Imaging

Cardiac perfusion imaging aims to assess perfusion in the myocardium to characterize different tissue types and aid the diagnosis of certain cardiac diseases. The typical tissue types characterized with cardiac perfusion imaging are normal and ischemic myocardial tissue. Ischemic myocardial tissue suffers from reduced blood flow compared to normal myocardial tissue. In clinical practice, the most common disease cardiac perfusion imaging helps diagnose is coronary artery disease (CAD), which is a well established cause of congestive heart failure. Other applications of cardiac perfusion imaging that are actively being researched are early detection of rejection in transplanted organs [1, 2], in vivo cell tracking [3], and measurement of the biodistribution of new and tagged drugs at desired locations [4]. In the clinical setting, the nuclear medicine imaging modalities, single photon emission computed tomography (SPECT) and positron emission tomography (PET), are frequently used. However, these modalities lack the spatial resolution to detect subendocardial infarcts and they suffer from false positives due to the interpretation of the female breast attenuation shadow or obesity attenuation shadow as a defect [5]. Magnetic resonance imaging (MRI) is an attractive alternative to nuclear medicine due to its higher spatial resolution, lack of radiation exposure, and no attenuation shadow problem.

Although cardiac perfusion MR imaging can be performed with arterial spin labeling techniques [6], the arterial spin labeling techniques have limited application in the clinical practice [7]. Instead, contrast agents are used to aid assessment of perfusion in the myocardium. Contrast agents, such as the frequently used gadolinium, typically consist of paramagnetic substances that act to slightly increase the local magnetic field. As a consequence of this
phenomenon, the $T_1$ relaxation time is reduced [8]. Thus, proper $T_1$ weighted MR imaging sequences allow visualization of the contrast agent as it perfuses through the heart. Other contrast agents do exist that affect the $T_2$ and $T_2^*$ relaxation times, but these will not be reviewed in this study.

Since contrast agents allow assessment of blood flow characteristics in the myocardium, the various myocardial tissue types can be characterized and certain cardiac diseases can be diagnosed. More specifically, the myocardial blood flow is tracked by direct observation of enhancement with rate of uptake and detraction with rate of washout of the contrast agent on its first pass through the heart. Ischemic and infarcted (dead) myocardial tissue are known to display slower rates of both the uptake and the washout of the contrast agent. The uptake and the washout of the contrast agent in infarcted myocardial tissue, however, is too slow to be detectable using cardiac perfusion imaging. Detection of infarcted myocardial tissue using cardiac perfusion imaging is improving but delayed contrast enhancement imaging is currently the gold standard for its detection. The reason why the uptake and washout of infarcted tissue is extremely slow is that infarcted myocardium exhibits a larger extracellular volume than non-infarcted myocardium [9]. Delayed contrast enhancement imaging, however, only allows identification of infarcted tissue and does not indicate any of the perfusion characteristics in the myocardium that cardiac perfusion imaging indicates.

The techniques employed to perform assessment of the myocardium using cardiac perfusion imaging are both qualitative and quantitative. The qualitative methods involve visual assessment of perfusion throughout the myocardium. The quantitative methods consist of tracking the signal intensity over time of certain regions of the myocardium and extracting quantitative parameters from these curves. Some examples of the quantitative parameters include peak signal intensity, time to peak signal intensity, and rate enhancement of the contrast agent (also known as upslope).

1.2 Problem Statement

Cardiac perfusion MR imaging has been an actively researched field over the past 20 years and is gaining popularity in the clinical setting due to MRI’s advantages of higher spatial
Table 1.1: Desired Features of Cardiac Perfusion MR Perfusion Imaging for a Human

<table>
<thead>
<tr>
<th>Features</th>
<th>Desired Attributes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatial Coverage</td>
<td>Entire left ventricular myocardium</td>
</tr>
<tr>
<td>Temporal Resolution</td>
<td>High resolution to detect differences during first-pass (&lt; 1 – 2 sec)</td>
</tr>
<tr>
<td>Spatial Resolution</td>
<td>High resolution to detect subendocardial ischemia (&lt; 2 mm² in-plane)</td>
</tr>
<tr>
<td>Signal-to-noise Ratio</td>
<td>High SNR to differentiate normal and ischemic myocardium</td>
</tr>
<tr>
<td>Image Contrast</td>
<td>High contrast to differentiate normal and ischemic myocardium</td>
</tr>
<tr>
<td>Motion Artifact</td>
<td>Minimum</td>
</tr>
<tr>
<td>Contrast Concentration vs. Signal Intensity</td>
<td>Known and quantifiable relationship</td>
</tr>
</tbody>
</table>

resolution, lack of ionizing radiation exposure, and no attenuation shadow problem when compared to SPECT and PET. Nevertheless, challenges such as achieving a high temporal resolution without sacrificing spatial resolution or introducing motion artifacts still exist. A summary of the desired features of cardiac perfusion MR imaging in humans, as given by Lee [10] and Bogart et al. [5], is shown in Table 1.1. For example, a contrast agent’s first pass through the heart usually occurs in under a minute in humans. Therefore, in order to generate accurate signal intensity over time curves, a temporal resolution below one second is desired. To achieve this temporal resolution as well as satisfy the spatial coverage requirement, spatial resolution is sacrificed. However, high spatial resolution is also a desired feature to detect perfusion abnormalities in the subendocardium. A summary of the challenges to capture the first pass of contrast agent through the heart while satisfying the desired features in Table 1.1 is given by Burstein et al. [11].

Ever since the first publication in 1990 detailing successful application of cardiac perfusion imaging in humans by Atkinson et al. [12] where a fast $T_1$-weighted single-shot inversion-recovery imaging technique was used, the most commonly used imaging sequences for cardiac perfusion are either a fast spoiled gradient-echo or short-echo train echo-planar saturation/inversion recovery sequence. However, even with the advancement of imaging hardware, these techniques typically sacrifice spatial resolution for temporal resolution. To perform cardiac perfusion imaging while satisfying the desired features in Table 1.1, a large number of
dynamic imaging methods have been proposed. The main goals of these methods are to reconstruct a dynamic sequence with high spatial and temporal resolution with minimal motion artifacts. A few examples, which were used in 1990, are fast-scan methods that traverse k-space in a short time [13, 14]. Other examples include methods that use an estimate of the spatial-spectral support [15–17]; methods that incorporate parallel imaging to reduce data acquisition time [18–22]; methods that temporally model the dynamic sequence; and methods that attempt reconstruction of the dynamic sequence using severely reduced or sparse sampling [23–26]. Recent applications of these techniques include a parallel imaging technique called TSENSE introduced by Kellman et al. [27], a parallel technique called k-t SENSE that uses an estimated spatial-spectral support [28], and temporally constrained version of k-t SENSE called k-t PCA [29].

Another recent technique applied to cardiac perfusion imaging is the partially separable functions (PSF) model [30]. The PSF model temporally models the dynamic sequence model and has been shown to reconstruct cardiac sequences with good results [30–32]. The technique uses the theory of partially separable functions and linear algebra to obtain a reconstruction of a dynamic sequence with good spatial and temporal resolution while allowing sparse or reduced sampling. Although previous studies have demonstrated good results using the PSF model, a detailed analysis on the effect of the choice of sampling pattern has yet to be performed. This thesis will examine the effect of Cartesian and projection sampling on the accuracy of cardiac perfusion imaging using the PSF model. More specifically, this thesis will study which sampling patterns perform better for the PSF method when the perfusion characteristics of the heart exhibit spatial inhomogeneity that is common in ischemic or infarcted myocardium. Assessment of the sampling patterns will be accomplished by qualitative and quantitative comparison between the “gold standard” image sequence and reconstructed image sequence. A cardiac perfusion phantom of a rat with experimentally derived parameters will be used for the study. Since a rat is smaller in size and has a faster heart rate compared to a human, the desired spatial resolution and temporal resolution are more demanding than the ones listed in Table 1.1. The adjusted desired features of cardiac perfusion MR imaging for rats are shown in Table 1.2.
Table 1.2: Desired Features of Cardiac Perfusion MR Perfusion Imaging for a Rat

<table>
<thead>
<tr>
<th>Features</th>
<th>Desired Attributes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatial Coverage</td>
<td>Entire left ventricular myocardium</td>
</tr>
<tr>
<td>Temporal Resolution</td>
<td>High resolution to detect differences during first-pass (&lt; 100 – 200 ms)</td>
</tr>
<tr>
<td>Spatial Resolution</td>
<td>High resolution to detect subendocardial ischemia (&lt; 200 µm)</td>
</tr>
<tr>
<td>Signal-to-noise Ratio</td>
<td>High SNR to differentiate normal and ischemic myocardium</td>
</tr>
<tr>
<td>Image Contrast</td>
<td>High contrast to differentiate normal and ischemic myocardium</td>
</tr>
<tr>
<td>Motion Artifact</td>
<td>Minimum</td>
</tr>
<tr>
<td>Contrast Concentration vs. Signal Intensity</td>
<td>Known and quantifiable relationship</td>
</tr>
</tbody>
</table>

1.3 Summary of Results

Overall, the Cartesian sampling patterns provided better reconstructions in terms of image quality, image sequence NRMSE, and relative error of the quantitative perfusion parameters. The errors from the projection sampling patterns were, overall, only slightly higher. Also, the projection sampling patterns showed a robustness to noise that was lacking in the Cartesian sampling patterns. Within the Cartesian sampling patterns, the gaussian random sampling patterns consistently performed worse than the other Cartesian patterns. Within the projection sampling patterns, the random angle patterns performed worse than the other projection sampling patterns. For the simulated defects that represent spatially inhomogeneous perfusion characteristics, the projection sampling patterns performed worse for the smallest size defect. However, the best sampling pattern performer for the other size defects varied. Lastly, random sampling (for both Cartesian and projection sampling patterns) provided no benefits.

1.4 Organization of Thesis

The thesis will be organized into chapters. Chapter 2 gives a history of cardiac perfusion MR imaging, a background of imaging sequences used in cardiac perfusion MRI, and the
parameters used from the reconstructed images for the assessment of cardiac perfusion MRI. Chapter 3 introduces dynamic imaging, the partially separable functions (PSF) model, and \((k,t)\)-space sampling. Chapter 4 presents the simulation phantom used in the study, discusses the choice of model order for the PSF model, and describes the methods used to perform the analysis of the sampling patterns. Chapter 5 presents and describes the results. Concluding remarks are given in Chapter 6.
2.1 History of Cardiac MRI

At its introduction, MRI was primarily used to image static objects. When MRI was proposed to image the heart in the 1980s, one of the biggest challenges faced was managing the motions of the heart. Methods to image dynamic objects did not exist at the time, but a method known as gating where data acquisition is synchronized with periodic or quasi-periodic physiological signals was successfully applied to handle the motion of the heart. Gating was first studied in the mid 1980s [33–35] and proved useful for cardiac imaging due to the heart’s quasi-periodic motion. The successful application of gating to cardiac MR imaging opened the door for many different areas of cardiac imaging. One of these areas is cine imaging where a movie of a beating heart is generated using cardiac gating. Cardiac cine imaging was first studied in the late 1980s [36, 37] and is currently the foundation of functional cardiac MR imaging.

Methods that supplement different information about the heart were also developed in the late 1980s and early 1990s. Myocardial tagging, which uses a grid of saturation lines to track deformations in the heart caused by contraction, was one of the first significant methods [38]. Around the same time in the late 1980s that myocardial tagging was developed, flow quantification was first studied [39, 40]. Flow quantification uses the phase of the MR signal to encode blood flow information. Later, delayed contrast enhancement as a way to perform myocardial viability imaging, which is the detection of and distinction between infarcted and recoverable myocardium, was introduced in the late 1980s and early 1990s [41–43]. The topic of interest to this study, cardiac perfusion imaging, was first studied in the late 1980s at nearly the same time as myocardial viability imaging using a combination
of gated spin-echo and real-time imaging techniques [44,45]. The first publication detailing successful application of myocardial perfusion imaging with first-pass contrast enhancement in humans was published in 1990 by Atkinson et al. [12]. To characterize the perfusion within the myocardium, Atkinson et al. used a $T_1$-weighted single-shot inversion-recovery technique to acquire multiple images during each heart cycle.

During the early stages of cardiac imaging, the most frequently used imaging sequence was spoiled gradient-readout echo (GRE). However, as the hardware of MRI scanners improved such that a lower $T_R$ was achievable, the GRE imaging sequence limited the lowest useable $T_R$ due to its dependence on flow-enhancement [9]. Fortunately, an alternative imaging sequence known as steady-state free precession (SSFP), developed by Oppelt et al. [46] in the mid 1980s, proved to allow a shorter $T_R$ than GRE sequences for cardiac imaging [47]. In fact, all of the advantages of SSFP imaging sequences—relative independence of contrast from blood flow, speed of acquisition, and SNR efficiency—made it such an attractive alternative to GRE sequences that the current standard imaging sequence for cardiac MRI is SSFP [9]. The speed and spatial coverage of cardiac MR imaging sequences were further improved by the introduction of parallel imaging in the late 1990s and early 2000s [48–50]. Parallel imaging uses spatial sensitivity profiles of surface coils to provide additional information about the MR signal’s location, which can be used to increase acquisition speed or spatial coverage [49].

Although Cartesian sampling is the most commonly used sampling scheme in cardiac MRI, studies on the use of radial and projection sampling patterns in cardiac MRI were done in the early 2000s [51, 52]. These studies used projection sampling patterns to perform real-time ungated imaging and showed that projection sampling possessed higher motion artifact rejection than Cartesian sampling while providing comparable temporal resolution.

### 2.2 Cardiac Perfusion MR Imaging Sequences

Current cardiac perfusion imaging sequences, as noted by Finn et al., use a 90° saturation recovery pre-pulse or a 180° inversion recovery pre-pulse followed by a fast gradient echo, multishot echo planar, or fast SSFP readout acquisition [9]. Advances in imaging hardware
in recent years have allowed even faster acquisition sequences such that multi-slice acquisition within a heartbeat is now common. These imaging sequences are shown in Figure 2.1. For all sequences, there exists a trigger delay (TD) such that imaging artifacts commonly seen when imaging during systole, which is where the most violent contraction of the heart occurs, are diminished. The effective inversion time (T_{I_{\text{eff}}}) of these saturation and inversion recovery sequences occurs at the center of k-space to maximize contrast between the unenhanced myocardium and the enhancing myocardium. A more detailed look into these and other imaging sequences is given in the book by Bernstein et al. [53].

Use of these imaging techniques requires trade-offs of the desired features listed in Table 1.1 and Table 1.2 and calls attention to the challenges prevalent in cardiac perfusion imaging. For example, in spoiled GRE imaging sequences, maintaining a sufficient image contrast while keeping a low T_R to provide good temporal resolution is challenging. In echo planar imaging sequences, distortion artifacts that reduce image quality hinder its use in cardiac perfusion imaging. Steady-state free precession imaging sequences suffer from a lower temporal resolution due to a longer T_R to maintain steady state [10]. Also, all of these imaging sequences sacrifice spatial resolution (i.e., acquire a reduced number of phase encodings/projections) to satisfy the temporal resolution requirement. Motion artifacts can also occur for these imaging sequences due to their time-sequential sampling nature. The spatial coverage requirement is satisfied by acquiring multiple slices every heart beat. These artifacts are reduced, however, due to the reduced number of acquired phase encodings/projections that effectively lead to a faster temporal sampling rate. In practice, the spatial coverage and temporal resolution requirements are the most desired features.

More recent work on cardiac perfusion dynamic imaging methods has shown promise in improving the spatial and temporal resolution, imaging time, or spatial coverage features. In the work by Kellman et al. [27], a dynamic parallel imaging method called TSENSE was used to perform a slice-interleaved acquisition where multiple slices are acquired per saturation preparation as opposed to the original one slice acquired per saturation preparation shown in Figure 2.1. The benefits of this method are reduced imaging time with equivalent spatial coverage or extended spatial coverage with the equivalent imaging time when compared to the techniques presented in Figure 2.1. Other recent work by Plein et al. [28] showed that
Figure 2.1: Imaging sequences used for first-pass cardiac perfusion imaging. Top sequence shown is fast low-flip angle gradient echo sequence (also known as turboFLASH or spoiled GRE). Middle sequence shown is multishot echo planar imaging (also known as segmented EPI). Bottom sequence is steady-state free precession (SSFP) imaging. Trigger delay is referred to as TD; effective inversion time is referred to as $T_{\text{I\text{eff}}}$. $\alpha$ refers to the flip angle.
the dynamic imaging method known as k-t SENSE can be used to accelerate data acquisition while increasing spatial resolution. This method exploits spatiotemporal data correlations of dynamic sequences. Another dynamic imaging technique, proposed by Pedersen et al. [29], is k-t PCA where temporal basis functions determined through principal component analysis (PCA) can be used to constrain the reconstruction such that the temporal resolution is improved.

2.3 Assessment of Cardiac Perfusion in MRI

Cardiac perfusion assessment of resulting images generated by the above sequences falls into two categories: qualitative and quantitative analysis. Qualitative analysis involves visual assessment of the perfusion in the heart. Defects are indicated by visually abnormal perfusion characteristics. Quantitative analysis consists of generating signal intensity over time (time-signal intensity) curves for various regions of the heart. Since this method does not provide a pure quantitative analysis where perfusion can be measured in typical perfusion units of mL/min/g, the method is often referred to as semi-quantitative analysis. However, this study will refer to this type of analysis as a quantitative analysis. An example of first-pass cardiac perfusion time-signal intensity curves is shown in Figure 2.2 for normal, ischemic,
Table 2.1: Semi-quantitative Parameters for Cardiac Perfusion MRI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak signal intensity</td>
<td></td>
<td>$SI_p$</td>
</tr>
<tr>
<td>Peak contrast enhancement</td>
<td></td>
<td>$CE_{peak}$</td>
</tr>
<tr>
<td>Time to peak</td>
<td>Time to peak SI from onset of enhancement</td>
<td>$T_{peak}$</td>
</tr>
<tr>
<td>Upslope</td>
<td>Slope of initial rise in myocardium</td>
<td>Upslope</td>
</tr>
<tr>
<td>Upslope ratio</td>
<td>Ratio of myocardial upslope to left ventricular upslope</td>
<td>Upslope Ratio</td>
</tr>
<tr>
<td>Mean transit time</td>
<td>Average time for contrast agent to pass through heart region</td>
<td>MTT</td>
</tr>
</tbody>
</table>

and infarcted myocardium. As described in Section 1.1, ischemic and infarcted myocardium show a lower rate of uptake of the contrast agent compared to normal myocardium.

In practice, the acquired time-signal intensity curves of the first-pass cardiac perfusion are fit to gamma-variate curves that were first proposed by Thompson et al. [54]. The first-pass signal intensity over time gamma-variate curve is

$$SI(t) = SI_p \left( \frac{e}{\alpha \beta} (t - T_A) \right)^\alpha e^{-\left( \frac{t - T_A}{\beta} \right)} + SI_0$$

(2.1)

where $SI_p$ is the peak signal intensity, $SI_0$ is the pre-contrast signal intensity, $T_A$ is the time of appearance of the contrast agent, and $\alpha$ and $\beta$ are the adjusted parameters used to fit the curve to the data using a nonlinear least-squares fit. The quantitative parameters derived from the time-signal intensity curves are given in Table 2.1 with a short description of each parameter along with its symbol. Also, a graph with some of the listed quantitative parameters depicted in Table 2.1 is shown in Figure 2.3. The calculation of some of these parameters when the data is fit to the gamma-variate curve in Equation (2.1) is

$$CE_{peak} = \frac{SI_p - SI_0}{SI_0}$$

(2.2)

$$T_{peak} = T_A + \alpha \beta$$

(2.3)

$$MTT = T_A + \beta(\alpha + 1).$$

(2.4)
Figure 2.3: Typical time-signal intensity curves for the left ventricle and myocardium with certain quantitative parameters shown. Note that the left ventricle time-signal intensity curve depicts a second-pass of the contrast agent. This phenomenon also occurs in the myocardium, but to a lesser extent, and is ignored in this diagram.

Calculation of the upslope consists of least-squares fitting of a linear function to the inflow of contrast agent. Since the time-signal intensity curve flattens out before the peak signal intensity is reached, attention to the region of inflow of contrast agent to which a linear function is fit is important. A proper range of Equation (2.1) to fit the linear function is \((T_A + \alpha) \leq t \leq (T_{peak} - \frac{\beta}{1.25})\). These values work for a wide range of \(\alpha\) and \(\beta\) values. Then, the upslope is simply the slope of the fitted linear function. The upslope ratio is the ratio of the upslope of the myocardium to the upslope of the left ventricular blood pool.

The most used quantitative parameters to characterize cardiac perfusion are upslope, upslope ratio, time to peak, and peak signal intensity [8]. Upslope ratio is more commonly used than upslope since the upslope value is affected by the contrast agent’s bolus injection condition and the subject’s cardiac output. As a result, the myocardium upslope value is normalized against the left ventricular upslope value to better accommodate the different bolus injection conditions and the subject’s cardiac output. In order to calculate an accurate upslope and upslope ratio, the temporal resolution requirement given in Table 1.1 and Table 1.2 need to be satisfied for a human and rat, respectively.
CHAPTER 3
THEORY

3.1 Introduction to Dynamic Imaging and (k,t)-Space

Magnetic resonance imaging (MRI) has proven to be a useful imaging modality in both clinical and research settings by providing anatomical and functional properties of the imaged object. In MRI, samples in the spatial frequency domain, which is referred to as k-space, of the object \( \rho(\mathbf{r}) \) are collected according to

\[
S(\mathbf{k}) = \int_{-\infty}^{\infty} \rho(\mathbf{r}) e^{-i2\pi \boldsymbol{k} \cdot \mathbf{r}} d\mathbf{r} \tag{3.1}
\]

where \( \mathbf{r} = (x, y) \) corresponds to the 2D spatial coordinates and \( \mathbf{k} = (k_x, k_y) \) corresponds to the 2D k-space coordinates. In the “real-world,” a continuous system is not realizable. As a result, it is more practical to model the object discretely as

\[
\rho(x, y) = \sum_{m \in \mathbb{Z}} \sum_{n \in \mathbb{Z}} c_{m,n} \phi(x - m\Delta_x, y - n\Delta_y) \tag{3.2}
\]

where \( \phi(x, y) \) is some basis function that is applied at the coordinates \((m\Delta_x, n\Delta_y)\) where \(m, n \in \mathbb{Z}\). For simplicity, \( \phi(x, y) \) is chosen to be a Kronecker delta function basis since it allows quick analysis of the discretely sampled k-space. For a discretely sampled k-space of \(M\) samples along the x-direction and \(N\) samples along the y-direction, the collected k-space samples are

\[
S(k_x, k_y) = \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} c_{m,n} e^{-i2\pi (mk_x \Delta_x \Delta_k + nk_y \Delta_y \Delta_k)} \tag{3.3}
\]
Figure 3.1: (a) Classical $k$-space. (b) View when rotating $k$-space counterclockwise as referenced from the top of the page. (c) $(k,t)$-space, which can be thought of as a rotated $k$-space stacked at each time point.

where

$$\Delta_x = \frac{1}{M \Delta_{k_x}}, \quad \Delta_y = \frac{1}{N \Delta_{k_y}}$$

(3.4)

when the sampling is treated separately along each dimension. From Equations (3.3) and (3.4), it is seen that the 2D discrete Fourier transform (DFT) relationship can be used for image reconstruction, which is a very useful feature since it can be computed quickly and it has well characterized artifacts.

The above approach must be slightly modified since, as with cardiac perfusion MR imaging, the object being imaged is a time-varying object. Consequently, Equation (3.2) is transformed into

$$\rho(x, y, t) = \sum_{m \in \mathbb{Z}} \sum_{n \in \mathbb{Z}} \sum_{p \in \mathbb{Z}} c_{m,n,p} \phi(x - m \Delta_x, y - n \Delta_y, t - p \Delta_t)$$

(3.5)

and the samples are collected in a higher dimensional $(k,t)$-space that was first proposed by Xiang and Henkelman [55],

$$S(k_x, k_y, t) = \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} \sum_{p=0}^{P-1} c_{m,n,p} e^{-i2\pi (mk_x \Delta_x \Delta_{k_x} + nk_y \Delta_y \Delta_{k_y})} \phi(t - p \Delta_t).$$

(3.6)

A graphical representation of $(k,t)$-space derived from $k$-space is shown in Figure 3.1. Fortunately, $(k,t)$-space can be considered $k$-space over time where the frequency encoding axis
is oriented perpendicular to the page in Figure 3.1c. The key assumption in this representation is that the temporal sampling rate for $k_x$ samples is considered to be fast enough to enable perfect reconstruction of the dynamic object along the $x$-axis assuming bandlimitness. Thus, $k_x$ is treated as being collected instantaneously in $(k,t)$-space such that its notation is dropped. This assumption is fairly justified since, in modern MRI systems, $k_x$ samples are acquired at a temporal sampling interval around 4 $\mu$s and physiological motion, such as cardiac and respiratory motion, for mammals occurs with periods in the hundreds of milliseconds. Conversely, $k_y$ samples, which are acquired at a temporal sampling interval around 3 ms, are considered to be the limiting factor when sampling dynamic sequences.

As a result of the slow temporal sampling interval for $k_y$ samples, special attention is given to sampling dynamic sequences. More specifically, phase encoding lines and projection lines are acquired once per time point in Cartesian and projection sampling, respectively. This type of sampling is referred to as time-sequential sampling (TSS) or real-time imaging in MRI. The Cartesian and projection sampling patterns are shown for both normal $k$-space sampling and time-sequential $(k,t)$-space sampling in Figure 3.2. For Cartesian sampling, when the time-sequential sampling is reconstructed using the inverse two-dimensional DFT by combining phase encoding lines from different time points into one frame, the motion artifact known as ghosting occurs if the number of phase encodings times the sampling interval violates the temporal Nyquist sampling criterion for the dynamic sequence.

Ghosting is when dynamic objects appear on the reconstructed sequence as a low amplitude signal. Ghosting was first described by Xiang and Henkelman [55] for reconstructing dynamic MRI sequences in Cartesian sampling. It can be described using the projection-slice theorem for Fourier transforms where temporally varying structures of the image are projected onto the final reconstruction or by multi-dimensional lattice sampling theory that was first looked at by Jan P. Allebach [56] and further explored by Willis and Bresler [57,58]. In cases where the dynamic region of the object covers much of the image’s field of view (FOV), ghosting severely affects the reconstructed image sequence’s quality. Projection sampling reconstruction techniques, on the other hand, have been shown to exhibit diminished motion artifacts when compared with Cartesian sampling [59]. The motion artifacts for projection sampling reconstruction techniques appear as pixel blur and streaking artifacts, which are
Figure 3.2: Sampling shown where each dot represents an acquired sample and each line represents an acquire phase encoding/projection line for $\mathbf{k}$-space and $(\mathbf{k},t)$-space, respectively. (a) Cartesian (also known as rectilinear) sampling in $\mathbf{k}$-space. (b) Projection sampling in $\mathbf{k}$-space. (c) Cartesian time-sequential sampling in $(\mathbf{k},t)$-space. Notice that each phase encoding line is acquired once per time point. (d) Projection time-sequential sampling in $(\mathbf{k},t)$-space. Notice that each projection line is acquired once per time point.
Figure 3.3: Diagram of ECG gating. After the R wave, the first phase encoding/projection line is acquired for the first cardiac phase followed by the first line of the remaining cardiac phases up to Np total phases. In the following cardiac cycle, the second phase encoding/projection line is acquired for all Np cardiac phases. This type of acquisition continues until all N phase encoding/projection lines are acquired, which takes a total of N heartbeats.

considered to be more acceptable in the MR imaging community [52].

One way to overcome these motion artifacts in cardiac imaging is to use gating. Gating involves synching acquisition with quasi-periodic physiological signals, such as the cardiac and respiratory cycles. A simple example of prospective electrocardiogram (ECG) gating known as ECG triggering where signal acquisition is synched with the cardiac cycle is shown in Figure 3.3. It should be noted that the example in Figure 3.3 is not typically used in clinical practice. Instead, a $k$-space segmented version where multiple phase encoding/projection lines are acquired each cardiac phase is used. However, for the example in Figure 3.3, one phase encoding line or projection line is acquired each cardiac phase at a rate of one line per cardiac phase per heartbeat. In other words, Np phase encoding/projection lines are acquired for the $N^{th}$ line/angle number during each heartbeat such that Np frames of the heart cycle are generated. Thus, a full set of phase encoding/projection lines is essentially acquired at the same time point in $(k,t)$-space for each cardiac phase. When reconstructing the sequence, a motion artifact free heartbeat is produced (ignoring respiratory motion).

The total scan time for this type of acquisition for one heart cycle is $T_{\text{scan}} = N \cdot RR$ where N is the number of phase encoding/projection lines and RR is the average time between
two R phases of the ECG. To accommodate respiratory motion, breath holding, respiratory
gating in combination with ECG gating, and averaging are typically employed in practice.
The entire cardiac cycle can be sampled when the ECG gating is done retrospectively with
interpolation, which also improves scan time efficiency.

Although ECG gating has been very useful in the development of cardiac MRI, particu-
larly cardiac cine imaging, it has limited use in first-pass myocardial perfusion imaging since
the contrast agent’s first pass through the heart occurs over several heart cycles. Instead,
 acquisition is triggered after a certain interval after the R wave. Although this ECG trig-
gering is different than the ECG triggering described in Figure 3.3, it is still referred to as
ECG triggering since signal acquisition is synchronized with the systolic peak of the ECG
signal. One of the first studies done on myocardial perfusion MR imaging by Miller et al. [45]
used ECG triggering in combination with time-sequential sampling to qualitatively image
contrast enhancement during diastole. Drawbacks of implementing effective ECG gating
include requirement of a strong ECG signal and absence of severe arrythmia. However, ev-
idence of the usefulness of ECG gating is made apparent by the fact that the standard for
cardiac cine imaging has become using breath-held ECG-gated steady-state free precession
sequences.

3.2 Partially Separable Functions Model

The partially separable functions (PSF) dynamic imaging model aims to reconstruct a dy-
namic sequence using highly sparse sampling of (k,t)-space [25]. In MRI, data acquisition
of dynamic sequences is described by

$$S(k, t) = \int_{-\infty}^{\infty} \rho(r, t)e^{-i2\pi k \cdot r} dr$$  \hspace{1cm} (3.7)
where $S(k, t)$ is the measured data and $\rho(r, t)$ is the dynamic object [55]. In the PSF model, the measured data is modeled by a $M^{th}$-order partially separable function,

$$S(k, t) = \sum_{m=1}^{M} \alpha_m(k) \phi_m(t) \quad (3.8)$$

where $\{\alpha_m(k)\}$ represents the $k$-space basis functions that describe the variations in $k$-space and $\{\phi_m(t)\}$ represents the temporal basis functions that describe the temporal variations.

This model can also be transformed to image space,

$$\rho(r, t) = \sum_{m=1}^{M} c_m(r) \phi_m(t) \quad (3.9)$$

where $c_m(r)$ is the inverse Fourier transform of $\alpha_m(k)$.

In order to determine the $k$-space and temporal basis functions, two data sets are acquired. One of the data sets, denoted as $S_1(k, t)$, is a high temporal resolution data set that satisfies the Nyquist temporal sampling criterion and is often referred to as the training data. The second data set, denoted as $S_2(k, t)$, is a high $k$-space resolution data set that satisfies the spatial Nyquist sampling criterion. The temporal basis functions, $\{\phi_m(t)\}$, are determined via a singular value decomposition,

$$A = \sum_{m=1}^{\min(p,q)} \lambda_m u_m v_m^H \quad (3.10)$$

where

$$A = \begin{bmatrix}
S_1(k_1, t_1) & S_1(k_2, t_1) & \cdots & S_1(k_p, t_1) \\
S_1(k_1, t_2) & S_1(k_2, t_2) & \cdots & S_1(k_p, t_2) \\
\vdots & \vdots & \ddots & \vdots \\
S_1(k_1, t_p) & S_1(k_2, t_p) & \cdots & S_1(k_p, t_p)
\end{bmatrix} \quad (3.11)$$

and $\lambda_m$ are the singular values of $A$ in descending order, $\{u_m\}$ are the left singular vectors, and $\{v_m\}$ are the right singular vectors. The temporal basis functions are then set to the
left singular vectors for \( m = 1, 2, \ldots, M \),

\[
[\phi_m(t_1), \phi_m(t_2), \ldots, \phi_m(t_p)]^T = u_m. \tag{3.12}
\]

The \( k \)-space basis functions are determined by fitting the model to the measured data, \( S_2(k, t) \). This task is accomplished by solving

\[
\begin{bmatrix}
\phi_1(t_{1,d}) & \phi_2(t_{1,d}) & \cdots & \phi_M(t_{1,d}) \\
\phi_1(t_{2,d}) & \phi_2(t_{2,d}) & \cdots & \phi_M(t_{2,d}) \\
\vdots & \vdots & \ddots & \vdots \\
\phi_1(t_{L,d}) & \phi_2(t_{L,d}) & \cdots & \phi_M(t_{L,d})
\end{bmatrix}
\begin{bmatrix}
\alpha_1(k_d) \\
\alpha_2(k_d) \\
\vdots \\
\alpha_M(k_d)
\end{bmatrix}
= \begin{bmatrix}
S_2(k_d, t_{1,d}) \\
S_2(k_d, t_{2,d}) \\
\vdots \\
S_2(k_d, t_{L,d})
\end{bmatrix} \tag{3.13}
\]

for \( \{\alpha_m(k_d)\} \) independently for each \( k \)-space location (referred to as \( k_d \)) where \( L \) is the number of measured data for each \( k_d \) and \( d = 1, 2, \ldots, D \) where \( D \) is the total number of \( k \)-space locations. Equation (3.13) may be written as \( \Phi_d \alpha_d = s_d \) for simplicity. Usually, the model order of the PSF model, \( M \), is less than the number of measured data, \( L \), for each \( k \)-space location (i.e., \( M < L \)). As a result, Equation (3.13) is an overdetermined system and can be solved in a least-squares sense for \( \{\alpha_m(k)\} \). Also, the solution to Equation (3.13) is not unique. Therefore, a Moore-Penrose pseudoinverse (for an overdetermined system) of \( \Phi_d \) as given by

\[
\Phi_d^\dagger = (\Phi_d^T \Phi_d)^{-1} \Phi_d^T \tag{3.14}
\]

is used to solve the equation in a minimum norm sense. If \( M > L \), then Equation (3.13) is an underdetermined system and, again, has no unique solution. The equation can be solved in minimum norm sense using the undetermined version of the Moore-Penrose pseudoinverse, but a good result is not guaranteed. Therefore, it is important that the PSF model order is chosen with proper care. The PSF model order typically corresponds to the number of significant singular vectors. Also, the eigenvalue decay indicates a proper choice for \( M \). Moreover, \( M \) is also often determined by evaluating the reconstructed dynamic sequences for a certain range of \( M \) and then chosen by which reconstructed sequence is the best.

The PSF model was previously used by Liang et al. in the dynamic imaging by model
estimation (DIME) reconstruction algorithm [23]. The DIME algorithm is a special case of the PSF model where the temporal basis functions in Equation (3.8) and Equation (3.9) are expressed in parametric form. More specifically, the temporal basis functions are denoted by a weighted sum of harmonic functions,

\[ \phi_m(t) = e^{i2\pi f_m t} \] (3.15)

for \( m = 1, 2, \ldots, M \) where \( \{f_m\} \) are the motion frequencies. These motion frequencies can be determined from \textit{a priori} information or the training data. The model order, \( M \), is determined by the number of finite locations where energy occurs in the spectral domain. The DIME algorithm is equally as good as the PSF algorithm in the case of periodic or quasi-periodic motion. However, the PSF model is not restricted to periodic or quasi-periodic motion since it can handle arbitrary motion.

From the theory of partially separable functions, the matrix \( A \) in Equation (3.10) has rank \( M \) where \( M < \min(p, q) \) if Equation (3.8) is exact. Therefore, the singular value decomposition can be truncated

\[ \hat{A} = \sum_{m=1}^{M} \lambda_m u_m v_m^H \] (3.16)

since \( \lambda_m = 0 \) for \( m \geq M \). In general, the partial separability of the (k,t)-space signal is not exact. Also, since the temporal basis functions are determined by setting them equal to the \( M \) most significant left singular vectors, it is apparent that the choice of \( M \) will severely affect the resulting image quality of the reconstructed sequence when the PSF model is used. As such, an inquiry into the effect of the model order of the SVD approximation on the dynamic image sequence will give an indication of the resulting image quality and viability of the PSF model.

3.3 Sampling in (k,t)-Space

Cartesian and projection sampling, as previously shown in Figure 3.2, are types of sampling frequently used in MRI. The first images produced using MRI were done with projection
type sampling patterns and used backprojection to reconstruct an image [60]. However, technical shortcomings like eddy currents and chemical shift severely reduced image quality using backprojection. These shortcomings led to the use of Cartesian sampling patterns that allowed usage of the Fourier transform for image reconstruction. But, with the vast improvement in technology of MRI scanners and the incorporation of gridding, projection sampling has resurfaced as a viable sampling pattern. Projection sampling has been shown to be advantageous over Cartesian sampling when sampling dynamic objects since motion artifacts appear as a radial streak with its amplitude lowest near the dynamic region [59]. The temporal resolution of reconstructions using projection sampling has also been shown to be comparable to traditional Cartesian methods [61]. Also, angular undersampling of a dynamic object has been shown to provide better temporal resolution while reducing SNR and spatial resolution [62].

3.3.1 Cartesian Sampling

Cartesian sampling, for static objects, involves collecting $k$-space samples on the Cartesian grid along the frequency encoding ($k_x$) axis and phase encoding ($k_y$) axis. If the object being imaged, $I(x, y)$, is support limited along the $x$-axis ($I(x) = 0$ for $|x| < W_x$) and support limited along the $y$-axis ($I(y) = 0$ for $|y| < W_y$), then the $k$ sampling interval along the each axis needs to follow the spatial Nyquist sampling criterion

$$\Delta k_x \leq \frac{1}{W_x}$$

$$\Delta k_y \leq \frac{1}{W_y}$$

for the $k_x$ axis and $k_y$ axis, respectively. If this criterion is not satisfied, then the familiar spatial wrap-around artifact occurs. The spatial Nyquist sampling criterion still extends to ($k,t$)-space Cartesian sampling, as shown in Figure 3.2c, for dynamic objects. However, an additional temporal Nyquist sampling requirement is introduced for each $k$-space point. If this temporal Nyquist sampling requirement is violated, then the previously described ghosting artifact occurs.
Figure 3.4: The partially separable functions model \((k,t)\)-space sampling pattern for Cartesian sampling. The frequency encoding \((k_x)\) axis is oriented perpendicular to the page. The open circles represent the training data, \(S_1(k,t)\), and the closed circles represent the dynamic data, \(S_2(k,t)\).

The PSF method for reconstruction of dynamic sequences was originally proposed using Cartesian sampling [25]. Although not realizable in practice, acquisition of \((k,t)\)-space that satisfies both the spatial and temporal Nyquist sampling criterion should be acquired to ensure the number of temporal basis functions needed to adequately represent the dynamic sequence is minimal. Instead, a certain number of phase encoding lines is chosen that is determined to well represent the dynamics of the object. Unfortunately, the dynamics of an object are encoded at all spatial frequencies. Thus, it is desired to acquire \((k,t)\)-space that satisfies the spatial Nyquist sampling criterion for the training data. However, acquisition of this form cannot be done to also satisfy the temporal Nyquist sampling criterion for each \(k\)-space point. As a result, lines near the center of \(k\)-space are typically acquired for the training data since the center of \(k\)-space contains a large amount of information about the object. An example of the type of Cartesian sampling pattern used in the PSF method is described in Figure 3.4. In this sampling pattern, the training data is collected along \(k_y = 0\) at a high temporal rate. Extending the training data collection to use more than one phase encoding line is possible provided that sampling for each \(k\)-space point satisfies the temporal Nyquist sampling criteria. Also, in the example sampling pattern, the dynamic data is collected to satisfy the spatial Nyquist sampling criterion.
3.3.2 Projection Sampling

Projection sampling, for static objects, involves sampling along projection lines. Sampling along these projection lines can be described by acquiring $k_x$ and $k_y$ samples at

\begin{align}
    k_x &= r \cos \theta \\
    k_y &= r \sin \theta
\end{align}

(3.19) (3.20)

where \( r \) is a vector that determines the location of samples acquired along the projection line and \( \theta \) is a vector that determines the angle orientation of the projection line. For a support limited object, the spatial Nyquist sampling criterion is defined as

\[
k_{\text{max}} \Delta \theta \leq \frac{1}{W}
\]

(3.21)

where \( k_{\text{max}} \) is the radius of the projection line (or the sampled point furthest away from the center of \( k \)-space), \( \Delta \theta \) is the angular sampling interval, and \( W \) is the diameter of the largest circle than encloses the entire object [53]. As with Cartesian sampling, the temporal Nyquist sampling criterion needs to be satisfied for each \( k \)-space point when sampling dynamic objects.

Projection sampling for the PSF method is handled in a fashion similar to Cartesian sampling. Since each projection line samples the center of \( k \)-space, it is possible to acquire an arbitrary number of projection lines for the training data provided the temporal Nyquist criterion is satisfied. Also, acquisition of different angles for projection lines is desired since projection lines cannot capture motion encoded in a direction perpendicular to it. However, it is also feasible to acquire the training data along \( k_y = 0 \) at a high temporal rate just like it is acquired in Cartesian sampling. For the dynamic data, a projection line is acquired at each time point instead of a phase encoding line. In order words, the \( \theta \) vector in Equations (3.19) and (3.20) is fixed for a certain number of projections. A projection line is acquired at \( \theta_1 \) during the first time point, \( \theta_2 \) during the second time point, and so on until \( \theta_p \) where \( p \) is the number of projections. Then, this pattern is repeated \( L \) times to form \( s_d \) in Equation (3.13).
3.3.3 Deterministic versus Random Sampling

The most standard deterministic time-sequential Cartesian sampling pattern used in practice, which is shown in Figure 3.2c, falls into the category of lexicographic sampling that was described by Allebach [56]. This type of pattern can be described by the multidimensional \((k,t)\)-space sampling matrix

\[
V = \begin{bmatrix}
N_{pe} \Delta t & \Delta t \\
0 & \Delta k_y
\end{bmatrix}
\]

(3.22)

where \(\Delta t\) is the time between acquisition of consecutive phase encoding lines, \(\Delta k_y\) is the space along \(k_y\) between phase encoding lines, and \(N_{pe}\) is the total number of phase encodings. With this sampling matrix, a reciprocal periodicity matrix in the reciprocal \((y,f)\)-space is defined by

\[
U = (V^{-1})^T = \begin{bmatrix}
\frac{1}{N_{pe} \Delta t} & 0 \\
-\frac{1}{N_{pe} \Delta k_y} & \frac{1}{\Delta k_y}
\end{bmatrix}
\]

(3.23)

The physical representation of the reciprocal periodicity matrix is that the spatial-spectral \((y,f)\) support function of the dynamic sequence is densely packed in \((y,f)\)-space. With this dense packing, energy from one of the replicas typically leaks into the original spatial-spectral function, which causes the aforementioned ghosting artifact. Of course, the occurrence of leaking energy is dependent upon the actual spatial-spectral support function of the dynamic sequence; however, leaking typically occurs due to the dense packing. This multidimensional sampling approach can be used to design different sampling patterns, as was done by Allebach [63] and Willis and Bresler [64], when the spatial-spectral support function of the dynamic sequence is known or can be estimated.

Random sampling, although not as well characterized as Cartesian sampling, provides some benefits when compared to Cartesian sampling. For Cartesian sampling of a dynamic sequence, random sampling typically means that the order of each acquired phase encoding line is based upon some probability distribution. For projection sampling of a dynamic sequence, the angle displacement between consecutive projection lines can be random or the order in which the projection lines are acquired can be random. Benefits of random sampling, as described by Allebach [56], include incoherent aliasing artifacts and increased SNR for
acquisition of fewer phase encoding/projection lines compared to Cartesian sampling. More specific to the PSF method, random sampling can help avoid ill-conditioning of the temporal basis matrix in Equation (3.13) by choosing samples for different time points between k-space samples. Liang et al. described how random sampling over time can help avoid ill-conditioning of the temporal basis matrix in the presence of strong sinusoidal varying objects [23]. Random sampling has also been used in compressed sensing in MRI as a generic acquisition scheme to recover images with a sparse representation [65].
4.1 Simulation Phantom

A two-dimensional cardiac MR simulation with first-pass perfusion characteristics in the left ventricular blood pool and myocardium of a rat was developed to use for the sampling pattern analysis. The simulation was created from an ECG triggered and respiratory gated fast low angle shot (FLASH) imaging sequence of the short-axis view of a healthy rat using a four channel MRI scanner with no application of parallel imaging (i.e., no $k$-space undersampling was performed). The reconstructed image sequence contained a single heartbeat of a rat with no respiration. Cardiac phases were generated though the use of cubic spline interpolation between successive frames of the image sequence. Respiratory motion was created by deforming the interpolated image sequences based on a thin-plate spline transformation [66]. These respiratory deformations are applied separately from the cardiac cycle such that the heartbeat is not synchronized with the respiration motion. For the respiratory deformation, an ellipse was used to model the expansion and contraction of the chest during the breathing process. An advantage of using a thin-plate spline type deformation is that it introduces displacement and deformation of the heart, which is consistent with recent biological studies [67]. Also, cardiac and respiration cycle variabilities were imposed on the simulation based on statistics from experiments similar to the experiment from which this phantom was derived. Overall, a mean period of 970 ms with 1% variability was used for respiration and a mean period of 197 ms with 10% variability was used for cardiac motion. A snapshot of this phantom is shown in Figure 4.1a.

To add perfusion to the left ventricular blood pool and left ventricular myocardium, masks of these regions were created on each frame of the experimental image sequence. These
masks were then interpolated and deformed in the same manner as the original cardiac MR simulation to account for cardiac and respiratory motion, respectively. As a result, the masks accurately portray the movement of their represented regions whereby a perfusion overlay can be applied. The type of perfusion curve applied to the phantom was the gamma-variate curve shown in Equation (2.1) with an asymptotic recirculation term that was proposed by Golish et al. [68],

\[
SI(t) = SI_p \left( \frac{e}{\alpha \beta} (t - T_A) \right)^\alpha e^{-\left(\frac{t - T_A}{\beta}\right)} + SI_r \left( 1 - e^{-\left(\frac{t - T_A}{\tau}\right)} \right)
\]

where \(SI_r\) is the recirculated signal intensity and \(\tau\) is designed such that the recirculation term reaches its maximum when the original gamma-variate curve falls off to about 5% of its peak. Note that no precontrast signal intensity, \(SI_0\), is shown in Equation (4.1) since its value is already contained in the original phantom. To simulate spatially inhomogeneous perfusion characteristics of the heart, four small regions (with pixel sizes: one, four, nine, and sixteen) inside the left ventricular myocardium were defined. These defect masks remained stationary (i.e., the masks were not interpolated and deformed to account for cardiac and respiratory motion, respectively). The defect locations, however, were defined such that they mostly
Figure 4.2: Perfusion curves for applied to the left ventricular blood pool, left ventricular myocardium, and left ventricular defect locations.

remained within the left ventricular myocardium throughout the physiological motions of the rat. Separate perfusion curves were added to these defect locations to simulate spatially inhomogeneous perfusion characteristics. The parameters for all perfusion curves applied to the phantom are shown in Table 4.1 with the actual curves shown in Figure 4.2. Also, a snapshot the phantom with perfusion is shown in Figure 4.1b.

Since the analysis of sampling patterns is not performed with experimental data, the simulation parameters were restricted to parameters realizable in an experimental setting. Also, constraining the simulation parameters to be consistent across the analyzed sampling patterns ensures a more fair comparison. Therefore, the following characteristics, which are based on modern MRI scanners, of the simulation are:

| Table 4.1: Parameters for Overlayed Perfusion Terms |
|-----------------|---------------|---------------|---------------|
| Parameter       | LV Blood Pool | LV Myocardium | LV Defects    |
| $SI_p$          | $M$           | 0.7$M$        | 0.1$M$        |
| $\alpha$        | 1             | 1             | 1             |
| $\beta$         | 9.5           | 9.5           | 9.5           |
| $T_A$           | 5             | 5             | 5             |
| $SI_r$          | 0.12$SI_p$    | 0.12$SI_p$    | 0.12$SI_p$    |
| $\tau$          | 5             | 5             | 5             |

$M = 8 \cdot 10^4$
• Acquisition of two echoes in 15 ms

• Isotropic spatial resolution of approximately 200 µm
  – Digital resolution of 256 x 256
  – In-plane field-of-view (FOV) of 5 cm by 5 cm
  – Slice thickness of 2 mm

• 180 second experiment time
  – Maximum duration of 180 sec for the dynamic data collection
  – Maximum duration of 180 sec for the training data collection

4.2 Analysis of Model Order of the PSF Model using SVD Approximation to the Phantom

The SVD approximation of the phantom was performed in order to get a sense of the proper model order, $M$, to use in the analysis of sampling patterns. The analysis is similar to Eckart-Young theorem where a matrix is approximated by another lower rank matrix using SVD. For model order analysis, 95 seconds ($t_{exp} = 95$) of the phantom with and without perfusion was used and arranged according to

$$ A_{phn} = \begin{bmatrix}
\rho(r_1, t_1) & \rho(r_2, t_1) & \cdots & \rho(r_Q, t_1) \\
\rho(r_1, t_2) & \rho(r_2, t_2) & \cdots & \rho(r_Q, t_2) \\
\vdots & \vdots & \ddots & \vdots \\
\rho(r_1, t_P) & \rho(r_2, t_P) & \cdots & \rho(r_Q, t_P)
\end{bmatrix} \tag{4.2} $$

where $P = \lfloor \frac{t_{exp}}{\Delta t} \rfloor$ with $\Delta t = T_R = 15$ ms, and $Q = N_x N_y$ with $N_x = N_y = 256$. Then, the SVD of $A_{phn}$ was performed using the MATLAB function `svds` to find the $M$ largest singular values and their corresponding left singular and right singular vectors. For this analysis, the model order was swept from 1 to 20. Also, the sequence was reconstructed via the SVD matrix multiplication.
Examining the SVD approximation of the image sequence reveals that, for all model orders, there are no apparent ghosting motion artifacts introduced. This result is expected since each spatial point of the original image is represented in $A_{\text{phan}}$ every $\Delta t$. Conversely, the model order is expected to affect the temporal characteristics of the SVD approximate image sequence since the model order choice is essentially equivalent to choosing the number of temporal basis functions to represent the sequence. And, as expected, low model orders ($M \leq 5$) fail to properly model cardiac and respiration motion in the sequence without perfusion. Temporal blurring of the chest wall during respiration is also seen for model orders of $M \leq 10$. The same temporal artifacts seen in the SVD approximate sequence existed for the SVD approximate image sequence with perfusion. Also, some minor temporal blurring artifacts near the boundaries of the perfusion enhanced left ventricular blood pool and myocardium were also seen.

Additionally, the normalized root mean square error (NRMSE) was calculated for the SVD approximate image sequence using

$$\sqrt{\frac{\sum_n |\hat{\rho}(r, t_n) - \rho(r, t_n)|^2}{\sum_n |\rho(r, t_n)|^2}} \tag{4.3}$$

where $\hat{\rho}(r, t)$ represents the SVD approximate image sequence and $\rho(r, t)$ is the gold standard sequence. The NRMSE for each model order is shown in Figure 4.3a. The NRMSE curves for the SVD approximation with and without perfusion have similar shapes, but the curve for the approximation with perfusion experiences higher levels of NRMSE for all model orders. This result is expected since the sequence with perfusion possesses additional dynamics that require a higher model order to capture when compared to the sequence without perfusion.

For a given choice for the model order, the root mean square error (RMSE) can be calculated according to

$$\|\hat{A}_{\text{phan}} - A_{\text{phan}}\|_F = \sqrt{\min\{P,Q\} \sum_{m=M+1}^\infty \lambda_m^2} \tag{4.4}$$

where $\hat{A}_{\text{phan}}$ is the SVD approximate matrix and $\lambda_m$ is the $m$-th singular value of $A_{\text{phan}}$ [25]. The model order can be chosen by specifying a desired RMSE value and then using
Figure 4.3: (a) Normalized root mean square error of the SVD approximate image compared to the actual image with and without perfusion. (b) Singular values of $A_{\text{phn}}$ with and without perfusion. The model order used in this study is highlighted with a dashed vertical line.

Equation (4.4) to determine the model order that satisfies this performance bound. A similar approach is used in other fields as described by Candes [69] and Aggarwal and Bresler [16]. For reference, the singular values are given in Figure 4.3b. From this plot, the singular value at the model order choice of 16 is at a level of about 40 decibels (dB) lower than the highest singular value for the image with perfusion and at a level of about 50 dB lower than the highest singular value for the image without perfusion.

In most cases, a proper model order choice to avoid image artifacts is the model order where the knee of the singular value curve occurs. This criterion can also be applied to the knee of the NRMSE curve since the related RMSE metric can be calculated from the singular values. It is seen that perfusion adds about a factor of two for all NRMSE values. The knee of the NRMSE curve occurs around $M = 8$. However, this study uses $M = 16$. This model order has previously been used in cardiac MRI experiments and was shown to reconstruct the image sequence with little artifacts. Additionally, a model order of 16 was found experimentally to provide a good balance between flexibility and low noise amplification [30]. Noise amplification occurs due to the higher temporal basis functions modeling image noise as opposed to modeling the dynamics of the image.
4.3 Data Acquisition

Since the dynamics of an object are encoded at all spatial frequencies and the center of k-space contains a large amount of information about the object, the training data will be collected along the $k_x$ axis of k-space for both Cartesian and projection sampling patterns. In past studies, this type of training data collection has proven sufficient to represent the dynamics of cardiac motion [30]. Also, in this study for both Cartesian and projection sampling patterns, the acquisition of a phase encoding/projection line occurs at the same time a training data sample is collected. Although this method may not seem realizable in practice, it is possible by either using a fast imaging sequence to minimize time between echoes or acquiring two separate echoes. In both cases, temporal interpolation can be performed to temporally align the training and dynamic data.

Since the $T_R$ for the simulation is set to 15 ms, the training data is acquired with a temporal sampling interval of 15 ms. With a mean period of 197 ms and 10% variability used for the cardiac cycle of the phantom, the Nyquist sampling interval is approximately 16 ms when considering the 5th harmonic of the highest frequency of the cardiac cycle as highest frequency component of the phantom. Thus, the temporal Nyquist criterion is satisfied for the training data. Also, an advantage of acquiring a phase encoding/projection line and a training data sample at the same time is that no temporal interpolation is needed since the temporal basis functions exist at each time instant a phase encoding/projection line of the dynamic data is acquired.

4.4 Image Reconstruction

The image reconstruction process consists of three or four steps depending upon the type of sampling pattern (Cartesian or projection) used. Step one is to determine the temporal basis functions from the training data. Step two is to estimate the k-space coefficients from the dynamic data. Step three, which is only performed for projection sampling, is to perform gridding on the k-space coefficients to transform them into image space on the normal Cartesian grid. Step four is to obtain the image sequence by applying the PSF.
model. This process clearly shows the influence of the sampling patterns on the resulting image sequence since it is the only variable changed in the process.

In step one, the temporal basis functions, \( \phi_m(t) \), were determined by first constructing \( A \) from the training data and then performing the truncated SVD operation shown in Equation (3.16). In the second step, the k-space coefficients \( \alpha_m(k) \), were determined by solving Equation (3.13) for each k-space location. A pseudo-inverse was performed on the temporal basis coefficient matrix, denoted as \( \Phi_d \), to solve the equation. Step three consisted of applying the standard gridding algorithm [70] to transform the k-space coefficients to image space. Gridding involves transforming k-space data acquired in a non-Cartesian manner to a Cartesian grid. Gridding for signals in k-space is written as

\[
\hat{M}(k_x, k_y) = \left[ \frac{M_S(k_x, k_y)}{\xi(k_x, k_y)} \right] * C(k_x, k_y) \cdot \text{III} \left( \frac{k_x}{\Delta k_x}, \frac{k_y}{\Delta k_y} \right) 
\]  

(4.5)

where \( M_S(k_x, k_y) \) represents the non-Cartesian k-space samples such that

\[
M_S(k_x, k_y) = M(k_x, k_y) \cdot S(k_x, k_y)
\]  

(4.6)

and

\[
S(k_x, k_y) = \sum_i 2\delta(k_x - k_{x,i}, k_y - k_{y,i})
\]  

(4.7)

where \( \xi(k_x, k_y) \) is the density compensation function, \( C(k_x, k_y) \) is the gridding convolution kernel, and \( \text{III} \left( \frac{k_x}{\Delta k_x}, \frac{k_y}{\Delta k_y} \right) \) represents the Cartesian grid. For this study, the density compensation function is given by

\[
\xi(k_x, k_y) = S(k_x, k_y) * C(k_x, k_y)
\]  

(4.8)

and the \( C(k_x, k_y) \) is the Kaiser-Bevel convolution kernel \((W = 4 \text{ and } \beta = 18.5547)\) used by Jackson et al. [71]. The last step is accomplished by evaluating Equation (3.9) to obtain the image sequence.
4.5 Qualitative and Quantitative Analysis Parameters

The qualitative analysis of the reconstructed image sequence mainly consisted of identifying artifacts in images that degrade its quality. Some of the artifacts that were sought out included spatial ringing, spatial streaking, ghosting, temporal blurring, and spatial blurring. Other more obvious artifacts such as severe ghosting were also identified. For the quantitative analysis, a comparison of the reconstructed imaging sequence in addition to a comparison of the time-signal gamma-variate perfusion curves was performed. The normalized root mean square error (NRMSE) was calculated for the reconstructed image sequence using Equation (4.3).

For the time-signal intensity curves, the first step in the comparison was to fit the gamma variate curve in Equation (4.1) to the data by adjusting $\alpha$, $\beta$, $SI_p$, $SI_r$, $\tau$, and $T_A$. Gamma-variate curves were fit to the following regions using prior knowledge of their locations:

- Left ventricular blood pool (LV BP).
- Left ventricular myocardium (LV Myo).
- One pixel size left ventricular defect.
- Four pixel size left ventricular defect.
- Nine pixel size left ventricular defect.
- Sixteen pixel size left ventricular defect.

The fitting was performed using non-linear least-squares data-fitting command `lsqnonlin` in MATLAB. The normalized root mean square error was calculated for the perfusion curves using

$$\sqrt{\frac{\sum |SI(t_n) - SI_{gs}(t_n)|^2}{\sum |SI_{gs}(t_n)|^2}}$$

where $SI(t_n)$ is the fit perfusion curve and $SI_{gs}(t_n)$ is the true perfusion curve. The semi-quantitative signal intensity peak, time to peak, mean transit time, and upslope parameters were also extracted from the curves. The time to peak and mean transit time parameters...
were calculated using Equations (2.3)-(2.4), respectively. The upslope was calculated for all regions by using a linear least-squares fit to the inflow of contrast agent (i.e., the signal intensity curve in the range \((T_A + \alpha) \leq t \leq (T_{\text{peak}} - \frac{\alpha}{1.25})\). The upslope ratio was calculated for all regions except the left ventricular blood pool since its curve is used for the normalization to obtain the upslope ratio. Lastly, the absolute and relative errors of these semi-quantitative parameters were calculated.

4.6 Cartesian and Projection Sampling Analysis

The analysis of Cartesian versus projection sampling was done using a total of 10 sampling patterns: five Cartesian patterns and five projection patterns. The five Cartesian sampling patterns used were a full set of time-sequentially sampled phase encoding lines referred to as “normal full,” a Monte Carlo uniform random pattern, a uniform random pattern, a Monte Carlo Gaussian random pattern, and a Gaussian random pattern. The five projection sampling patterns used were a set of consecutively ordered projections spaced according to the spatial Nyquist criterion and referred to as “Nyquist angle,” a set of randomly ordered projections spaced according to the spatial Nyquist criterion and referred to as “Nyquist angle random order,” a Monte Carlo set projections randomly spaced referred to as “random angle,” a set of randomly ordered projections randomly spaced and referred to as “random-angle random-order,” and a pattern that approximates the golden angle.

Monte Carlo random sampling patterns were implemented because, in practice, it is difficult to implement a truly random sampling pattern across all time instances that the object is sampled. A repeatable sampling pattern is much easier to program into an MRI scanner. Thus, a Monte Carlo random sampling pattern may be used in place of a truly random sampling pattern during experiments and, as a result, it was analyzed in this study. A Cartesian uniform random sampling pattern was used as it seemed the most standard random sampling pattern to use when testing if random sampling may help improve conditioning of the temporal basis matrix. Gaussian random sampling patterns were analyzed to see if the over-sampling of the center of \(k\)-space provides advantages. Implementation of the Monte Carlo method consisted of repeating a group of five random permutations of 1, 2, 3, \ldots, \(N_{pe}\). The
truly uniformly distributed random sampling pattern was generated across all time instances using the MATLAB function randi.

Implementation of the Cartesian Gaussian random sampling patterns included the following steps:

- Calculate a discrete Gaussian cumulative distribution function for the phase encoding sampling indices \(1 \leq j \leq N_{pe}\) with the mean set to \(\frac{N_{pe}}{2}\) and the standard deviation set to \(\frac{N_{pe}}{6}\).

- Generate a uniform random number with mean equal to zero and variance equal to one.

- Assign a phase encoding index based on where the generated random number falls in the cumulative distribution function.

For this study, the mean of the Gaussian distribution was set to \(\frac{N_{pe}}{2}\) and the standard deviation was set to \(\frac{N_{pe}}{6}\) such that the center of k-space had the highest probability of being sampled. Also, all phase encoding lines are represented by 99.7% of the probability density function. For the Monte Carlo method, a group of five random patterns was repeated using the same procedure outlined above.

The Nyquist angle projection sampling pattern was implemented by repeating a set of projections where the first projection line was set to be acquired at \(\theta = 0\) and then the angle of each successive projection line was incremented by \(\Delta\theta\) according to Equation (3.21). For this particular study, the number of projections in a set was equal to 403. This number of projections was used for all sets in each projection sampling pattern. The Nyquist angle random order sampling pattern used the projection lines from the Nyquist angle pattern, but randomly ordered the time at which each projection was acquired. Implementation of the random angle sampling pattern included repeating a set projection lines where the first projection line was set to be acquired at \(\theta = 0\), and then the angle of each successive projection line was incremented by a random angle described by a uniform distribution on the interval \([\frac{\pi}{2}, \pi]\). The random-angle random-order sampling pattern used the technique from the random angle pattern, but randomly ordered the time at which each projection
was acquired.

Since projection sampling has advantages over Cartesian sampling, there have been studies of an optimal angle displacement between projection based on the golden ratio \([72, 73]\). Winkelmann et al. studied the use of the angle displacement based on the golden ratio and concluded that it is advantageous for sampling a dynamic sequence with an arbitrary number of projections while showing comparable image quality in terms of SNR and artifacts to an equal angular distribution sampling pattern \([74]\). Due to its popularity for projection sampling patterns, it was analyzed in this study. However, it is unclear how this sampling pattern will affect the reconstructed image sequence when using the PSF model. Implementation of this golden angle sampling pattern was similar to implementation of the Nyquist sampling pattern. The only difference is that a constant angle displacement of 111.246° is used between successive projection line. Also, no random sampling pattern based on the golden angle pattern was used since it violates the golden angle approximation theory.

A equivalent experiment time of 180 seconds was used in all simulations. For all sampling patterns involving a random variable, 10 separate reconstructions were performed and the calculated quantitative parameters were averaged using these 10 separate cases. A caveat to the generation of the sampling patterns is that each phase encoding index was forced to be sampled at least once in a frame of the Monte Carlo Gaussian random pattern and at least once for the true Gaussian random pattern. The simulation time of 180 seconds gives a sufficiently large number of data samples to assume each phase encoding line is sampled at least once in the true uniform sampling pattern. Also, the sampling patterns were generated such that the same phase encoding line or projection line could not be acquired twice in a row. This enforcement was performed to make the rows of the temporal basis matrix for that particular \(k\)-space point less dependent because acquiring the same phase encoding/projection line twice in row is equivalent to sampling below the temporal Nyquist criterion.
CHAPTER 5
RESULTS AND DISCUSSION

5.1 Sliding Window Reconstruction

A basic and frequently used approach to reconstructing a dynamic sequence is to use sliding window reconstruction. Sliding window reconstruction is a way to perform real-time imaging in MRI by taking the time-sequentially sampled (k,t)-space data that is acquired in a Cartesian sense, sliding a window a desired amount of time over the data, and performing Fourier reconstruction of the data that falls within the window. The temporal resolution of the data is essentially equivalent to the window step time. However, the frames of the reconstructed sequence experience temporal blurring which effectively diminishes the actual temporal resolution of the reconstruction. The severity of the blurring depends on how badly the Nyquist criterion is violated and on the motions of the dynamic sequence. Also, the technique still suffers from motion artifacts if the temporal Nyquist criterion is violated.

To show that use of sliding window reconstruction when trying to suppress motion artifacts is infeasible for cardiac perfusion imaging, a dynamic sequence was reconstructed via the sliding window technique using four phase encoding lines. The window time step was set to the $T_R$ to make the temporal resolution comparable to the PSF method. Also, four phase encoding lines were used since they nearly satisfy the temporal Nyquist criterion. To truly satisfy Nyquist when considering the 5th harmonic of the highest frequency of the cardiac cycle as the highest frequency component of the phantom, the sampling interval for each point in k-space would need to be the $T_R$. However, this acquisition scheme is only possible when one phase encoding line is acquired, which will give absolutely no spatial information along the $y$ direction. When four phase encoding lines are used, the sampling interval for each k-space point is $4T_R$, which satisfies Nyquist when considering the fundamental frequency.
Figure 5.1: Snapshot of the reconstructed image sequence using the sliding window technique when acquiring (a) four phase encoding lines and (b) sixteen phase encoding lines. The reconstruction was performed using zero-filling such that the resulting images digital resolution match the digital resolution of the phantom.

of the heart as the highest frequency component of the phantom. Of course, the use of four phase encoding lines will give very little spatial information as seen in a snapshot of the reconstructed image sequence shown in Figure 5.1a. To obtain a sequence with more spatial information, a sliding window reconstruction using sixteen phase encoding lines, as shown in Figure 5.1b, was also performed. Although using sixteen phase encoding lines does violate the temporal Nyquist criterion, its primary use is to obtain a sequence with more spatial information while keeping good temporal resolution to see if more accurate parameters can be extracted from the reconstructed sequence.

When the quantitative parameters are calculated from the fit time-signal intensity curves as shown in Table 5.1 and Table 5.2 when using four and sixteen phase encoding lines, respectively, it is apparent that the sliding window reconstruction techniques are very much inadequate for cardiac perfusion imaging. The normalized root mean square error (NRMSE) of the signal intensity curves for both the left ventricular blood pool and left ventricular myocardium are approximately one for each reconstruction. The NRMSE of the left ventricular
Table 5.1: Semi-Quantitative Errors for Sliding Window Reconstruction using Four PE

<table>
<thead>
<tr>
<th>Region</th>
<th>SI</th>
<th>$SI_p$</th>
<th>$T_{peak}$</th>
<th>MTT</th>
<th>Upslope</th>
<th>Upslope Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error Parameter</td>
<td>NRMSE</td>
<td>Relative Error (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV BP</td>
<td>0.999</td>
<td>0.999</td>
<td>0.006</td>
<td>0.065</td>
<td>1.000</td>
<td>N/A</td>
</tr>
<tr>
<td>LV Myo</td>
<td>0.985</td>
<td>0.991</td>
<td>0.026</td>
<td>0.008</td>
<td>0.997</td>
<td>6.909</td>
</tr>
<tr>
<td>One Pixel Defect</td>
<td>2.0393</td>
<td>2.0819</td>
<td>0.007</td>
<td>0.010</td>
<td>2.055</td>
<td>8012</td>
</tr>
<tr>
<td>Four Pixels Defect</td>
<td>0.933</td>
<td>0.931</td>
<td>0.004</td>
<td>0.011</td>
<td>0.928</td>
<td>188.9</td>
</tr>
<tr>
<td>Nine Pixels Defect</td>
<td>0.143</td>
<td>0.145</td>
<td>0.001</td>
<td>0.001</td>
<td>0.159</td>
<td>2205</td>
</tr>
<tr>
<td>Sixteen Pixels Defect</td>
<td>0.950</td>
<td>0.942</td>
<td>0.002</td>
<td>0.002</td>
<td>0.917</td>
<td>217.2</td>
</tr>
</tbody>
</table>

Table 5.2: Semi-Quantitative Errors for Sliding Window Reconstruction using Sixteen PE

<table>
<thead>
<tr>
<th>Region</th>
<th>SI</th>
<th>$SI_p$</th>
<th>$T_{peak}$</th>
<th>MTT</th>
<th>Upslope</th>
<th>Upslope Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error Parameter</td>
<td>NRMSE</td>
<td>Relative Error (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV BP</td>
<td>0.998</td>
<td>0.999</td>
<td>0.033</td>
<td>0.008</td>
<td>0.999</td>
<td>N/A</td>
</tr>
<tr>
<td>LV Myo</td>
<td>0.990</td>
<td>0.993</td>
<td>0.001</td>
<td>0.004</td>
<td>0.996</td>
<td>4.4831</td>
</tr>
<tr>
<td>One Pixel Defect</td>
<td>2.054</td>
<td>2.718</td>
<td>0.010</td>
<td>0.016</td>
<td>4.829</td>
<td>7950</td>
</tr>
<tr>
<td>Four Pixels Defect</td>
<td>0.700</td>
<td>0.633</td>
<td>0.004</td>
<td>0.003</td>
<td>0.407</td>
<td>807.8</td>
</tr>
<tr>
<td>Nine Pixels Defect</td>
<td>0.116</td>
<td>0.239</td>
<td>0.017</td>
<td>0.004</td>
<td>1.059</td>
<td>2808</td>
</tr>
<tr>
<td>Sixteen Pixels Defect</td>
<td>0.745</td>
<td>0.698</td>
<td>0.003</td>
<td>0.003</td>
<td>0.546</td>
<td>618.4</td>
</tr>
</tbody>
</table>

defects’ signal intensity curves is lowest for the nine pixel size size, but is significantly higher for the other size defects. A possible reason why the nine pixel size defect signal intensity curve better represents the actual signal intensity curve is that its location is near the center of mass along the $y$-direction of each defect location. Thus, each defect gets somewhat smeared into the location of the nine pixel size defect. The $T_{peak}$ and MTT parameters, however, are well estimated using the sliding reconstruction technique. This result is expected since the perfusion covers a large enough spatial location, the heart, to capture the shape of the signal intensity curves during enhancement and detraction. It also is attributed to the fact that the $\alpha$, $\beta$, and $T_A$ parameters for the signal intensity curves are the same for all heart regions. The $SI_p$, upslope, and upslope ratio parameters are poorly estimated, which is expected since the NRMSE of the signal intensity curve is high. Also, the NRMSE of the reconstructed image when compared to the gold standard is 1.3024 when using four phase encoding lines and 1.3967 when using sixteen phase encoding lines. The lower NRMSE of the sliding window reconstruction using four phase encoding lines is attributed to its higher temporal resolution.
Figure 5.2: Noiseless phantom reconstructed image sequence NRMSE for all sampling patterns.

5.2 Cartesian and Projection Sampling Analysis

5.2.1 Noiseless Phantom Simulation

The NRMSE for the reconstructed image sequence for all sampling patterns is shown in Figure 5.2. The NRMSE for all reconstructed image sequences using projection sampling patterns is higher than the NRMSE of all the reconstructed image sequences using Cartesian sampling patterns. The higher NRMSE for the projection sampling patterns results from the increased spatial coverage of the motion artifacts in the image compared to spatial coverage of the motion artifacts from the reconstructions using Cartesian sampling. The motion artifacts of the reconstructions using Cartesian sampling appear as ghosting artifacts as shown in Figure 5.3a, whereas the motion artifacts for projection sampling appear as radial steaks as shown in Figure 5.3b. The Cartesian motion artifact’s spatial coverage spans the entire $y$ dimension but with a width equal to that of the heart. The projection motion artifacts extend outside the body of the rat and span the entire image.

The NRMSEs of the fitted time-signal intensity curves are shown in Figure 5.4. The NRMSEs of both the Cartesian and projection time-signal intensity curves for the left ventricular blood pool and myocardium are low and nearly equivalent. For all of the left ventricular
Figure 5.3: Snapshot of the reconstructed image sequence for the noiseless phantom using the PSF method for a (a) Cartesian sampling pattern and (b) projection sampling pattern. Motion artifacts exist in each image. The motion artifacts in the Cartesian case consist of heart ghosts, whereas the motion artifacts in the projection case appear as radial streaks.

defects, the NRMSE for each sampling pattern is fairly low. However, the projection sampling patterns involving random angles have higher NRMSEs than all other patterns. The relative errors of the fit MTT and $T_{\text{peak}}$ parameters are not shown, but were all less than 1% and comparable across each region of the heart. The relative errors of the fit $SI_p$ parameter are shown in Figure 5.5. Again, the relative error for left ventricular blood pool and myocardium regions are relatively low and similar across both the Cartesian and projection sampling patterns. Also, for the one pixel size left ventricular defect, the relative error for all projection sampling patterns is significantly higher than relative error for the Cartesian patterns. This trend is also true, but the error is not as significantly different, for the nine pixel size defect case. For the other size defects, the errors of the Cartesian sampling patterns are regularly similar to or slightly worse than the errors for the projection sampling patterns if the random angle cases of the projection patterns are ignored.

The relative errors of the fit upslope parameter are shown in Figure 5.6. Again, the errors across all patterns are comparable for the left ventricular blood pool and myocardium
regions. The projection sampling patterns perform worse for the one pixel size and nine
pixel size defect. Also, the errors of the Cartesian sampling patterns are regularly similar to
or slightly worse than the errors for the projection sampling patterns for the four pixel and
sixteen pixel size defect if the random angle cases of the projection patterns are ignored. The
relative errors for the fit upslope ratio as shown in Figure 5.7 also follow the same trends as
the relative errors of the upslope.

The motion artifacts seen in the reconstructed image sequence when using both the Carte-
sian and projection sampling patterns are due to poor fitting of the PSF model to the data.
This poor fitting manifests itself as motion artifacts when solving Equation (3.13). The mo-
tion artifacts originate from the large edge of the heart regions during contrast enhancement.
Oddly, the random sampling patterns for both Cartesian and projection sampling patterns
show no apparent improvement in image quality. It was expected that the random patterns
would provide slight improvement over the deterministic patterns due to the presence of a
the quasi-periodic heart and respiration cycle that tends to make the temporal basis matrix
ill-conditioned. Instead, the NRMSE for the reconstructed image sequence was about the
same for the deterministic and random patterns. This trend was also true for the calculated
quantitative perfusion parameters.

The low errors for all calculated quantitative perfusion parameters for the left ventricular
blood pool and left ventricular myocardium are attributed to the large spatial area of these
regions. In other words, even when there is an error in several pixels of the reconstructed
image sequence within these regions, the spatial area of the blood pool and myocardium
regions is large enough such that these errors insignificantly contribute to the average cal-
culated quantitative perfusion parameter. However, it is a different case for the small left
ventricular defect regions.

Within each set of Cartesian and projection sampling patterns, there are patterns that
consistently perform worse than the other patterns. For the Cartesian sampling patterns,
these two patterns are the Monte Carlo Gaussian random and Gaussian random patterns.
These two patterns perform worse than the other Cartesian sampling patterns because the
number of samples from the outer portions of \( k \)-space are typically lower than the model
order. Therefore, the temporal basis matrix is ill-conditioned for these \( k \)-space locations
Figure 5.4: Signal intensity over time curve’s NRMSE for the noiseless phantom for (a) left ventricular blood pool, (b) left ventricular myocardium, (c) one pixel size defect, (d) four pixel size defect, (e) nine pixel size defect, (f) sixteen pixel size defect.
Figure 5.5: Signal intensity peak relative error for the noiseless phantom for (a) left ventricular blood pool, (b) left ventricular myocardium, (c) one pixel size defect, (d) four pixel size defect, (e) nine pixel size defect, (f) sixteen pixel size defect.
Figure 5.6: Upslope relative error for the noiseless phantom for (a) left ventricular blood pool, (b) left ventricular myocardium, (c) one pixel size defect, (d) four pixel size defect, (e) nine pixel size defect, (f) sixteen pixel size defect.
Figure 5.7: Upslope ratio relative error for the noiseless phantom for (a) left ventricular myocardium, (b) one pixel size defect, (c) four pixel size defect, (d) nine pixel size defect, (e) sixteen pixel size defect.
and, as a result, noise is amplified. Also, since the outer portions of k-space contain information about the higher spatial frequencies, the small left ventricular defect regions are negatively affected. This effect agrees with the errors shown in Figures 5.4-5.7. For the projection sampling patterns, the two patterns that consistently perform worse than the other patterns are the random angle and random-angle random-order patterns. The reason for the consistently worse performance is similar to the reason for the Cartesian Gaussian patterns. More specifically, high spatial frequency features in the phantom are expected to be missed with random angular distribution sampling patterns since angular undersampling can possibly occur.

Upon comparing the errors of the quantitative perfusion parameters for the left ventricular defect regions for the group of Cartesian and projection sampling patterns that consistently perform well (the normal full and uniform random Cartesian patterns, and the Nyquist and golden angle projection patterns), one sees that the errors of the projection sampling patterns are regularly worse than the errors for the Cartesian sampling patterns for the one pixel and nine pixel size defects. Conversely, the errors of the Cartesian sampling patterns are regularly similar to or slightly worse than the errors for the projection sampling patterns for the four pixel and sixteen pixel size defects. Two possible explanations of the results for the defect errors are the high spatial resolution along the x dimension for the Cartesian sampling patterns and the actual location of the defects. For the Cartesian sampling patterns, high spatial resolution along the x dimension is always obtained and can help provide more accurate signal intensity curves. The actual defect locations can affect the reconstructed image sequence for the projection sampling patterns due to the defect’s neighboring image features’ spatial amplitude dominance in a particular set of projections. Since the relative performance of the sampling patterns (Cartesian versus projection) for each defect size is independent of the size of the defect, it seems likely that the location of the defects is a large contributing factor to proper reconstruction.
Figure 5.8: Image sequence NRMSE for all sampling patterns when setting $L$ equivalent for the Cartesian and projection sampling patterns.

5.2.2 Effect of Having $L$ Equivalent for the Cartesian and Projection Sampling Patterns

Since satisfaction of the spatial Nyquist criterion for projection sampling requires 403 projections as opposed to 256 phase encodings to satisfy the criterion for Cartesian sampling patterns, the number of measured data, $L$, for each k-space location for the projection patterns is, on average, lower than for the Cartesian patterns. Since this discrepancy between the two types of patterns could result in a more ill-conditioned temporal basis matrix, a simulation where the number of projections was set equal to the number of phase encodings was performed. The implementation of all projection sampling patterns remained the same except for the Nyquist angle patterns. For the Nyquist angle pattern, the spacing between successive projections was set to $\Delta \theta = \frac{\pi}{N_{\text{proj}}}$. The Nyquist angle random order sampling pattern was implemented the same way except it used the spacing described in the previous sentence. The procedure of setting the number of projections equal to the number of phase encodings is equivalent to performing angular undersampling that results in lower SNR and spatial resolution [62].

The NRMSE for the reconstructed image sequence for all sampling patterns is shown in Figure 5.8. Similar to the NRMSE when using the spatial Nyquist criterion for projec-
Figure 5.9: Snapshot of the reconstructed image sequence when setting $L$ equivalent for the Cartesian and projection sampling patterns using the PSF method for a (a) Cartesian sampling pattern and (b) projection sampling pattern. Motion artifacts exist in each image. The motion artifacts in the Cartesian case consist of heart ghosts, whereas the motion artifacts in the projection case appear as radial streaks.

The NRMSE for all reconstructed image sequences using projection sampling patterns is higher than the NRMSE of all the reconstructed image sequences using Cartesian sampling patterns. The NRMSEs for the projection sampling patterns are slightly higher than the NRMSEs when the Nyquist spatial criterion is satisfied, which is a result of the lower spatial resolution. The motion artifacts of the reconstructions using Cartesian sampling still appear as ghosting artifacts shown in Figure 5.9a and the motion artifacts still appear as radial streaking shown in Figure 5.9b, which affect a larger spatial area than the motion artifacts for Cartesian sampling.

The errors for the calculated quantitative perfusion parameters when using projection sampling patterns that have the number of projections equal to the number of phase encodings follow all the same trends as the errors when using projection sampling patterns that satisfy the spatial Nyquist criterion. However, the errors for the projection sampling patterns are slightly higher. Also, the left ventricular defect errors feature a larger percentage increase than the errors for the left ventricular blood pool and myocardium. Again, the
increase in errors for all regions is attributed to the lower spatial resolution of the reconstructed image sequences, which also explains why the small sized left ventricular defects experience a larger increase in error. Overall, there is no apparent gain when setting the average number of measured data, $L$, for each k-space location equal between the Cartesian and projection sampling patterns.

5.2.3 Effect of Noise

All of the previous analyses were performed using a noiseless phantom. Since a noiseless object is not realizable in practice, an analysis of the effect of noise on the reconstructions and calculated quantitative perfusion parameters was performed. Also, a motivating factor for using the Cartesian Gaussian random and projection sampling patterns is that they are known to give reconstructions with higher SNR due to oversampling of the center of k-space. This oversampling can result in better conditioning of the temporal basis matrix for noisy cases. For this analysis, the reconstruction and calculation of quantitative perfusion parameters was performed at a SNR of 25, 15, and 5, decibels (dB). Also, the spatial Nyquist criterion was used for the projection sampling patterns as opposed to setting the number of projections equal to the number of phase encodings. This type of projection sampling pattern was used since the other type of pattern proved to provide no benefits as shown in Section 5.2.2.

The NRMSE for the reconstructed image sequence for each SNR (including the noiseless case) is shown in Figure 5.10. The motion artifacts seen in the noiseless cases still exist in the reconstructed sequence, except they are washed out by the noise in the image. Again, the NRMSE for all reconstructed image sequences using projection sampling patterns is higher than the NRMSE of all the reconstructed image sequences using Cartesian sampling patterns. Also, all NRMSEs significantly increase for the 5 dB SNR case suggesting a possible breaking point of the PSF algorithm. However, the NRMSE for all SNR cases except 5 dB stays nearly the same for the projection sampling pattern, whereas the NRMSE for the Cartesian sampling patterns continually increases. Even when the SNR is 5 dB, the increase in NRMSE for the Cartesian patterns is higher than the increase in NRMSE for the
Figure 5.10: Image sequence NRMSE for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
projection patterns. This behavior suggests a robustness to noise for the projection sampling patterns.

For the calculated quantitative perfusion parameters, the quantitative parameters for the left ventricular blood pool and myocardium are nearly equivalent across all SNR cases. But the error of the Cartesian sampling patterns increases as the SNR decreases, whereas the error for the projection sampling patterns stays nearly equivalent. The signal intensity NRMSE for the left ventricular blood pool and myocardium regions is shown in Figure 5.11 and Figure 5.12, respectively. Also, the upslope relative error for the left ventricular blood pool and myocardium regions is shown in Figure 5.17 and Figure 5.18, respectively on pages 62 and 63. The other quantitative perfusion parameters are not shown due to similarities between the shown parameters. All errors do experience a significant increase for the 5 dB SNR case, reaffirming that the 5 dB SNR case is a possible breaking point of the PSF algorithm. Nevertheless, similar behavior would need to be experienced when analyzing multiple data sets to support this claim.

For the calculated quantitative perfusion parameters of the left ventricular defect, the errors follow the general trend described in Section 5.2.1. The signal intensity NRMSEs for the left ventricular defect regions are shown in Figure 5.13 through Figure 5.16. Also, the upslope relative errors for the left ventricular defect regions are shown in Figure 5.19 through Figure 5.22.

Similar to the previous noiseless analysis, the Gaussian random patterns are typically the worst performers within the Cartesian sampling patterns and the random angle patterns are typically the worst performers within projection sampling patterns. However, the left ventricular defects’ quantitative perfusion parameters for the Gaussian patterns show a robustness to noise when it is introduced, which is expected since the center of k-space is oversampled for these patterns. Again, the errors of the projection sampling patterns are regularly worse than the errors for the Cartesian sampling patterns for the one pixel and nine pixel size defects; and the errors of the Cartesian sampling patterns are regularly similar to or slightly worse than the errors for the projection sampling patterns for the four pixel and sixteen pixel size defects. Moreover, the projection sampling patterns show an expected robustness to noise. The Nyquist angle random order and golden angle projection sampling
patterns hover around the same error level for the noiseless, 25 dB SNR, and 15 dB SNR cases but then significantly increase for the 5 dB SNR case. The other projection sampling pattern errors slightly increase and decrease across all noise cases.
Figure 5.12: Signal intensity NRMSE in the left ventricular myocardium for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.13: Signal intensity NRMSE in the one pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.14: Signal intensity NRMSE in the four pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.15: Signal intensity NRMSE in the nine pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.16: Signal intensity NRMSE in the sixteen pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.17: Upslope relative error for the left ventricular blood pool for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.18: Upslope relative error for the left ventricular myocardium for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.19: Upslope relative error for the one pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.20: Upslope relative error for the four pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.21: Upslope relative error for the nine pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
Figure 5.22: Upslope relative error for the sixteen pixel size defect for (a) noiseless image, (b) 25 dB SNR, (c) 15 dB SNR, (d) 5 dB SNR.
A simulation phantom was designed for and used to study the effect of various Cartesian and projection sampling patterns on the PSF method for cardiac perfusion MR imaging. A total of 10 sampling patterns (five Cartesian and five projection) were analyzed. The analysis considered the effect of the sampling pattern choice on the quality of the reconstructed image sequence and the accuracy of the quantitative perfusion parameters. Overall, the Cartesian sampling patterns provided better reconstructions in terms of image quality, image sequence NRMSE, and relative error of the quantitative perfusion parameters. However, the errors from the projection sampling patterns were, overall, only slightly higher. The higher errors were initially thought to result from a more ill-conditioned temporal basis matrix caused by the number of data measurements for each k-space point for projection sampling patterns being lower than the number for Cartesian sampling patterns. However, it was shown in this study that this reasoning was mistaken since the errors for the projection sampling patterns increased due to angular undersampling.

Within the Cartesian sampling patterns, the Gaussian random sampling patterns consistently performed worse than the other Cartesian patterns. These patterns performed worse due to the ill-conditioning of the temporal basis matrix for the outer portions of k-space caused by the low number of samples (i.e., number of samples less than the model order) for these points. Within the projection sampling patterns, the random angle patterns performed worse than the other projection sampling patterns. For the random angle patterns, angular undersampling, which causes poor spatial resolution and increases reconstruction error, was considered to be the culprit. For the remaining Cartesian sampling patterns, no one particular sampling pattern performed consistently better than the others. This result was somewhat unexpected since some of the patterns used random sampling that was thought
to improve the conditioning of the temporal basis matrix due to the quasi-periodic motions in the phantom. The same result was true for the projection sampling patterns. A possible explanation is that the variability of the motions in the phantom are large enough that random sampling provides no benefit. Furthermore, it cannot be discarded that a different randomization strategy might perform better.

Additionally, the quantitative perfusion parameter errors for the one pixel size left ventricular defect were always lower for the Cartesian sampling patterns. The reason for the smaller error is likely due to the Cartesian sampling pattern’s high spatial resolution along the \( x \) dimension. However, the projection sampling patterns did provide slightly smaller errors for the four pixel and sixteen pixel size defect’s quantitative perfusion parameters. Thus, it seems that the actual locations of the defects, not their size, was the largest contributing factor to the projection sampling’s quantitative perfusion parameter errors. A study of the effect of the defect’s location would need to be done to confirm this hypothesis.

One of the biggest advantages of projection sampling over Cartesian sampling was its robustness to noise. When noise was introduced into the dynamic sequence, the quantitative perfusion parameter errors in the defects as well as the reconstructed image sequence’s NRMSE for the Cartesian patterns consistently increased, whereas the errors for the projection patterns stayed nearly the same. Although the projection sampling patterns still performed worse than Cartesian sampling patterns for the noisy cases, this characteristic of the projection sampling patterns makes them intriguing for experimental use where noise levels can be high.

Future lines of work may include implementing a joint solution of the PSF method and a study of more advanced PSF reconstructions including regularization. A joint solution for the PSF model fitting was proposed by Brinegar et al. [32] and is expected to help alleviate motion artifacts seen in the reconstructed image sequences as well as improve the results from projection sampling patterns. The method solves for the \( k \)-space basis functions, \( \{\alpha_m(k)\} \), in a joint way by using a generalized Tikhonov regularization solution while incorporating \textit{a priori} spatial-spectral information. In the study done by Brinegar et al., this method has been shown to reduce the motion artifacts seen in Figure 5.3. When certain regularization schemes are used in the PSF method, projection sampling may offer an SNR advantage
that may provide a benefit for regularization since the optimal regularization parameter is
dependent on the noise in the data. One such type of regularization the may benefit from
an SNR advantage is $\ell_1$ regularization. Also, if projection sampling is advantageous for a
physical reason (e.g., short $T_E$, reduced susceptibility artifacts, reduced flow artifacts), then
projection sampling may provide results comparable to Cartesian sampling.
REFERENCES


