REAL-TIME FLOW QUANTIFICATION TECHNIQUES IN CARDIOVASCULAR
MRI APPLICATIONS

DISSERTATION

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ABSTRACT

Velocity measurement based on phase-contrast magnetic resonance imaging (PC-MRI) is firmly recognized as a valuable and accurate technique to assess hemodynamics in a variety of clinical applications. However, conventional PC-MRI requires the acquisition of two separate and complete k-space dataset with different flow sensitivities. Real-time MR velocity measurement experiences limited success due to the insufficient temporal sampling rate to depict hemodynamic prosperities within each cardiac cycle.

Accelerated data acquisition strategies described by this dissertation were developed to reduce the reference data requirements. Time-efficient PC-MRI methods accelerate the acquisition of phase-reference data in the spatial and temporal domain with minimum loss of velocity accuracy. Root-Mean-Square error estimation demonstrates the accuracy of the proposed accelerated velocity measurement methods as compared to the conventional PC-MRI reconstruction.

As an alternative accelerated PC-MRI, shared velocity encoding (SVE) method was developed to achieve the same temporal sampling rate comparing to standard MR cine scans. In SVE method, phase-difference images from alternative polarity pairs (+ -), (- +), (+ -), etc. can be reconstructed and resulted in a factor of 2 increase in the effective temporal resolution. With the SVE method implementation, the local pulse wave
velocity (PWV) measurement becomes practical and useful in the common carotid arteries in current clinical 1.5T MRI scanners.

Echo-planar imaging (EPI) is an ultra-high-speed MRI method that is capable of producing snap-shot MR images in the ranges of 10-100 msec. Recently, EPI sequence has been used in attempts to acquire real-time cardiac cine images in a standard MR scan. Consequently, we propose to utilize the advantage of high acquisition speed of EPI combining with PC-MRI to achieve real-time velocity measurement in the major vessels. However, chemical shift artifacts resulting from the off-resonance effect of fat spins limit the use of long echo train length, which compromises acquisition speed of the EPI method. This work investigated the problem of off-resonance artifacts and developed a fat-suppression method not only applicable to the EPI but also to the SSFP cine sequence. With the fat-suppression EPI sequence, we demonstrate the potential capability of using the SVE technique for real-time velocity mapping in both in-vitro pulsatile flow phantom and in-vivo volunteer studies.

Long scan time of multiple-directional velocity measurement is the common difficulties to perform in clinical routines. With an echo-planar readout sequence combined with SVE reconstruction, we conduct a feasibility study that shows the 2D multiple-directional and 3D single-directional velocity measurement become feasible in standard MRI scanners.
Dedicated to my loving family in Taiwan
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CHAPTER 1

INTRODUCTION

1.1 SIGNIFICANCE

According to the latest report of the National Center for Health Statistics, cardiovascular disease (CVD), including heart attack, stroke, vascular malfunction and abnormal circulation, has been the greatest killer of all races and genders in the United States since 1950 (1). Approximately 8.7 million American lives were directly claimed because of CVD or related complications in 2004 (2). This is equal to an average of 1 death every 36 seconds. CVD is the most life-threatening disease in the United States, costing a heavy financial burden on the society; in 2007 alone, the direct and indirect costs attributable to CVD were about $431.8 billion (3). CVD claimed more
American lives than the next seven leading causes of death combined from 1960 until 2004. Recent developments in modern medicine and cardiac surgery have played an important role in lowering CVD mortality from decade to decade. The annual deaths caused by CVD were dramatically decreased by 60% from 1960 (559 deaths per 100,000 population) to 2004 (217.5 deaths per 100,000 population). The advent of non-invasive diagnosis using advanced medical imaging modalities has helped to lower the CVD death rate by providing accurate diagnostic information for subsequent therapeutic decision. Cardiac Magnetic Resonance Imaging (MRI) is one of the promising non-invasive imaging techniques that offer not only anatomical but also functional information to assist in the clinical evaluation of patients with cardiovascular disease.

1.2 Cardiovascular Magnetic Resonance Imaging

Of all the organ systems, the cardiovascular system is the most challenging imaging subject because of complex blood flow and respiratory and cardiac motions. These result in only a narrow time window for acquiring MRI data that can be contaminated by motion artifacts and insufficient spatial and/or temporal resolution. Therefore, cardiac MRI has seen only limited clinical
application since its advent in the 1980s (4-7). Over the last few years, high-performance gradient hardware development (8), parallel acquisition acceleration methods combined with multiple phased-array coils (9-11), and high-field-strength clinical magnets (12-14) have extended the diagnostic capability of cardiac MRI in routine clinical applications. Recently, cardiac MRI has become firmly established as an essential tool to evaluate morphology of the heart (15,16), myocardial contractility (17,18), and myocardial perfusion (19,20).

In addition to ischemic heart disease, cardiac valvular diseases contribute to considerable morbidity and mortality in the United States even through they are relatively less common compared to other heart diseases. Echocardiography is now regarded as the non-invasive technique of choice for evaluation of patients with valvular heart disease. The principal advantage of routine echocardiography, which utilizes electronic transducer and ultrasound wave to generate a two or three dimensional image of the heart, is its real-time imaging capability, portability and cost efficiency. Cardiovascular MR (CMR) was originally developed to provide accurate structural information about cardiothoracic anatomy. Nevertheless, CMR methods are also available to
provide functional information regarding myocardial motion and hemodynamics in the major vessels (21-23). Phase-contrast MR imaging (PC-MRI), which is based on the phase shift of moving spins in a magnetic field, is an accurate and clinically proven technique to measure blood flow velocity. It provides unique features including pixel-by-pixel velocity mapping and quantitative multi-directional analysis of flow dynamics. Recently, ECG-triggered, segmented phase-contrast velocity mapping has been commonly employed for both quantitative and qualitative assessment of hemodynamics in the heart and great vessels (24-26) in a wide variety of cardiovascular diseases. However, the intrinsic insufficient temporal sampling rate of PC-MRI is a remaining issue which has not been satisfactorily addressed to date. This dissertation will introduce new methods that advance the capabilities of real-time velocity measurement with sufficient temporal resolution, spatial resolution, and image quality to be incorporated into routine diagnostic imaging.
1.3 CURRENT METHODS OF VELOCITY MEASUREMENT IN THE MAJOR VESSELS

1.3.1 Cardiac Catheterization

Cardiac catheterization is a medical procedure used to evaluate and treat certain conditions of the heart muscle, valves and vessels. During cardiac catheterization, a thin plastic tube or catheter is inserted through a blood vessel in the leg or arm into the heart, as shown in Figure 1.1 (27). Contrast media is administered to the patient through the angiography catheter while x-ray images are taken. The contrast media alters the signal contrast between blood and surrounding tissue in x-ray images. Coronary artery stenosis, cardiac function and hemodynamic status, can all be characterized and diagnosed during cardiac catheterization.
Cardiac catheterization is the conventional and most widely accepted standard for the assessment of vascular flow velocity. During the cardiac catheterization procedure, a thermal transducer is attached in the catheter probe and placed in the region of interest. Electrically generated heat is dissipated by thermal convection into the blood stream. Blood flow velocity can be determined based on the thermal conductivity of the blood and thermal attenuation rate.
Although heart catheterization is an accurate and reliable method for velocity measurement and in widespread use, several limitations restrict its utility. During conventional heart catheterization, the catheter is routinely guided toward the heart by x-ray fluoroscopy. However, accumulative ionizing radiation is a definite risk factor for cancer development that restricts the use of fluoroscopy for routine monitoring and repeated procedures in a patient (28). Heart catheterization is also an invasive operation, with finite risk for morbidity and mortality, which shows a total risk of major complications under 2% for all patients and 0.11% risk of death from cardiac catheterization (29).

1.3.2 Doppler Echocardiography

Doppler echocardiography is the most extensively used non-invasive imaging modality for diagnosis of vascular stenosis and valvular disease. The fundamental concept of the Doppler Effect was initially described by Johann Christian Doppler in 1842. He discovered that the frequency shift of the reflecting wave is dependant on the relative motion between observer and wave source. In Figure 1.2, the Doppler frequency shift is governed by the speed of sound in tissue, velocity of the blood and angle of incidence between
ultrasound beam and the direction of the flow, as expressed by the Doppler equation (30).

![Doppler Frequency Diagram]

**Figure 1.2:** Schematic diagram for the concept of blood velocity measurement using Doppler ultrasound and the mathematic expression of the Doppler equation (30).

Doppler echocardiography is an imaging procedure used to assess the flow velocity of moving blood *in vivo* from the frequency shift of a particular blood volume. In the standard velocity measurement using Doppler echocardiography, the ultrasound machine transmits a series of pulses (usually in the frequency range of 2 to 18 megahertz) to soft tissues or internal organs. When the ultrasound pulse encounters a boundary or interface between tissues of different density or compactness, some of the energy is
reflected back and detected by the receiver of the Doppler machine. The reflected ultrasound waves are collected and analyzed. The basis of Doppler echocardiography is to measure the relative change in the returned ultrasound frequency when compared to the transmitted frequency. Depending on the relative changes of the reflected frequencies, a Doppler echocardiographic system can measure the relative velocity of blood flow. For example, the received ultrasound wave from stationary tissue shows no frequency change from wave to wave because tissue typically has no relative motion. On the other hand, the received wave from moving blood flow has a frequency shift that indicates the relative velocity of blood flow.

However, several limitations, such as inadequate acoustic window and insufficient anatomic resolution, deteriorate the capability of two-dimensional Doppler echocardiography to accurately assess velocity and morphology through the vascular structure. Additionally, Doppler echocardiography has been successful in measuring blood velocity in superficial vessels; however, velocity results in deeply lying vessels are highly variable because of the limitations in ultrasound penetration (31). Furthermore, the skill of the sonographer can limit the accuracy of Doppler echocardiography and image
quality is dependent on subject anatomy and slice orientation (32). Therefore, recent literature suggested that Doppler echocardiography still cannot substitute for catheterization and cannot be considered an accurate method for blood-velocity and pressure measurement (33,34). Consequently, an alternative non-invasive method that provides accurate estimation of velocity is highly sought after.

1.3.3 Phase-contrast MR Velocity Measurement vs. Cardiac Catheterization and Doppler Echocardiography

Cardiac phase-contrast MRI (PC-MRI) has been proven as a non-invasive alternative for evaluation of hemodynamic information that includes valvular regurgitation (35-38), pulmonary pressure gradient (39), left-to-right shunt flow (40), ventricular filling (41), and assessment of stenotic aortic valves (42,43). PC-MRI provides unique advantages for non-invasive imaging with no radiation exposure, high reproducibility, and integrated assessment with CMR protocols providing both anatomic and functional information. Even so, phase-contrast MR velocity measurement is unlikely to replace cardiac catheterization or echocardiography as the initial imaging test on routine clinical applications. With a superior temporal resolution and accuracy of
measurement, cardiac catheterization has been recognized as a standard approach to measure blood-flow velocity in cases of suspected valvular disease. Nevertheless, it is an invasive procedure and ionizing radiation might cause potential complications after heart catheterization (29). Furthermore, poor soft tissue contrast and lack of three-dimensional imaging capability also limit its utility. Echocardiography is the dominant non-invasive imaging modality for evaluation of patients with valvular heart disease and has a number of inherent advantages, including real-time capability, availability and cost. However, recent technologic advances in cardiac MR velocity measurement methods have made PC-MRI a non-invasive alternative approach to measure velocity. A strong agreement of velocity measurement between PC-MRI and Doppler echocardiography demonstrate its capability to measure peak jet velocity and to evaluate mitral stenosis (44,45). This justifies the use of PC-MRI as an appropriate tool for detection and assessment of the severity of vascular disease in routine diagnosis or follow-up monitoring. However, the role of PC-MRI in valve disease has been limited because, in contrast to cardiac catheterization and Doppler echocardiography, PC-MRI can be limited by insufficient temporal resolution to capture adequate velocity information during rapid cardiac activity.
1.4 OBJECTIVES

Conventional ECG-triggered, segmented PC-MRI is an accurate and clinically proven technique to characterize blood flow velocity. However, this method requires reliable cardiac gating, regular cardiac rhythm, and either signal-averaging, respiratory gating, or breath-holding to suppress respiratory motion artifacts. Furthermore, the resulting velocity information is a weighted temporal average of information acquired over multiple cardiac and respiratory cycles; short-term hemodynamic variations are lost. Real-time PC-MRI, which is defined as acquiring beat-to-beat (i.e. actual velocity without temporal averaging) hemodynamics rather than real-time image display, has been previously proposed using echo-planar imaging (46) and spiral acquisitions (47), but limited performance has precluded routine clinical application. The aim of the present work is to design and demonstrate a novel method for rapid real-time velocity measurement with sufficient temporal resolution to eliminate the need for ECG synchronization and breath-holding, and to provide beat-to-beat hemodynamic information.

The minimum number of sampling points to accurately describe an aortic velocity wave was investigated by McDonald in 1974. In normal physiological
states, aortic flow is a smooth curve with limited high temporal frequency components. McDonald concludes that 99.5 percent of the variance (i.e. energy) in typical aortic pressure and flow velocity waveforms is contained within the first 7 or 8 harmonics. Based on this estimate, at a normal heart rate of 72 beats per minute (i.e. RR interval ~ 833ms), an effective temporal resolution of 59.5 ms is sufficient to achieve 99.5 percent accuracy in characterization of a given velocity waveform.

This project aims to improve the effective temporal resolution of the PC-MRI method in order to extend the capability of MR velocity measurement to real time. The major goal of this project is to develop a real-time MRI technique that is insensitive to artifacts caused by respiratory motion or variations in the cardiac cycle and can provide continuous monitoring of hemodynamic variations with sufficient temporal resolution.

1.5 ORGANIZATION OF DISSERTATION

The remaining work in this dissertation is presented as follows. Chapter 2 begins by summarizing the historical developments and fundamentals of PC-MRI techniques in cardiovascular applications. In addition, an overview
of current fat suppression techniques is included to provide background knowledge for the proposed rapid water-excitation fat-suppression method in Chapter 5. Chapter 3 and 4 describe three acceleration methods that aim to reduce data requirements in the conventional PC-MRI algorithm. Chapter 3 examines the feasibility of employing partial phase-reference data or temporal view-sharing techniques to extract velocity information from limited phase-reference data. In chapter 4, a novel PC-MRI algorithm designed to improve temporal resolution, i.e. the shared velocity encoding (SVE) method, is developed and evaluated. With the proposed SVE method, local pulse wave velocity (PWV) measurement becomes practical. A preliminary study in PWV measurement by using SVE will be described in Chapter 4. For further improvement in the acquisition speed of PC-MRI, echo-planar imaging (EPI) provides the sampling efficiency needed to measure velocity in real time. However, off-resonance artifact is one of the existing limitations imposing restrictions on the echo-train-length (ETL) and limiting the efficiency of EPI. To address this issue, a rapid phase-modulated water-excitation method is developed for fat-suppressed cine MRI based on EPI or steady-state free precession in Chapter 5. In Chapter 6, the combination of EPI and SVE is proposed and evaluated in a flow phantom and volunteer studies. The
proposed method enhances the capability of real-time velocity quantification to achieve beat-to-beat hemodynamic characterization in the major vessels. Chapter 7 provides a framework for developing in-plane velocity measurement using EPI with SVE reconstruction. Through-plane and in-plane flow quantification is evaluated by theoretic analysis and numerical simulations. Finally, the summary of this dissertation and recommendations for future research are addressed in Chapter 8.
This chapter summarizes the MRI physics of phase-contrast magnetic resonance imaging (PC-MRI) necessary for the comprehension and understanding of the present work. Additionally, the concept of echo-planar imaging (EPI), which we have utilized for real-time velocity mapping, is explained in this chapter. The imaging artifacts caused by the EPI trajectory are addressed as well. Moreover, this chapter describes the fundamentals and the limitations of the existing fat suppression techniques that provide the background knowledge and motivation for the proposed rapid phase-modulated water-excitation method for fat-suppressed cine MRI in Chapter 5.
2.1 Origins of Flow Effect in MRI

Understanding the origins of the phase shift due to motion in the direction of a magnetic field gradient is important in developing new methods of PC-MRI. Movement of spins induces two types of effects that cause the signal from moving spins to differ from stationary spins. First, Time-of-flight (TOF) phenomenon usually refers to the flow-related enhancement, as shown in Figure 2.1 (48).
Figure 2.1: Schematic diagram of flow-related enhancement effect (48)

- Partially saturated energy
- Unsaturated (maximum) signal
When using two-dimensional selective excitation, unsaturated blood, i.e. blood that has not been excited by prior RF pulses, flows into the imaging slice and yields full magnetization in gradient-echo sequences. The total signal amplitude of blood within an imaging slice is governed by the flow velocity, slice thickness and imaging repetition time (TR). Consequently, pulsatile flow results from signal amplitude modulation over the acquisition period because of wash in or wash out and the ratio of unsaturated and partially saturated spins in the imaging slice.

Consider turbulent flow in the cardiovascular circulation; the spins in the same voxel move with different velocities that induce phase variations within the voxel. Intravoxel phase dispersion results from a spin isochromat containing a variety of velocity components. When the accumulated phases vary over $180^\circ$ within a given spin isochromat, spin dephasing leads to considerable signal loss (49). The signal variation due to TOF effects and turbulence is difficult to quantify, leading to the need for phase-based flow measurement that we will discuss in the later chapters.
Flow-related phase fluctuations are another source of error that is extremely important in flow quantification applications. Flow related phase error can be classified into three categories (50). First, velocity-dependent phase shift ($\Phi_v$) linearly depends on the flow velocity ($v$). When spins move in the presence of a magnetic field gradient, they may accumulate phase shifts relative to static spins. This additional velocity-related phase modulation in each k-space line induces the ghosting artifact spread out in the MRI image because of pulsatile characteristic of blood flow in a normal physiologic condition.

Gradient moment nulling (GMN) or velocity-compensation (51) is used to eliminate the phase sensitivity to motion. The fundamental idea of velocity-compensation is to balance the zero and the first gradient moments at the echo time by adding an additional bipolar gradient waveform, as shown in Figure 2.2 (48). The gradient waveform pattern of the GMN method causes the signal vector of all spins to have zero accumulated phases independent of velocities.
Figure 2.2: A gradient waveform and phase accumulation in the slice-select axis using velocity-compensation (48)

The pitfall of the GMN method is a prolonged echo time because of the additional gradient lobe. The conventional GMN method can be adapted to any logical axes in an MRI sequence (i.e. slice-select, frequency-encoding and phase-encoding) and treated independently.

The last type of phase error only occurs in the presence of in-plane blood flow that is defined as spins moving with a direction that is oblique to the orientation of the phase-encoding and frequency-encoding axes. The displacement misregistration occurs because spins are spatial-encoded and
signal-collected in different time points. Any spatial shift due to motion between the phase-encoded gradient and center of frequency-encoded gradient induces spatial inconsistency. Although it is well known that the GMN concept in a magnetic field gradient can attenuate in-plane flow artifact, little has been reported about in-plane velocity compensated MR imaging either using GRE (52,53) or EPI (54-56).

2.2 PHASE-CONTRAST MR VELOCITY MEASUREMENT

2.2.1 Quantitative Description of Phase Shift of Moving Spins in a Magnetic Gradient

The historical development of PC-MRI began with Carr and Purcell when described the phase shift of moving spins in MRI in 1954 (57). To understand how velocity measurement can be achieved using MRI, several groups have investigated and evaluated the phase shift due to motion in the direction of a magnetic field gradient (58-60). In the past 40 years, the velocity mapping PC-MRI technique has undergone substantial development both in technical methodology (61-65) and clinical applications (25,66,67). Phase-contrast imaging with the PC-MRI method has provided new opportunities for in-vivo velocity measurement.
In this chapter, we analyze the phase modulation due to motion along the through-plane direction by theoretical derivation. For simplicity we consider a simple illustrative situation where an object moves at a constant velocity \(v\) along the \(x\) axis under the influence of constant magnetic field in the \(x\) direction. In MR imaging, the velocity-dependent phase shift, \(\Phi_v\), is expressed as

\[
\Phi_v = \gamma \int_0^{TE} G(t)x(t)dt \tag{2.1}
\]

where \(\gamma = 42.6\) MHz/Tesla is the gyromagnetic ratio, \(G(t)\) is the time-varying gradient, \(x(t)\) is the spatial position at specific time and \(TE\) is the time duration between the center of RF pulse and the center of central echo.

The spatial location of the moving object can be extrapolated with the Taylor series expansion:

\[
x(t) = x_0 + v_0t + \frac{1}{2} a_0 t^2 + \ldots \tag{2.2}
\]

The velocity-dependent result is obtained by substituting equation (2.2) into equation (2.1) as
\[ \Phi_v = \gamma \int_0^t G(t) \ast (x_0 + v_0 t + \frac{1}{2} a_0 t^2 + ....) dt \]  \hspace{1cm} (2.3)

To further simplify the analysis, the equation (2.3) can be analyzed in a condition that assumes plug flow and neglects acceleration and higher terms.

The equation (2.3) can be simplified as

\[ \Phi_v = \gamma \int_0^t G(t) \ast (x_0 + v_0 t) dt = \gamma G(t) x_0 t + \gamma G(t) v_0 \frac{t^2}{2} \] \hspace{1cm} (2.4)

As a result, the velocity-dependent phase shift not only depends linearly on gradient amplitude and velocity but also quadratically on the duration of the gradient pulse.

Another form to describe velocity-dependent phase shift by defining the zeroth and first gradient moments, \( M_0 \) and \( M_1 \), is

\[ M_0 = \int_0^t G(t') dt' \] \hspace{1cm} (2.5)

\[ M_1 = \int_0^t t' G(t') dt' \] \hspace{1cm} (2.6)

Thus, equation (2.3) can be decomposed by substituting equation (2.5) and (2.6) and yielded as

\[ \Phi_v = \gamma M_0(t) + \gamma M_1(t) v_0 \] \hspace{1cm} (2.7)
2.1.2 Background Phase Subtraction in PC-MRI

It is important to mention that a conventional phase-velocity measurement requires the acquisition of two separate and complete k-space datasets with different velocity sensitivity (68). Phase subtraction of two datasets is commonly performed to eliminate residual non-zero phase shifts that stem from undesired phase variation other than motion, such as field inhomogeneity, eddy currents, imperfect radiofrequency excitation and magnetic susceptibility. Two methods are commonly used, one acquiring datasets with equal and opposite velocity sensitivity (69), and the other collecting velocity-encoded and velocity-compensated phase-reference datasets (70). However, both approaches acquire additional information that doubles the amount of data required relative to other MRI pulse sequences. Thus, velocity mapping requires extended scan times to achieve sufficient spatial and/or temporal resolution, reducing the performance of breath-hold and real-time flow quantification techniques, and making three-dimensional acquisition impractical.
In an attempt to address these issues, accelerated PC-MRI that is based on minimum acquisition of phase-reference data has been investigated and evaluated. Jhooti (71) proposed a time-efficient PC-MRI method that acquires only the lower spatial frequencies of the phase-reference image with zero-filling for the peripheral “missing” regions in a conference proceedings in 1995. In Chapter 3, we extend the idea of reduced spatial resolution phase-reference to both spatial and/or temporal domains in order to reduce the acquisition time. Our proposed method aims to demonstrate this concept by collecting phase reference data with reduced spatial resolution and temporal view-sharing to improve PC-MRI acquisition efficiency.

In order to achieve a high-temporal resolution pulse wave or real-time velocity measurement, we propose a novel accelerated PC-MRI method, i.e. Shared Velocity Encoding (SVE), by sharing between consecutive alternating polarities velocity-encoding data. The comprehensive analysis and validation will be described in chapter 4, 6 and 7 in this dissertation.

2.1.3 Concomitant Gradient Terms Correction

MRI requires magnetic field gradients to encode the spatial position of a
given spin onto its precession frequency and phase. The main magnetic field
and additional magnetic field gradients are combined and form a linear
relationship between position and precession frequency over the entire sample
volume. When a desired linear magnetic field is applied, however, it
simultaneously induces additional nonlinear spatially dependent phase
variations based on Maxwell’s equations. This concomitant gradient effect
was first discovered and described by Norris and Hutchison (72) in 1990. It is
a consequence of Maxwell’s equations for the divergence and curl of the
magnetic field.

\[
div(B) = \nabla \cdot B = \frac{\partial B_x}{\partial x} + \frac{\partial B_y}{\partial y} + \frac{\partial B_z}{\partial z} = 0
\]

\[
curl(B) = \nabla \times B = \begin{vmatrix}
\frac{\partial}{\partial y} & \frac{\partial}{\partial z} \\
\frac{\partial}{\partial z} & \frac{\partial}{\partial x} \\
\frac{\partial}{\partial x} & \frac{\partial}{\partial y}
\end{vmatrix} = 0
\]

where \( \nabla \) indicates the Nabla operator, \( \cdot \) the vector product and \( \times \) cross
product.
Such concomitant gradients cause the precession frequency within the sampling volume to be a nonlinear function of position; this results in background phase variations in the image. Therefore, correction of the additional concomitant gradient terms is essential for any phase-based MR methods. PC-MRI is based on phase information to assess velocity, and concomitant gradient terms have been found to be a significant source of error in PC-MRI (73).

A number of phase correction algorithms have been proposed to mitigate the effects of concomitant gradients in MRI. One simple and practical concomitant gradient correction methods was developed by Bernstein and his colleagues (73). This method corrects the first-order concomitant terms. The concomitant magnetic field to the lowest order is:

\[
B_c(x, y, z, t) = \frac{1}{2B_0} \left\{ G_x z^2 + G_y z^2 + G_z \frac{x^2 + y^2}{4} - G_z G_x z x - G_y G_z y z \right\}
\]

The phase-contrast reconstruction is based on phase difference operation between alternating the polarity of velocity encoding gradients. The residual concomitant field phase error can then be expressed as
\[ \Delta \phi_c = \phi_{c,fe1}(x, y, z) - \phi_{c,fe2}(x, y, z) = \arg \left( \frac{Z_{c,fe1}}{Z_{c,fe2}} \right) = \arg(Z_{c,fe1}^* Z_{c,fe2}) \]

where \( f_e \) is the flow encoding index, \( Z_{c,fe1} \) and \( Z_{c,fe2} \) are complex after Fourier transformation of the \( fe_1 \) and \( fe_2 \) datasets respectively, * denotes complex conjugate, and "arg" represents the phase of a complex number.

(73)

The concomitant gradient correction algorithm is summarized as below:

1. Collect the detailed information about the gradient waveforms (ex. gradient ramp time, duration, amplitude, etc.) based on pulse sequence diagram

2. Calculate the correction coefficients

\[
A = \frac{\gamma}{2B_0} \int \left( \left( G_z^2(t) + G_y^2(t) \right)_{fe1} - \left( G_z^2(t) + G_y^2(t) \right)_{fe2} \right) dt
\]

\[
B = \frac{\gamma}{8B_0} \int \left( \left( G_z^2(t) \right)_{fe1} - \left( G_z^2(t) \right)_{fe2} \right) dt
\]

\[
C = -\frac{\gamma}{2B_0} \int \left( \left( G_z(t)G_z(t) \right)_{fe1} - \left( G_z(t) + G_z(t) \right)_{fe2} \right) dt
\]

\[
D = -\frac{\gamma}{2B_0} \int \left( \left( G_y(t)G_z(t) \right)_{fe1} - \left( G_y(t) + G_z(t) \right)_{fe2} \right) dt
\]

where time integrals are defined as a duration that all gradient lobes change between a pair of velocity encoding
3. The estimated concomitant field phase variation can be expressed by physical spatial coordinates and previous correction coefficients

\[ \Delta \phi_c(x, y, z) = Az^2 + B(x^2 + y^2) + Cxz + Dyz \]

4. Correct \( \Delta \phi_c \) for all pixels in image domain and pixel-by-pixel basis to obtain concomitant terms corrected accumulated phases

2.2 Echo-Planar Imaging Pulse Sequences

Echo-planar imaging (EPI) is one of the fastest MRI pulse sequence and was first described by Sir Peter Mansfield in 1977 (74). With modern gradient and RF hardware performance, the EPI sequence is able to acquire all k-space data required to reconstruct a MR image within the period of 30-100msec. Figure 2.3 (75) shows the time scale of physiologic motion in a normal human subject. The ultrafast acquisition speed of EPI is an important advantage in developing cardiovascular imaging applications, such as dynamic contrast imaging, non-breath-hold imaging and real-time imaging, as shown in Figure 2.4 (75).
Figure 2.3: Time scale of physiologic motion in a normal human subject (75)

Figure 2.4: Acquisition time and corresponding matrix size in different pulse sequences (75)

Figure 2.5 shows the pulse sequence diagram of a conventional EPI technique (48). The echo-planar readout strategy collects k-space data using
a markedly distinct approach compare to the standard MRI k-space trajectory.

One of the major differences is to employ rapidly oscillating gradients in the frequency-encoding axis and serial blip gradients in the phase-encoding axis. As a result, a train of gradient-echoes are generated by multiple reversals of the gradient polarity from positive to negative and vice versa. However, specific imaging artifacts associated with the EPI technique deteriorate image quality and limit its use in clinical applications. We summarize several particular artifacts that should be considered when applying the conventional EPI technique.

![Diagram of a segmented echo-planar imaging sequence.](image)

Figure 2.5: Diagram of a segmented echo-planar imaging sequence.
2.2.1 N/2 Ghosting

N/2 ghosting artifacts commonly occur if the MRI signal received from a voxel alternates in amplitude and/or phase in every other phase encoding line. Conventional echo-planar readout is performed by acquiring every other line in k-space with a readout gradient of opposite polarity. Thus, gradient-induced eddy currents, sequence timing mismatches and hardware imperfections yield N/2 ghosting artifacts in echo-planar imaging. In Figure 2.6, a pair of navigator echoes is commonly used to eliminate N/2 ghosting artifacts in echo-planar imaging (76). Navigator echoes are acquired without the application of phase encoding gradients prior to actual MR images. Fourier-transformation of navigator echoes determines the time delay of the echoes associated with each gradient polarity. As an alternative, k-space data can be acquired using only data collected with readout gradients of the same polarity in order to suppress N/2 ghosting artifacts.
2.2.2 Chemical Shift Artifacts

The resonance frequency depends on the magnetic field strength. Deviations in magnetic susceptibility between tissues will cause local gradients in the magnetic field, altering the resonance frequency which causes undesired imaging artifacts. The EPI k-space trajectory has an intrinsic low bandwidth along phase-encoding axis which introduces severe chemical shift artifact. The sampling bandwidth expressed in units of Hz/pixel corresponds to the frequency difference between adjacent pixels. Therefore, an appropriate bandwidth per pixel of any MR acquisition should be larger than the fat-water frequency shift, which is 220 Hz in 1.5 T, to avoid fat-water shift of
more than one pixel. Echo-planar acquisition uses an ultrafast sampling rate (i.e. high bandwidth per pixel) in the real-out axis; however, multiple echo readout with blipped jump in the phase-encoding axis results in an extremely low bandwidth in the phase-encoded direction. Echo-planar imaging uses bandwidth on the order of 30 Hz/Pixel, which causes undesired fat-water shift artifacts to appear along the phase-encoding axis as shown in Figure 2.7. The chemical characteristics of fat and water can either enhance or reduce the precession frequency resulting in spatial misregistration. Several fat suppression or water-excitation methods have been demonstrated to reduce the chemical shift artifacts in a variety of clinical applications. More detailed description in current fat-suppression methods are summarized in the Chapter 2.4 and 5.
2.2.3 Geometric Distortions

Geometric distortion artifacts commonly appear in the phase-encoding direction because the effective bandwidth in the phase-encoding direction is much smaller than in the readout direction. The effectively long sampling time in the phase encode direction allows the effects of small amplitude field variations to be amplified, leading to significant distortion. Image distortion mainly results from magnetic field inhomogeneity and susceptibility variations. Typical image distortions in EPI are represented by stretching or compressing of image voxels. Additionally, the brightness of a given voxel is also altered by distorted volume size. Thus, compression results in higher signal, and stretching results in lower signal relative to undistorted voxels. Several
distortion correction methods have been developed and implemented to eliminate image distortion in the EPI sequence (77-79). Common registration algorithms that correct for geometrical distortions are based on collecting a residual field map from a phase map so that pixel-relocation can be achieved (80,81). The degree of distortion is proportional to the duration of the echo train, motivating the use of segmented EPI techniques.

2.2.4 T2* Filtering

EPI sequence is one of the fastest MRI sequences, generating single-shot images in less than 100 msec. However, EPI is not fast enough to neglect the T2* decay that occurs during the echo-planar readout, as shown in Figure 2.8 (48). Thus, blurring caused by substantial signal intensity variation during data collection is another image artifact in EPI sequence. This T2* filtering effect can be minimized by shortening echo train and echo time. In single-shot EPI this can compromise spatial resolution in the phase-encoding direction, but segmented EPI can overcome this by keeping echo train short, at the expense of overall acquisition time.
2.2.5 Segmented and Single-Shot EPI

In the echo-planar trajectory, k-space data can be collection by a single shot or in multiple shots (using segmented k-space acquisition). With single-shot EPI, the entire k-space data is acquired following one excitation pulse, and hence the acquisition speed is superior to segmented EPI. Therefore, reduced sensitivity to motion and improved temporal resolution are major advantages of single-shot acquisition. On the other hand, this technique is sensitive to magnetic susceptibility inhomogeneities, which result in distortions as mentioned in the previous section. Therefore, we utilize the
segmented k-space approach to eliminate typical EPI artifacts in our development of real-time PC-MRI.

Segmented echo-planar has been implemented to acquire beat-to-beat hemodynamic information by taking its advantage of speed (82,83). Multiple shot EPI reduces the flow sensitivity compared to conventional single-shot echo-planar by keeping the echo time and echo train length short. While even echoes are inherently first moment nulled (velocity compensated), the odd echoes will exhibit increasing sensitivity to velocity with TE. Furthermore, susceptibility artifacts are also mitigated by shorter of echo-train-length.

An additional technique called echo time shifting (ETS) is required for multiple-shot echo-planar readout in order to eliminate the ghosting artifacts that can result due to the combination of phase errors that accumulate over the course of the echo train and interleaved segmented k-space acquisition (84). Phase errors due to field inhomogeneity, chemical shift and tissue susceptibility differences evolve accumulate over the echo train. An interleaved segmented acquisition uses the same echo of the echo train (i.e., echo 1, echo 2, etc.) to fill a contiguous segment of k-space. Assuming the
phase errors are static, each k-space segment will have a constant phase error, resulting in a stair-stepping increment of phase from one k-space segment to the next. These phase discontinuities result in ghost artifacts with the number and spacing of ghosts dependent on the k-space segmentation and number of shots. The ETS method increments a time shift between the RF pulse and the echo train readout from one shot to the next. This effectively smooths the phase variation from one segment to the next, converting the stair-steps of phase error to a continuous ramp of phase, and effectively suppressing segmentation ghost artifacts. The trade-off is in extended TE and TR as sufficient time between the RF pulse and the readout must be allowed to shift the equivalent of the time between echoes (echo spacing) over the course of all shots in the multi-shot EPI acquisition.

2.3 Temporal Resolution in Cardiac MRI

Cine imaging techniques provide an anatomic depiction of the heart and vessels in motion and are widely used to evaluate cardiac function, valve function, and blood flow. True temporal resolution is defined by the time spent acquiring data for a single image frame. With modern image acquisition and reconstruction methods, the reconstructed frame rate can be
significantly higher than the true temporal resolution through the use of digital interpolation or temporal window filtering techniques. The purpose of this section is to clarify the differences between the true temporal resolution and the effective temporal resolution that are often misinterpreted.

**True Temporal Resolution:** The most intuitive definition of true temporal resolution is the period of data acquisition for a complete cine-frame within a cine-loop (85). The intermediate cine-frame that is generated by image reconstruction techniques does not affect the true temporal resolution because data acquisition is completed and unchanged during image reconstruction. However, the cine loop displays smoother motion due to the higher number of frames in a given cine-loop after imaging reconstruction.

**Effective Temporal Resolution:** It is increasingly common to use a variety of image reconstruction methods to increase the image frame rate in order to produce smoother MR cine loops. The number of temporal frames in a cine-loop can be completely unrelated to the true temporal resolution, which we defined in the previous section. The effective temporal resolution is defined as the time interval between each reconstructed temporal-phase or
image frame in a cine-loop (85). Numerous intermediate cine-frames can be reconstructed by data interpolation or sharing methods. The quality of the MR cine images is improved by additional intermediate cine-frames; however, no additional information is acquired in the intermediate dataset. Visualization of moving structures can be improved by increasing the effective temporal resolution, although the true temporal resolution remains unchanged (86). Note that some acquisition and reconstruction techniques, such as echo-sharing, can generate MR images that a frame rate somewhere in between true and effective temporal resolutions. This is achieved by more frequent sampling of some lines of k-space. One extreme form of echo-sharing is the keyhole technique, in which only a center segment of k-space is updated in each frame, while the outer parts of k-space are sampled only once and shared among all frames.

2.4 Fundamentals of Fat-Suppression Techniques in MRI

Before discussing the fat-suppression technique which is specialized for echo-planar acquisition, a brief description of clinical fat-suppression methods provides useful background information. Suppression of the bright fat signal is essential in a variety of cardiovascular MRI applications to improve lesion
conspicuity, suppress motion and chemical shift artifacts, and minimize shifting and blurring in long readout acquisitions. Bright fat signal can reduce image contrast between normal and pathological tissues, and obscure lesion detection as illustrated in Figure 2.9. Therefore, the ability to identify some disease can be improved by fat-suppression techniques.

Figure 2.9: Single end-systolic frame from cine-SSFP series acquired without (a) and with (b) fat-suppression technique in a healthy volunteer.
Figure 2.10 illustrates the hydrogen protons in fat resonate at a frequency of 220 Hz less than water (i.e. 2.2 msec time delay) in a 1.5 Tesla MRI system (87). Additionally, the T1 of fat is much shorter than water-based tissues, providing another opportunity to suppress fat signal. These features of the fat signal can be exploited to suppress fat in MRI.

A variety of techniques have been developed to provide signal suppression from normal adipose tissue, such as chemical shift selective (CHESS) imaging (88,89), short tau inversion recovery (STIR) preparation (90,91), and the multi-point Dixon method (92). The CHESS imaging technique is currently the most commonly used fat-suppression strategy: it utilizes a
frequency-selective pre-saturation pulse that excites and tips into the transverse plane only the unwanted fat component prior to a conventional imaging sequence. The fat signal component is dephased by subsequent magnetic field gradient spoiling. A water-only MR image results because the water component is unaffected by the CHESS pulse. However, the prohibitively long acquisition times, steady-state disturbance, and sensitivity of field inhomogeneity may limit the utility of this method in some routine cardiovascular MRI applications.

The STIR sequence offers an alternative method of fat suppression with insensitivity to field homogeneity. The basic idea of STIR is to use a 180° radiofrequency pulse to invert spins to the negative longitudinal axis. Because the T2 of fat is significantly shorter than other tissues, a short inversion recovery time (TI) can be used to selectively null the signal from fat. Unfortunately, the STIR sequence has not been widely adaptable to steady-state free precession (SSFP) or other cine sequences because the inversion pulses perturb the normal steady-state equilibrium.

The multi-point Dixon method takes advantage of the relative difference in
precession frequency of fat and water to create water and fat images from at least two full acquisitions (93-96). But it also introduces a minimum scan time penalty to be able to achieve uniform water-fat separation by correcting for B0 field inhomogeneity.

2.5 Binomial Water-Excitation Pulses

Spectral-spatial fat suppressed MR imaging can be achieved by selectively exciting water protons using a binomial RF pulse train (1-1, 1-2-1, 1-3-3-1, etc.) instead of applying a conventional slice-selective RF excitation. Figure 2.11 represents the simplest excitation scheme (i.e. 1-1 binomial pulses) to tip water protons towards the transverse plane while maintaining fat protons on the longitudinal axis. The first pulse rotates both fat and water magnetization from initial equilibrium (Figure 2.11a) toward the transverse plane, as shown in Figure 2.11b. With a 2.2ms delay time, fat and water are $180^\circ$ out-of-phase, (Figure 2.11c), the second pulse, identical to the first in both amplitude and phase, tips water protons further down towards the transverse plane while tipping fat protons back up to the longitudinal axis, as shown in Figure 2.11d. This binomial pulse combination effectively reverses the initial excitation of fat and the resultant tip angle for water is the sum of the individual component
pulse angles. The standard MRI data acquisition scheme is applied after slice-excitation pulses to acquire a water-only MR image. This method and its application to EPI and SSFP sequence will be further developed in Chapter 5.
Fat undergoes no net excitation

Water is excited to transverse plane

Figure 2.11: Binomial water-excitation pulse pattern that tips water spins toward to transverse plane while maintains fat spins in the longitudinal axis
2.6 Summary

This chapter provided background information to help the reader understand the essential techniques previously developed by other research groups, such as sensitivity of moving spins, existing invasive and non-invasive velocity measurement methods and fat-water separation techniques, etc. Our study is based on prior achievements combined with several new concepts to meet the goal of this project which we described in Chapter 1. We start with an accelerated phase-reference method for rapid flow measurement in the following chapter 3.
CHAPTER 3

ACCELERATED PHASE-REFERENCE PHASE-CONTRAST MAGNETIC RESONANCE IMAGING

We implemented and evaluated two different acceleration approaches to achieve rapid velocity measurement with phase-contrast magnetic resonance imaging (PC-MRI) in this dissertation. First, in this chapter, accelerated data acquisition strategies (i.e. reduced spatial resolution and temporal view-sharing of phase-reference techniques) were developed to reduce the reference data requirements in PC-MRI. Second, an echo-planar imaging sequence was implemented in order to enhance the acquisition efficiency in PC-MRI, as described in Chapter 6. This chapter presents a time-efficient PC-MRI method that accelerates the acquisition of phase-reference data in the spatial and temporal domains with minimum loss of velocity accuracy.
3.1 INTRODUCTION

Velocity measurement based on PC-MRI (58) is firmly recognized as a valuable and accurate technique to assess hemodynamics in a variety of clinical applications (97). As we mentioned in Chapter 2, a conventional phase-velocity measurement requires the acquisition of two separate and complete k-space datasets with different flow sensitivities (68). The standard PC-MRI scan requires either velocity-encoded and velocity-compensated datasets (70), or a pair of equal and opposite polarity velocity-sensitized k-space datasets (69). Phase-difference reconstruction is performed on each complex data pair to eliminate any residual non-zero phase variation due to effects other than velocity. Thus, conventional MR velocity mapping requires twice as much data as standard MRI scans; this requirement either degrades the temporal sampling rate by a factor of two, or doubles the acquisition time to maintain sufficient temporal resolution.

Several techniques have been developed to reduce the data requirements in PC-MRI (98-100). To decrease total acquisition time, Man (98) proposes non-subtractive spiral phase-contrast velocity imaging that only required a velocity-encoded dataset. Instead of acquiring an additional phase-reference
map, the background phase characteristic is estimated and corrected directly from the single velocity-encoded dataset. However, non-subtractive velocity mapping has not been widely adopted because rapid spatial variations of magnetic susceptibility and imperfect background phase estimation can impair the velocity accuracy with this method. A similar method, velocity single-shot parameter assessment by retrieval from signal encoding (V-SS-PARSE), is implemented in PC-MRI by estimating independent parameters by solving an inverse problem based on a parametric equation (99,100). In V-SS-PARSE, multiple shots might be required for providing sufficient data for phase estimation to include off-resonance and T2* relaxation effects in the calculation model. Additionally, solving this inverse problem requires highly intensive computations that may extend reconstruction time. This may limit its utility in real-time cardiac applications.

The importance of the central region of k-space and its correlation with the majority of image information including background phase variations was previously discussed by Margosian (101) and MacFall (102) in the 1970s. We hypothesize that the residual phase effects slowly vary in both space and time domains in PC-MRI, and thus, the spatial and/or temporal resolution of
the phase-reference data can be significantly reduced without affecting the accuracy of the resulting velocity measurement. A simple and practical accelerated PC-MRI, which only acquires the central region of phase-reference data with zero-filling in the peripheral “missing” region was previously described by Jhooti et al. (71). We developed an alternative method that operates on the assumption that phase errors are slowly varying in time to improve temporal efficiency by sparse temporal sampling of phase reference data (103) This method was subsequently recently described by another research group (104). These methods use either a reduced spatial resolution phase-reference or a reduced temporal resolution phase-reference in PC-MRI reconstruction. The current work aims to demonstrate these concepts by off-line reconstructing phase-velocity images using phase-reference data with either reduced spatial resolution or temporal view-sharing in order to improve image acquisition efficiency. Reducing the spatial resolution of the phase-reference image data by zero-filling in peripheral k-space or reducing the temporal resolution of the phase-reference image data by using the view-sharing technique both create the potential benefit of accelerating the acquisition speed of PC-MRI. In order to preserve the highest accuracy of velocity measurement, the velocity-encoded image
data for both proposed accelerated methods was maintained in the original form and was unmodified in spatial or temporal resolution.

3.2 MATERIALS AND METHODS

3.2.1 Reduced Spatial Resolution of Phase-Reference Technique

The importance of the central region of k-space has been described in detail in previous publications (101,102). The assumption of this study is based on the slowly background phase variations in both space and time domains. Imaging time reduction can be achieved by partial k-space coverage with the zero-filling reconstruction method (105). Please note that this acceleration method only applies to the phase-reference data while maintaining the full resolution of the velocity-encoded data. This sampling strategy was performed here by dividing the k-space into a central lower spatial-frequency region that was fully sampled and a peripheral higher spatial-frequency region that was unsampled and filled by zero values, as shown in Figure 3.1.
Figure 3.1: Schematic illustration shows that two separated acquisitions are performed in reduced spatial resolution accelerated PC-MRI technique. (a) Velocity-encoded data with full spatial sampling and (b) velocity-compensated data that only acquired lower spatial samples incorporating with zero-padding of higher spatial frequency and window smoothing for Gibbs ringing suppression. Two datasets are subtracted to generate a phase map that is proportional to flow velocity corresponding to the direction of velocity-encoding.

In this study, we implemented and tested the proposed reduced spatial resolution and temporal view-sharing algorithm in an off-line image reconstruction without changing the acquisition scheme. Conventional phase-contrast MR k-space dataset was acquired; however, the raw data was off-line reconstructed by proposed algorithms. In the reduced spatial resolution of phase-reference method, Matlab off-line reconstruction was performed by filling zero value the peripheral k-space regions of the phase-reference dataset. The central region of phase-reference data and the peripheral region of zero-filled data were combined to yield a phase-reference
dataset with the same number of pixels as the full resolution velocity encoded data for phase-contrast reconstruction. A smooth roll-off of the transitional k-space data was implemented in order to eliminate the Gibbs ringing artifact that results from the potentially sharp discontinuity between the two k-space regions. We examined the use of a reduced spatial resolution phase-reference, utilizing only the lower 50% and 33% of k-space for the phase-reference data. It should be stressed that this method would allow additional cardiac phases to be sampled by acquiring the combination of two distinct sampling densities of phase-reference data, which is shown schematically in Figure 3.2. As proposed, cutting 50% of the reference data would result in a 25% improvement in scan efficiency (since the reference data comprises ½ of the total data acquired in PC-MRI).

![Figure 3.2](image)

Figure 3.2: Schematic diagram of the maximal number of cardiac phases that is acquired by conventional vs. reduced spatial resolution accelerated PC-MRI technique. This technique substantially decreases total acquisition time for velocity mapping by skip the higher spatial frequency region of phase-reference data.
3.2.2 Temporal View-Sharing of Phase-Reference Technique

To increase the acquisition efficiency for the PC-MRI technique, full k-space phase-reference data was generated by sharing data with earlier and later cardiac phases. In Figure 3.3, given an acceleration rate equal to 3, the phase-reference k-space was filled using data from current (1/3), previous (1/3) and next (1/3) cardiac phases. Note that the spatial resolution of the phase-reference dataset does not change because the full spatial sampled data is used for phase reconstruction. However, it may be possible to combine the approaches to reduce both the spatial and temporal sampling of reference data for further improvements in efficiency. The first/last velocity measurement point is reconstructed by sharing phase-reference data from the previous/later cardiac phases. Temporal view-sharing by factors of 3 and 11 were tested in the current study. In all reconstructions, full temporal and spatial resolution of the velocity-encoded data was maintained; these acceleration methods were only applied to the phase-reference data.
Figure 3.3: Sliding window view-sharing was used to simulate reduced temporal resolution phase-reference scan from fully sampled dataset. After data combining from adjacent velocity-compensated data from previous and later acquisition, a complete spatial resolution of phase-reference data is generated for velocity mapping.

3.2.3 Human Subject Imaging Studies

We recruited six healthy volunteers that had no prior history of cardiovascular disease. All scans were acquired in planes perpendicular to the vessel being studied, and aortic velocity curves with through-plane velocity-encoding were generated in a regions of interest (ROI). We analyzed aortic mean and peak velocity from six normal, healthy volunteers (mean age, 44 ± 13.1 years old). A conventional spoiled gradient-echo PC-MRI sequence was implemented on a 1.5 T Avanto system (Siemens Healthcare Inc., Erlangen, Germany) capable of producing a gradient of 45 mT/m and slew rate of 200 mT/m/msec with 12-channel surface coil array, and electrocardiography signal gating. Off-line image reconstruction was
performed using computer routines implemented in MATLAB software (Mathworks, Natick, MA). The image acquisition parameters were as follows: TE/TR = 3.8/7.1 ms, flip angle = 20°, acquisition matrix = 108 × 192, VENC = 120 cm/s, typical resolution 2.5mm × 1.8mm × 6 mm slice, no k-space segmentation and two averages to suppress respiratory motion artifacts.

3.2.4 Image Reconstruction

Full temporal and spatial resolution in both velocity-encoded and phase-reference datasets was considered to be the gold standard velocity measurement and all reconstructions using reduced phase reference data were compared data reconstructed from the full datasets. In the reduced spatial resolution phase-reference technique, a window smoothing filter was applied, which consisted of 1/16 of the number of k-space lines in the central lower spatial frequency region to roll-off the discontinuity between two separated regions and suppress Gibbs ringing artifacts (Figure 3.1b). The true phase-encoding spatial resolution of zero-filled phase reference k-space for 50% and 67% zero-filling are 5 and 7.5 mm, respectively. In the temporal view-sharing technique, the temporal resolution by offline reconstruction of
view-shared phase-reference k-space for 3 and 11 lines segmentation are 57 and 209 msec, respectively.

### 3.2.5 Data Analysis

ROI from each subject was drawn manually on the anatomical images, and then copied to the flow-encoded images. Correlation coefficients ($r$) were calculated between conventional PC-MRI with complete phase-reference and proposed accelerated PC-MRI methods. Differences in aortic mean, peak velocity, and Root-Mean-Square (RMS) error were calculated between full spatial/temporal resolution reference data and reduced phase-reference PC-MRI from six subjects. The differences in mean and peak velocity were expressed as a percentage of conventional PC-MRI technique to validate accuracy of velocity measurement. Velocity bias between conventional and proposed PC-MRI from each volunteer is normalized and expressed as a percentage of peak velocity when comparing data from other volunteers.

### 3.3 RESULTS

In-vivo images from one of the six volunteers are shown in Figure 3.4. Illustrative magnitude and phase PC-MRI images with conventional data
acquisition and full spatial and temporal resolution of phase-reference are shown in Figure 3.4a and b. The results of Figures 3.4c and d demonstrate coincidental phase information including only 50% (Figure 3.4c) and 33% (Figure 3.4d) of central phase-reference k-space lines after zero-padding in the remaining region and phase reconstruction. Figures 3.4e and f are examples of phase-velocity images at temporal view-sharing acceleration factors of 3 and 11, respectively.
Figure 3.4: Single frames of MR images reconstructed showing magnitude image (a) with full phase-reference k-space data, and phase-velocity images with (b) full phase-reference k-space data, (c) 50% phase-reference k-space data, (d) 33% phase-reference k-space data, (e) temporal view-sharing acceleration factor of 3, and (f) temporal view-sharing acceleration factor of 11.
To investigate the accuracy of velocity measurements, the aortic mean, peak velocity curves and RMS error were calculated using each of the acceleration techniques and the conventional technique from all subjects. Comparison of hemodynamic information acquired with the temporal view-sharing technique to those acquired with the standard PC-MRI method shows no discernible difference for clinical diagnosis. Figure 3.5 shows the flow velocity in the descending aorta of the normal volunteer shown in Figure 3.4 measured with conventional and accelerated PC-MRI techniques. Figure 3.5a shows separately the flow velocity during the cardiac cycle in a single volunteer measured with 100% (diamonds ♦), 50% (squares ■) and 33% (triangles ▲) data. Note the excellent correspondence between the three velocity curves despite the significantly reduced phase-reference spatial resolution. In the same volunteer, flow velocity curves comparing full temporal resolution (diamonds ♦), sharing factor of 3 (squares ■) and factor of 11 (triangles ▲) are displayed in Figure 3.5b. Phase information appears to be equivalent despite significant temporal resolution reduction in phase-reference dataset. All results demonstrate a high degree of similarity and the curves in Figure 3.5a and 3.4b are significantly overlapping except for the first velocity measurement points in Figure 3.5b since they were
reconstructed by sharing phase-reference data from the latter cardiac phases. Aortic mean, peak velocity differences and RMS from each individual subject expressed as a percentage difference from gold standard PC-MRI are listed in Table 3.1. A quantitative analysis of the measured velocities for all methods on six healthy volunteer data is summarized in Table 3.2. Velocity bias between conventional and proposed PC-MRI from each volunteer is normalized and expressed as a percentage of peak velocity when comparing data from other volunteers. The RMS error comparison displays a good agreement between different spatial and temporal resolution conditions compared to standard PC-MRI acquisition.
Figure 3.5: Accelerated PC-MRI scans were performed in the descending aorta in a healthy volunteer. Comparison of aortic flow curve versus phase of the cardiac cycle for the one normal volunteer obtained from (a) spatial resolution reduction of phase-reference with 100% (diamonds ♦), 50% (squares ■) and 33% (triangles ▲) data, and (b) temporal view-sharing methods of phase-reference data acceleration sharing factor of 3 (squares ■) and factor of 11 (triangles ▲).
In mean velocity measurement, insignificant mean velocity difference was obtained in human subject studies. These differences were \(-0.92 \pm 1.12\% (r = 0.98)\) for 50% spatial-resolution reduction, \(-1.68 \pm 3.43\% (r = 0.96)\) for 33% spatial-resolution reduction, \(-0.64 \pm 1.82\% (r = 0.98)\) for temporal view-sharing acceleration factor of 3 and \(-1.23 \pm 4.11\% (r = 0.96)\) for temporal view-sharing acceleration factor of 11. In peak velocity measurement, insignificant peak velocity difference \(-0.21 \pm 0.26\% (r = 0.99)\) for 50% spatial-resolution reduction, \(-0.31 \pm 0.68\%\) for 33% spatial-resolution reduction, \(0.07 \pm 0.52\% (r = 0.99)\) for temporal view-sharing acceleration factor of 3 and \(0.28 \pm 1.62\% (r = 0.95)\) or temporal view-sharing acceleration factor of 11) were obtained in all cases.
### TABLE 3.1
Mean, peak velocity difference and RMS from each individual subjects expressed as a percentage of conventional PC-MRI

<table>
<thead>
<tr>
<th>Difference</th>
<th>Subject</th>
<th>Volunteer # 1</th>
<th>Volunteer # 2</th>
<th>Volunteer # 3</th>
<th>Volunteer # 4</th>
<th>Volunteer # 5</th>
<th>Volunteer # 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Mean (V_{\text{orig}}) - Mean (V_{50% FC})) / Mean (V_{\text{orig}}) (%)</td>
<td>-1.04</td>
<td>0.64</td>
<td>-1.87</td>
<td>0.25</td>
<td>-1.46</td>
<td>-2.05</td>
<td></td>
</tr>
<tr>
<td>(Mean (V_{\text{orig}}) - Mean (V_{30% FC})) / Mean (V_{\text{orig}}) (%)</td>
<td>-3.98</td>
<td>-2.08</td>
<td>-4.93</td>
<td>2.21</td>
<td>2.88</td>
<td>-4.21</td>
<td></td>
</tr>
<tr>
<td>(Mean (V_{\text{orig}}) - Mean (V_{11%})) / Mean (V_{\text{orig}}) (%)</td>
<td>-0.19</td>
<td>-1.32</td>
<td>-0.91</td>
<td>-3.31</td>
<td>2.27</td>
<td>-0.38</td>
<td></td>
</tr>
<tr>
<td>(Mean (V_{\text{orig}}) - Mean (V_{11%})) / Mean (V_{\text{orig}}) (%)</td>
<td>-4.92</td>
<td>-3.48</td>
<td>-3.57</td>
<td>-3.11</td>
<td>5.39</td>
<td>2.34</td>
<td></td>
</tr>
</tbody>
</table>

Continued
Table 3.1: continued

<table>
<thead>
<tr>
<th>Expression</th>
<th>68</th>
</tr>
</thead>
<tbody>
<tr>
<td>((\text{Peak } V_{\text{origl}} - \text{Peak } V_{\text{50% FC}}) / \text{Peak } V_{\text{origl}}(%))</td>
<td>-0.28 0.72 1.52 3.09</td>
</tr>
<tr>
<td>((\text{Peak } V_{\text{origl}} - \text{Peak } V_{\text{30% FC}}) / \text{Peak } V_{\text{origl}}(%))</td>
<td>-0.31 -0.38 1.76 1.15</td>
</tr>
<tr>
<td>((\text{Peak } V_{\text{origl}} - \text{Peak } V_{\text{VS = 3}}) / \text{Peak } V_{\text{origl}}(%))</td>
<td>0.21 -0.38 1.68 2.61</td>
</tr>
<tr>
<td>((\text{Peak } V_{\text{origl}} - \text{Peak } V_{\text{VS = 11}}) / \text{Peak } V_{\text{origl}}(%))</td>
<td>-0.58 -0.77 1.17 3.11</td>
</tr>
<tr>
<td>\text{RMS}_{\text{50% FC}}(%)</td>
<td>-0.18 -1.01 1.45 3.52</td>
</tr>
<tr>
<td>\text{RMS}_{\text{33% FC}}(%)</td>
<td>-0.17 -0.72 1.23 3.71</td>
</tr>
<tr>
<td>\text{RMS}_{\text{VS = 3}}(%)</td>
<td>2.04 2.97 1.9 2.97</td>
</tr>
<tr>
<td>\text{RMS}_{\text{VS = 11}}(%)</td>
<td>0.28 1.92 1.31 3.97</td>
</tr>
<tr>
<td>\text{RMS}_{\text{VS = 3}}(%)</td>
<td>1.12 2.38 1.39 3.43</td>
</tr>
<tr>
<td>\text{RMS}_{\text{VS = 11}}(%)</td>
<td>1.08 1.29 1.48 3.07</td>
</tr>
<tr>
<td>\text{RMS}_{\text{VS = 3}}(%)</td>
<td>1.12 2.91 1.33 2.55</td>
</tr>
<tr>
<td>\text{RMS}_{\text{VS = 11}}(%)</td>
<td>0.98 1.24 1.32 1.24</td>
</tr>
<tr>
<td>Methods</td>
<td>50% Spatial Resolution</td>
</tr>
<tr>
<td>-----------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Difference</td>
<td></td>
</tr>
<tr>
<td>Mean Velocity (%)</td>
<td>-0.92 ± 1.12</td>
</tr>
<tr>
<td>Peak Velocity (%)</td>
<td>-0.21 ± 0.26</td>
</tr>
<tr>
<td>Root-Mean-Square Error (%)</td>
<td>1.11 ± 0.56</td>
</tr>
</tbody>
</table>
3.4 CONCLUSIONS

In principle, partial coverage of the phase-reference dataset could be used to shrink acquisition time or improve spatial and/or temporal resolution with minimal loss of accuracy of velocity measurement. Total scan time is proportional to the ratio of k-space coverage based on theoretical estimation. For example, acquiring the central region of 50% phase-reference data requires 75% of total scan time comparing to conventional phase-contrast MRI acquisition. Similar scan time estimation also applies to the temporal view-sharing of phase-reference method because it only reduces the sampling requirements for the phase-reference dataset. In this chapter, methods to increase the efficiency of PC-MRI by reducing the spatial or temporal resolution of the phase-reference data were presented and validated in human experiments. The reconstructed flow images reconstructed using both accelerated PC-MRI techniques correlated well with those generated by conventional PC-MRI using fully-sampled reference data (Figure 3.4).

The accuracy of the two accelerated approaches was compared to the standard, full phase-reference method for velocity measurement in six healthy volunteers. Excellent agreement between different spatial and/or temporal
resolution conditions compared to standard PC-MRI acquisition and a negligible RMS error difference of 1.11 ~ 2.87% was present in the descending aorta as reflected by a mean difference percentage of -0.64 and -1.68 %, respectively (Table 3.1)

The major advantage of the accelerated PC-MRI methods is that time-efficient data acquisition can be readily achieved by reducing the spatial and/or temporal resolution of the phase reference (velocity compensated) data without significantly affecting the accuracy of velocity measurement. Acquiring only the minimally required spatial and/or temporal resolution of phase-reference data maintains the quantitative accuracy of velocity measurement while significantly reducing data acquisition requirements. This method can be utilized to improve the spatial and/or temporal resolution of breath-hold and real-time PC-MRI techniques, and reduce the lengthy scan time of three-dimensional data acquisitions.

In conclusion, this study suggests that appropriate phase-reference data reduction can accelerate acquisition time for velocity measurement without any significant loss of accuracy in velocity mapping. This proposed method can

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be used in segmented acquisition without any additional limitation. Besides, this method is also compatible in combination with partial Fourier acquisition and parallel acceleration techniques, which could further increase scan efficiency and improve temporal and spatial resolution of real-time PC-MRI. The two methods described are also compatible with each other, and could potentially be combined for further time savings.

In the next chapter, we will propose a novel phase-velocity reconstruction algorithm, i.e. Shared Velocity Encoding (SVE) method, which improves the effective temporal resolution of real-time PC-MRI. Please note that the SVE method has technical success in real-time and non-segmented acquisitions.
CHAPTER 4

SHARED VELOCITY ENCODING RECONSTRUCTION

This chapter we present a novel phase-contrast magnetic resonance imaging (PC-MRI) method which uses a standard method of data acquisition, but a new, unique algorithm for phase-velocity reconstruction that results in improved temporal resolution. One conventional method of PC-MRI works by alternating the polarity of velocity-encoding gradients from one temporal frame to the next between positive [+] and negative [-] velocity-encoding sensitivities (i.e. [+ -], [+ -]). One phase-velocity map is reconstructed from each pair of frames, resulting in half the temporal sampling rate of a standard cine acquisition because two times the data must be acquired. In Chapter 3, we presented a time-efficient PC-MRI technique that acquires minimum phase-reference data with no significant loss of velocity accuracy. In this
In this chapter, to validate the improvement in temporal resolution achieved by SVE, we conducted a numerical simulation which compares the peak velocity and total flow volume measured using conventional PC-MRI (i.e. [+ 0], [+ 0]), velocity-encoded only (i.e. [+], [+]) and SVE methods (i.e. [+ -], [- +]). Furthermore, we developed a flow phantom using a constant flow pump, a mechanical valve and a wave function generator to provide constant and pulsatile velocity waveforms. Quantitative velocity measurements on this in-vitro pulsatile flow phantom were performed and analyzed in this chapter to evaluate the accuracy of SVE velocity measurements compared to PC-MRI methods.

4.1 THEORY

4.1.1 Conventional Phase-Contrast Reconstruction

Conventional phase-contrast MR images are commonly acquired using a spoiled gradient-echo sequence combined with a pair of velocity-sensitized bipolar gradients on one or more gradient axes. There are two basic
approaches to achieve quantitative and qualitative velocity measurement by
PC-MRI. Figures 4.1 and 4.2 illustrate the conventional PC-MRI sequence
diagrams that employ a pair of velocity-compensated and velocity-encoded
gradients (Figure 4.1), and equal and opposite polarity velocity-sensitized
gradients (Figure 4.2) to eliminate background phase variations. As
previously mentioned in Chapter 2, phase subtraction of two datasets is
performed to eliminate residual non-zero phase shifts that stem from
undesired phase variation other than motion, such as field inhomogeneity,
eddy currents, and magnetic susceptibility. However, the additional
acquisition of a phase-reference, which typically interleaves with the
velocity-encoding dataset, reduces the temporal resolution as compared to
standard cine image scans.
Figure 4.1: Spoiled gradient-echo phase-contrast pulse sequence for one-directional velocity encoding along the slice-selection direction using a pair of velocity-compensated and velocity-encoded gradients.

Similarly, the phase subtraction reconstruction is applied in PC-MRI using a pair of equal and opposite polarity velocity-sensitized gradients (Figure 4.2). To reduce the effects of background phase variations, and other unwanted contributions to the phase, two consecutive images are acquired. A pixel-by-pixel phase subtraction is performed to determine the difference in phase in these two images. In this manner, quantitative measurement of blood flow can be estimated from the phase difference between two velocity-sensitized datasets. The proposed SVE method adapts this velocity-encoding and acquisition strategy; however, the phase-contrast
images are reconstructed using a novel algorithm, which we will discuss in detail in the rest of this chapter.

Figure 4.2: Spoiled gradient-echo phase-contrast pulse sequence for one-directional velocity encoding along the slice-selection direction using a pair of equal and opposite polarity velocity-sensitized gradients.

Note that both conventional PC-MRI approaches require additional phase information that doubles the amount of data required relative to other MRI pulse sequences. As the result, PC-MRI requires either extended scan time or sacrifices in spatial and temporal resolution that make real-time flow quantification and three-dimensional acquisition impractical.
4.1.2 Shared Velocity Encoding Reconstruction

In an effort to address the temporal resolution limitations of PC-MRI, we developed a new sampling strategy to reconstruct the phase-velocity data acquired using alternate polarity velocity encodings. SVE is a PC-MRI reconstruction technique designed to improve temporal resolution by reusing adjacent k-space data to reconstruct twice as many frames as conventional PC-MRI reconstruction methods. As previously mentioned, one type of conventional PC-MRI method works by alternating the polarity of velocity encoding gradients from one k-space to the next between positive [+ ] and negative [-] velocity encoding (i.e., [+ -], [+ -]), as shown in Figure 4.3.

![Figure 4.3: Conventional non-segmented PC-MRI reconstruction. N/2 of numbered reconstructed phase contrast images compare to standard MR scans](image-url)
The velocity map is obtained by subtracting the negative velocity encoded image from the positive encoded k-space data. The temporal resolution of the velocity map is therefore half the image frame rate. In the conventional PC-MRI method, the phase-contrast images are calculated from consecutive pairs of [+ -] velocity encoded lines. This results in N/2 reconstructed temporal-phase images from N acquired full k-space datasets. In SVE, data are acquired in the same way, but the velocity map is reconstructed by sliding the pair of images for subtraction one frame at a time (instead of two), resulting in a factor of 2 improvement in effective temporal resolution (Figure 4.4).

Using SVE, velocity-sensitized data is reconstructed between consecutive images with alternate polarity velocity encoding. As a result, N-1 phase-difference lines from alternate polarity pairs (i.e. [+ -], [- +], [+ -]), etc., can be reconstructed from N acquired lines, resulting in nearly a factor of 2 increase in effective temporal resolution.
Improvement of temporal resolution is one of the critical parameters to evaluate the performance of the conventional and proposed PC-MRI methods. As previously mentioned in Chapter 2, there are two distinct definitions of temporal resolution used in dynamic digital imaging. The appropriate interpretation of each definition should be emphasized and re-visited when we compare the SVE method to conventional PC-MRI acquisition.

1. **True Temporal Resolution** is defined as the period of data acquisition for a complete cine-frame within a cine-loop (85). That is, it is the duration of time spent in each cardiac cycle collecting data for each image frame.
2. **Effective Temporal Resolution** is defined as the time interval between each reconstructed temporal-phase or image frame within a cine-loop (85).

Please note that the intermediate cine-frames that are generated by image reconstruction techniques do not affect the true temporal resolution because true temporal resolution is defined purely by the time spent acquiring data. Pure interpolation between reconstructed frames will have the effect of smoothing the display of moving structures. However, depending on the reconstruction and the method used to share data between frames, each individual frame may still contain unique information and may improve the representation of moving structures or dynamically changing image contrast.

In this study, we investigated and compared the characteristics of temporal resolution and accuracy of velocity measurement using conventional FL-FQ PC-MRI with velocity-encoded and velocity-compensated sensitivities (i.e. [+ 0], [+ 0], [+ 0]), velocity-encoding only (i.e. [+], [+], [+]) without acquisition of reference data, and SVE (i.e. [+ -], [- +], [+ -]) PC-MRI methods. In conventional FL-FQ PC-MRI, the true temporal resolution is the total period of
positive velocity-encoded [+] and velocity-compensated [0] acquisitions. Effective temporal resolution is equal to true temporal resolution because this type of reconstruction requires a pair of velocity-encoded and velocity-compensated images to yield one temporal cine-frame. In other words, FL-FQ PC-MRI utilizes one frame to acquire velocity sensitivity data and a second time frame to acquire phase reference data without velocity sensitivity; this reference data contributes no velocity information at the corresponding time point. There is no velocity-related information in the velocity-compensated dataset by design, since first order gradient moment nulling effectively eliminates any phase due to velocity. This implies, however, that short-term or high frequency velocity changes may not be detected if they occur during the velocity-compensated acquisition period. Thus, the conventional method of interleaving velocity compensated with velocity encoded data not only has the effect of reducing true temporal resolution, it also effectively introduces gaps in the sampling of velocity during the time frames when velocity compensated data are acquired.

Data acquisition sampling lines with positive velocity-encoding only (i.e. [+] [+], [+] [+]) was simulated to define the gold standard for true temporal resolution.
In this case, the reconstructed temporal resolution is equal to the true temporal resolution and is defined as the time to acquire only one frame. However, without background phase subtraction, this method is impractical since without a phase reference the accuracy of velocity measurement is adversely affected by residual phase variations due to local field inhomogeneities and other effects.

The proposed SVE method acquires a pair of k-space datasets with equal and opposite velocity-encoding sensitivities in each temporal cine-frame. Phase subtraction and phase-contrast reconstruction is performed on each successive pair of k-space datasets, but shifting only one frame instead of the usual two frames between subtractions. That is, each subtraction has one dataset in common with the previous frame, and one dataset in common with the next frame. A conventional PC-MRI reconstruction generates N/2 subtraction pairs from N acquired frames, but SVE reconstruction results in N-1 subtraction pairs. While similar to the methods of echo-sharing or view-sharing used in conventional cine imaging, each of the subtraction pairs used in the SVE method contains unique velocity information that corresponds to a weighted average of the velocity over the time of acquisition of the two
frames. As the result, the SVE method achieves twice the effective temporal resolution compared to conventional PC-MRI; however, SVE does not alter the true temporal resolution because it requires the same acquisition period to collect k-space data for each temporal cine-frame; two temporal cine-frames are used to calculate each velocity map. Both temporal cine-frames contribute equally to the velocity measurement at each time point. When velocity compensated data is used as the phase reference, only the velocity-encoded frames contribute to the measured velocity. In other words, the SVE method smoothes the velocity curve using a sliding local average window with width of two velocity-encoding acquisitions. Simulations were performed to evaluate the effect of this sliding window reconstruction on measurements of peak velocity and total flow volume in section 4.2 of this chapter.

4.1.3 Shared Velocity Encoding Reconstruction vs. Echo-Sharing Method

Cardiac echo-sharing was proposed to improve the effective temporal resolution in segmented cine and phase-contrast imaging in 1995 (86). One of the major differences of SVE comparing to echo-sharing method is that SVE
collects a full k-space data with a given velocity sensitivity followed by another k-space with an opposite velocity sensitivity. On the other hand, the echo-sharing method shares portions of k-space between adjacent images for both the velocity compensated and velocity encoded lines. Therefore, in the echo-sharing method, partial k-space data is shared and reconstructed from two or more temporally adjacent k-space data pairs, as shown in Figure 4.5. SVE, on the other hand, does not share parts of k-space with adjacent phases, but instead shares half of the data (V+ or V-) needed for PC-MRI reconstruction as shown in Figure 4.6.

Figure 4.5: Diagram shows the cardiac view-sharing PC-MRI method
There are several differences between SVE and echo-sharing that influence velocity measurements and the applicability of each technique due to difference in the ordering of k-space.

Because image characteristics are dominated by the central portion of k-space, echo-sharing methods require the acquisition of an additional central line or segment of k-space for each pair of reconstructed frames. Otherwise, if the central line(s) of k-space were shared between frames, those frames would contain substantially the same information. SVE does not require the acquisition of additional central lines; each frame has a unique combination of central line encodings ($V^+$ and $V^-$), and thus unique velocity information. In segmented acquisitions the smaller the number of segments the less efficient echo-sharing methods are due to requirement of acquiring additional center
lines. In the extreme case of one line per segment, or non-segmented acquisition, echo-sharing fails to provide any gain in temporal resolution while SVE can be successfully applied as demonstrated later in this chapter. As the number of segments increases, the efficiency of echo-sharing increases also, to the extreme of real-time imaging where typically only a single central line of k-space must be acquired uniquely for each image. However, in the particular implementation of real-time PC-MRI using a segmented echo-planar readout (see Chapter 6), echo-sharing would require the acquisition of an additional echo-train per encoded image, i.e., one for the V+ encoding and one for the V- encoding. This would result in a significant loss in efficiency when compared with SVE which requires no additional data or echo trains to ensure that each reconstructed frame has unique central k-space information.

It was mentioned previously that segmented view-sharing technique loses its capability in non-segmented high temporal PC-MRI. While segmented k-space PC-MRI has taken over most applications for velocity mapping, applications requiring extremely high temporal resolution, such as pediatric CMR and pulse wave velocity (PWV) measurements, still rely on non-segmented data acquisition. Estimation of local PWV in short sections of
central or peripheral arteries requires extremely high temporal resolution for
differentiation of short transit time-delays between the pulse waves measured
at points separated by short distances. The temporal resolution requirements
for local PWV measurements are beyond those achievable with k-space
segmentation, and even higher than attainable with conventional,
non-segmented PC-MRI acquisition. The SVE technique is similar to the
view-sharing method; however, view-sharing methods require some level of
segmentation of the acquisition and are not applicable when only one line of
k-space is acquired at a time. Thus, the ability of SVE to improve the
effective temporal resolution of non-segmented PC-MRI is a unique advantage
over echo-sharing methods.

4.2 NUMERICAL SIMULATIONS

4.2.1 Numerical Simulation

Numerical simulations were performed to predict the accuracy of peak
velocity and total flow volume measurements using (i) conventional FL-FQ
PC-MRI with velocity-encoded and velocity-compensated sensitivities (i.e. [+ 0], [+ 0], [+ 0]), (ii) velocity-encoded only (i.e. [+], [+], [+]), (iii) view-sharing
PC-MRI, and (iv) SVE (i.e. [+ -], [- +], [+ -]) PC-MRI methods. The numerical
vessel phantom and predefined hemodynamic properties were generated using Matlab software (MathWorks, Inc., Natick, MA.). The blood-velocity spatial profile, which was chosen to mimic normal laminar physiological flow, was defined as a parabolic curve (i.e. a maximum value at the center of parabolic curve and a zero value at the vessel boundary). For the purpose of simplicity, this simulation model does not include distensibility of the vessel wall. The predefined flow-vs-time profile was chosen as of the positive half of a sinusoidal function spanning one third of a cardiac cycle as shown in Figure 4.7.

All simulations were performed with the following simulation condition: a k-space matrix of 128 x 60, echo-planar readout with echo-train-length of 15, four shots (60 acquired lines) per image, repetition time (TR) of 13.8 ms, echo time of 5.6 ms, effective temporal resolution of 55 ms and echo-spacing of 0.56 ms. The region of interest, which is the vessel lumen with predefined flow profile, consists of 4 pixels. No parallel acceleration method was implemented in order to avoid undesired artifacts resulting from parallel imaging reconstruction. For the purpose of simplicity, we ignored the flow variations during the acquisition of each k-space line because negligible flow
changes are assumed within such a short period. However, we do consider the short-term flow changes that occur between k-space lines. The minimal temporal step of the simulated flow profile was chosen to match the duration of echo-spacing (0.56 ms). The average cardiac cycle (RR interval) was set to 784 ms which corresponds to 1400 defined temporal points on the flow curve. The flow results obtained using each of the three algorithms considered in the study were investigated. Qualitative assessment of the accuracy of peak flow and total flow volume measurements were conducted by comparing reconstructed flow curves to the simulated flow profiles.

4.2.2 Simulation Results and Discussions

The velocity curves computed from four phase-contrast reconstruction methods are shown in Figure 4.7. In Figure 4.7, as expected, the velocity-encoded only method demonstrates the best fidelity to characterize the predefined flow curve and the value of peak flow because it has the highest temporal sampling rate (56 msec) and no temporal averaging comparing to other methods. In an actual MRI acquisition, however, the background phase variations which we do not include in this model are inevitable and would seriously affect the accuracy of flow measurements. Conventional FL-FQ
PC-MRI with alternating velocity-encoded and velocity-compensated k-space may not accurately detect the value of peak flow because of its insufficient temporal sampling rate and temporal gaps between velocity encoded acquisitions. Echo-sharing PC-MRI effectively doubles the reconstructed frame rate, which is essential to detect short-term velocity variation in clinical routines, compared to conventional FL-FQ. The proposed SVE method acquires as many temporal sampling points as the velocity-encoded only method; that is, the effective temporal resolution of SVE is equivalent to the true temporal resolution of the velocity-encoded only method. However, as previously described, each temporal data point of SVE consists of data acquired over two frames. The maximal value of peak velocity may be suppressed due to the effect of averaging across frames.
Temporal sampling plays a key role in determination of peak velocity, a key physiological parameter with significant clinical relevance. With the relatively coarse sampling of real-time imaging, sharp peaks in the velocity waveform may fall between temporal samples causing an underestimation of peak velocity. Furthermore, the heart rate is variable and in the case of real-time imaging, data acquisition is not synchronized with cardiac cycle. The peak velocity observed in each cardiac cycle might fluctuate due to the asynchrony of temporal sampling. In other words, observed beat-to-beat fluctuations in
peak velocity may not be real; they may instead be caused by the combination
of sparse sampling and asynchrony of the acquisition with respect to the
cardiac cycle. Therefore, we conducted another numerical experiment in
order to understand the relationship between the accuracy of peak velocity
detection and temporal sampling. Figure 4.8 shows the peak velocity
measurement results obtained over a range of temporal shifts of data samples
within one cardiac cycle using previous four reconstruction methods. Across
the range of temporal shifts, the maximum peak velocity measured by the
conventional FL-FQ PC-MRI and the velocity-encoded only PC-MRI should be
the same if the acquisition covers enough cardiac cycles; the expectation is
that peak velocity will be sampled in at least one of the heartbeats if enough
beats are sampled. The SVE and echo-sharing PC-MRI method, on the other
hand, effectively average velocity over two time samples and is expected to
smooth out sharp peaks. However, the peak velocity measurement of
conventional FL-FQ PC-MRI shows greater fluctuation (i.e. as a function of
temporal shift) that because the sampling rate of the conventional FL-FQ
PC-MRI is effectively 50 percent lower than SVE and echo-sharing PC-MRI.
Thus, conventional PC-MRI encoding is expected to show greater variability in
peak velocity measurements than SVE, especially if only a few cardiac cycles
are sampled. SVE, on average, will provide a more consistent measurement of peak velocity with less potential for large errors, although it will consistently underestimate sharp peaks.

Figure 4.8: Temporal sampling phase shift vs. peak flow result from (i) conventional FL-FQ PC-MRI with velocity-encoded and velocity-compensated sensitivities, (ii) velocity-encoded (FE) only, (iii) Echo-sharing PC-MRI, (iv) SVE PC-MRI methods, and (v) predefined flow profile

Total flow volume, which is the time integral of flow within one cardiac cycle, is another important clinical parameter measured using PC-MRI. As shown in Figure 4.9, the temporal integral of the flow for the three PC-MRI acquisition/reconstruction methods are also a function of the temporal
sampling phase. Conventional FL-FQ PC-MRI shows a larger fluctuation because of its lower sampling rate. The velocity-encoded only PC-MRI and the SVE methods show exactly the same curve because SVE uses a sliding window average of velocity-encoded only PC-MRI. Therefore, it does not change the temporal mean. This result indicates that the SVE method will provide greater accuracy in measurement of volume flow than conventional PC-MRI reconstruction. While the peak-velocity measurement obtained by echo-sharing was very similar to that achieved by SVE (Figure 4.8), echo-sharing significantly underestimates the volume flow compared to SVE (Figure 4.9). The echo-sharing scheme simulated here did not incorporate additional central k-space lines, a strategy that would help to alleviate the inaccuracy in volume flow shown here. However, as mentioned in the previous section, the acquisition of additional central lines would significantly degrade the temporal resolution in real-time PC-MRI using segmented EPI readout.
4.2.3 Conclusions

The result from the numerical simulation demonstrates the proposed SVE method has a capability to improve effective temporal resolution while maintaining the accuracy of velocity and flow measurements. As previously mentioned, each temporal-phase image should possess a unique center line of k-space to differentiate velocity information from the adjutant temporal-frame. Therefore, appropriate choices of echo-train-length and
view-per-segment of EPI protocol is required for velocity measurement using EPI and SVE method.

4.3 FLOW PHANTOM STUDIES

4.3.1 Flow Phantom Introduction and Methods

As previously described in section 4.2, the numerical simulation of the conventional FL-FQ PC-MRI and proposed SVE methods demonstrate a factor of two effective improvement in temporal resolution and offers an important capability to detect the peak flow-velocity of MR velocity measurements. A pulsatile flow phantom experiment is conducted in this section to provide an in-vitro validation for the proposed SVE method comparing to current standard approaches.

In-vitro validation experiments were run using a pulsatile flow phantom to compare the results of standard FL-FQ PC-MRI with the SVE method. Two MR flow measurements were performed on a pulsatile flow phantom: (i) conventional segmented FL-FQ PC-MRI and (ii) segmented SVE. A static bottled water phantom doped with 1.25g NiSO$_4$ + 6 H$_2$O and 5g NaCl per 1000g water was placed with its long-axis along the z-axis in the isocenter of
the magnet. Two tubes with inside diameter of 3/8 inch were aligned with the z-axis of the magnet before they were connected to a flow pump. A single dose (0.1 mmol/kg) of Gd-DTPA contrast agent was doped in water to shorten T1 and minimize the T1 effects of incoming unsaturated spins. Thus, a static water phantom and two tubes with water flowing in opposite directions were included in the constant flow experiments.

For the pulsatile flow experiments, pulsatile flow resembling arterial flow was created by a constant flow pump (Figure 4.10, Commodity Axis, San Gabriel, CA), a mechanical valve (Figure 4.11, Ehcotech, Inc, Prescott, AZ), and a wave function generator (Figure 4.12, TekNet Electronics, Inc, Alpharetta, GA). In Figure 4.13, the schematic experiment layout is provided to describe the order and role of each hardware component in the pulsatile flow phantom.
Figure 4.10: Constant flow pump (Commodity Axis, San Gabriel, CA),
Figure 4.11: Mechanical valve (Ehcotech, Inc, Prescott, AZ)

Figure 4.12: Wave function generator (TekNet Electronics, Inc, Alpharetta, GA)
Figure 4.13: Schematic diagram of the pulsatile flow phantom experiment design

The basic concept in mimicking pulsatile flow is to control the desired pattern of open and closed stages of the mechanical valve in order to create the pulsatile flow pattern. The open and closed stages of the mechanical
valve are controlled by an input signal generated from the wave function generator. Thus, the customized pulsatile flow is created by adjusting the signal frequency and duration from the mechanical valve and the wave function generator. The generated wave signal is directed into the MR console system as an external signal for triggering MR acquisition. The imaging acquisition parameters performed in pulsatile flow experiments are listed as follows: FOV = 300 mm x 165 mm, flip angle = 25°, spatial resolution = 1.6 x 2.7 mm², VENC = 120 cm/s, echo time = 3.5 msec and repetition time = 7.3 msec.

4.3.2 Flow Phantom Results

In this pulsatile phantom study, we conducted a qualitative comparison and quantitative accuracy assessment on reconstructed flow curves. First of all, we compared reconstructed flow-velocity from conventional segmented FL-FQ PC-MRI (solid triangles ▲) and SVE method (hollow diamonds ◇), as shown in Figure 4.14. Pulsatile flow phantom results of the SVE method shows additional temporal-velocity information is extracted in the intermediate temporal point of phase-velocity time course. Thus, SVE demonstrates the expected twofold increase in effective temporal resolution compared to
conventional FL-FQ PC-MRI without any increase in scan time. Furthermore, the short-term flow change and the value of peak velocity are detected by improving the effective temporal resolution.

For the purpose of accuracy assessment on flow measurement, a non-segmented, high temporal resolution FL-FQ PC-MRI measurement was acquired and considered to be the gold standard flow measurement and all segmented PC-MRI methods were compared flow result from the gold standard. To investigate the accuracy of velocity measurements, the
Root-Mean-Square (RMS) error was calculated between the flow-velocity curves obtained using segmented FL-FQ PC-MRI and SVE techniques comparing to gold standard non-segmented acquisition. RMS error measurements shows a significant RMS error of 4.32 cm/sec between conventional segmented FL-FQ PC-MRI, while negligible RMS errors (2.24 cm/sec) between segmented SVE method. However, phase-velocity data points from non-segmented (i.e. high sampling frequency) show similar results compared with the SVE method except for high acceleration time points.

This section demonstrates the potential application of Shared Velocity Encoding (SVE) in the local pulse wave velocity measurement to improve the effective temporal resolution of non-segmented phase-contrast MRI (PC-MRI) without increasing scan time. With the SVE method, preliminary results indicate that local pulse wave velocity (PWV) measurement by PC-MRI may be practical in the common carotid arteries.

4.4 Demonstration of SVE for Carotid Artery Pulse Wave Velocity

4.4.1 Introduction

The stiffness and thickness of carotid arteries are known clinical indicators
of atherosclerosis and cerebrovascular disease (106-109). PWV measured by PC-MRI (110-112) provides a non-invasive method to estimate arterial stiffening that corresponds to the early stage of atherosclerosis. As we mentioned in Chapter 2, conventional PC-MRI requires either a pair of velocity-encoded and velocity-compensated datasets (70), or a pair of equal and opposite polarity velocity-sensitized k-space datasets (113). Phase-difference reconstruction is performed on each complex data pair to eliminate any residual non-zero phase variation due to effects other than velocity, such as eddy currents, gradient imperfection and field inhomogeneity. As a result, conventional MR velocity mapping requires twice as much data as standard MRI scans; this requirement either degrades temporal sampling rate by a factor of two, or doubles the acquisition time to maintain the sufficient temporal resolution. Echo-sharing methods are commonly employed to improve the effective temporal resolution in segmented k-space scans (86). However, estimation of local PWV in short sections of central or peripheral arteries requires extremely high temporal resolution for differentiation of short transit time-delays between the pulse waves measured at points separated by short distances.
The temporal resolution requirements for local PWV measurements are beyond those achievable with k-space segmentation, and even higher than those attainable with conventional, non-segmented PC-MRI acquisition. The aim of this section is to demonstrate the application of SVE reconstruction to improve the effective temporal resolution of non-segmented PC-MRI. The SVE method is demonstrated in the local PWV measurement of common carotid arteries in one subject to show improved effective temporal resolution over conventional PC-MRI with no prolongation of the MRI scan time.

4.4.2 Materials and Methods

The SVE method was evaluated in one healthy volunteer on a 1.5 T Avanto system (Siemens Healthcare, Inc. Erlangen, Germany) with head and neck phased-array coils and prospective ECG signal gating. In-plane MR velocity measurements were performed in the carotid artery using (i) a conventional non-segmented PC-MRI sequence with velocity compensated/encoded gradients and (ii) non-segmented PC-MRI with bipolar VENC and SVE reconstruction. Image acquisition parameters were as follows: TE/TR = 4.4/7.4 ms, flip angle = 15°, FOV = 350 mm x 263 mm, slice thickness = 8mm,
acquisition matrix = 192 × 144, two signal average, VENC = 120 cm/s and acquisition time < 3 minutes in the frequency-encoding direction (head-to-foot).

After obtaining a series of dynamic velocity maps from different time points within cardiac cycle, local PWV can be estimated by measuring the difference in arrival time of the velocity pulse wave at two or more locations separated by known distances along an artery. The quotient of distance over pulse wave transit time represents the estimated PWV over the measured length of vessel. The precision of the PWV measurement is determined by the temporal sampling frequency relative to the difference in arrival times.

4.4.3 Results

In vivo images from one healthy volunteer are shown in Figure 4.15. Conventional PC-MRI resulted in an effective temporal resolution of 14.8 msec per image, yielding 53 phases over the cardiac cycle. Bipolar velocity encoding with SVE reconstruction was used to reconstruct nearly twice as many (105) frames at an effective temporal resolution of 7.4 msec. The two regions of interest (ROIs) separated by 5 cm shown in blue and green in Figure 4.15b were used for local PWV estimation in the common carotid artery.
Figure 4.15: Carotid MRI magnitude and phase-contrast images. (a) Magnitude and (b) phase images obtained using the proposed SVE reconstruction method with velocity-encoded in head-to-foot.

Figure 4.16a illustrates the velocity profiles in the two ROIs obtained using conventional PC-MRI; the velocity profiles resulting from SVE reconstruction are shown in Figure 4.16b. Scan times were the same for the conventional and SVE acquisitions. This gives a velocity profile with more points (Figure 4.16b), enabling a more accurate estimate of the pulse arrival time. Figures 4.16b shows greater separation of the two velocity waveforms as a result of the higher temporal resolution, yielding an estimated PWV of 3.2 m/sec, within the expected normal range. Conversely, the pulse wave arrival times are
barely distinguishable in Figure 4.16a at the lower temporal resolution of the conventional PC-MRI scan, making accurate PWV estimation impossible.

Figure 4.16: Carotid pulse-wave velocity measurement using the conventional and proposed SVE reconstruction method. (a) Common carotid artery velocity curve from conventional velocity compensated/encoded PC-MRI (b) carotid velocity curve using SVE reconstruction to yield a factor of 2 increase in the number of sample points.

4.4.4 Conclusions

SVE reconstruction results in a factor of 2 improvement in the effective temporal resolution of non-segmented PC-MRI with no increase in scan time. Preliminary data demonstrates that non-segmented PC-MRI with SVE reconstruction provides sufficient temporal resolution to evaluate PWV in the common carotid artery and suggests that estimation of the local mechanical properties of an artery is feasible. The accuracy of any velocity measurements should be improved by the additional temporal sample points.
available to characterize the velocity waveform. In the future, we plan to apply SVE to assess local mechanical properties in central and peripheral arteries and extend the method to segmented and real-time acquisitions.

4.5 SUMMARY AND CONCLUSIONS

In this chapter, we developed a novel phase-contrast reconstruction that uses alternating polarity velocity-sensitized gradients to extract velocity information from the conventional PC-MRI method. The phase-contrast results are not only reconstructed from each consecutive pair of [+ -] velocity encoded datasets, but also from intermediate pairs of [- +] velocity encoded datasets. Numerical simulation and in-vitro pulsatile phantom studies demonstrate that SVE method provides an improvement of temporal resolution that impacts the accuracy of peak velocity and volume flow measurements without increasing scan time.

View-sharing, which uses a similar concept of temporal averaging, has been proposed to improve the accuracy of ventricular volume estimation and effective temporal resolution in phase-contrast imaging in 1995 (86). However, intermediate k-space data is shared and reconstructed from two
temporally adjacent k-space date pairs. As a result, view-sharing method improves the effective temporal resolution that deteriorates by the segmented k-space technique. However, segmented echo-sharing technique loses its capability in some applications, such as non-segmented velocity measurements. For example, estimation of local pulse wave velocity in short sections of central or peripheral arteries requires extremely high temporal resolution for differentiation of short transit time-delays between the pulse waves measured at points separated by short distances. The SVE method has a unique advantage over echo-sharing in non-segmented PC-MRI acquisitions demanding extremely high temporal resolution, such as estimation of pulse wave velocity. We presented a preliminary study on non-segmented PWV measurement using SVE method in this chapter.

Before we move to real-time velocity measurement by using PC-MRI, we will discuss the effect of off-resonance artifact in steady-state free precession and echo-planar imaging sequence in next chapter. Off-resonance artifacts, which are often caused by fat protons that resonate at a different frequency (-3.5 ppm) from water protons, is a major limitation that restricts the use of segmented EPI real-time flow imaging. Thus, we will propose the rapid
phase-modulated water-excitation method that can acquire a fat-suppressed MR cine without distributing steady-state equilibrium that is not only applicable to PC-MRI, but also in all types of gradient-echo and steady-state MR sequences.
CHAPTER 5

RAPID PHASE-MODULATED WATER-EXCITATION FOR

FAT-SUPPRESSED CINE MRI

Echo-planar imaging (EPI) is an ultra-high-speed MRI method that is capable of producing snap-shot MR images in the ranges of 10-100 msec. Recently, EPI sequence has been used in attempts to acquire real-time cardiac cine images in a standard MR scan. Consequently, we propose to utilize the advantage of high acquisition speed of EPI combining with the phase-contrast magnetic resonance imaging (PC-MRI) method to achieve real-time velocity measurement in the major vessels. However, chemical shift artifacts resulting from the off-resonance effect of fat spins limit the use of long echo train length, which compromises acquisition speed of the EPI method. The artifacts occur because spins accumulate phase shifts,
especially in the later echoes, under the EPI readout gradient. The general problem of off-resonance artifacts appeared not only in EPI but also in all variations of the steady-state free precession (SSFP) sequence. Since the EPI sequence acquires numerous echoes within the repetition time period, the multiple readout strategy of EPI sequence typically causes off-resonance artifacts and other image artifacts, such as shape distortion and ghosting artifacts. For the purpose of simplicity, we first develop and evaluate a fat-suppression method in the SSFP cine sequence, which is the most widely used sequence in the cardiovascular MRI scan. Secondly, the EPI cine scan is performed with proposed fat-suppression method on the patient study in this chapter and phase-contrast real-time velocity mapping in chapter 6.

This chapter proposes a rapid phase-modulated water-excitation method that provides fat-suppressed MR images both in EPI and SSFP sequences. With the development in the rapid phase-modulated water-excitation technique, the fat-suppressed SSFP and EPI with longer echo train length become practical and beneficial in cardiovascular imaging applications.
5.1 INTRODUCTION

Suppression of bright fat signal is important in a variety of cardiovascular magnetic resonance applications to characterize lesions, suppress chemical shift and motion artifacts, and distinguish fluid or tumor from adipose tissue. Numerous techniques such as chemical shift selective pre-saturation (CHESS) (114,115), short tau inversion recovery (STIR) (116,117), and the multi-point Dixon method (118) have been developed to provide suppression of signal from normal adipose tissue. These techniques all have limited success when applied to SSFP and EPI imaging as they disturb the steady-state equilibrium and/or prolong repetition time (TR) and acquisition time. A number of recent articles describe fat suppression methods designed to maintain the magnetization steady-state in SSFP imaging (119-127). Scheffler (126) first proposed a method of interleaving spectral fat-saturation pulses within the SSFP acquisition, utilizing an $\alpha/2$ flip-back pulse to store the established steady-state magnetization prior to each fat suppression pulse. While successful, this method is incompatible with cine MRI that requires continuous data acquisition without interruption. Reeder (125) proposed a water-fat separation method using an “iterative decomposition of water and fat with echo asymmetry and least squares estimation” (IDEAL) which decomposes
cine-SSFP images into separate water and fat images. IDEAL requires acquisition of three complete datasets and a longer TR, nearly tripling image acquisition time and increasing sensitivity to off-resonance artifacts. Hardy (120) proposed a method of maintaining an uninterrupted, fat-suppressed steady-state by cycling the SSFP RF-excitation pulse amplitude through a repeating binomial pattern. This approach utilizes the principle of binomial water-excitation (128), modulating the excitation pulse amplitudes to create a broad band of signal suppression centered on the fat frequency. However, Hardy’s technique required additional TR’s and a significant increase in total acquisition time. The method of alternating-TR (ATR-SSFP) proposed by Leupold (122) arrives at a similar pulse sequence design to that which we propose, but with differences in concept and in sequence design constraints that will be discussed.

A simple, practical method for spectrally and spatially selective water-excitation (WE) based on binomial pulse design (128) has been used in combination with spoiled gradient echo imaging for several years. Binomial water-excitation has been applied to abdominal and orthopedic MRI (129-131), and more recently to cardiac MRI (132) providing advantages of no disruption
of the steady-state and uniform fat-suppression. More recently, binomial water-excitation has been combined with 3D SSFP for orthopedic imaging (133). In this chapter, we combine a rapid phase-modulated binomial water-excitation pulse with SSFP for fat-suppressed cardiac cine imaging. Our hypothesis is that sufficient fat signal suppression can be achieved with minimal impact on TR, sensitivity to flow artifact, total scan time, and cine-SSFP image quality using rapid binomial water-excitation RF pulses.

While the combination of binomial WE with SSFP has similarities with the methods proposed by both Hardy (120) and Leupold (122), our design strategy removes the necessity for any additional data acquisition or constraints on the relationship between the TR and the WE pulse timing. Numerical simulation, phantom and healthy volunteer imaging trials were performed to provide experimental validation of the fundamental concepts and performance of WE-SSFP, and images in one patient are shown to demonstrate a potential clinical application.

5.2 MATERIALS AND METHODS

5.2.1 Phase-Modulated Water-Excitation

Spectral-spatial WE can be achieved using a spatially-selective RF pulse
train with flip angles following a binomial series (1-1, 1-2-1, 1-3-3-1, etc.) (128). Increasing the number of component pulses and therefore the order of the binomial pulse improves spectral selection, but at the expense of total RF pulse duration. The simplest binomial pulse (1-1) consists of two $\alpha^\circ$ pulses with inter-pulse delay ($\tau$) chosen to allow $180^\circ$ of phase evolution between water and fat spins ($\tau = 2.2$ ms at 1.5 Tesla). The first pulse rotates both fat and water magnetization toward the transverse plane. After time $\tau$, fat and water spins are $180^\circ$ out of phase and the second pulse, identical to the first in both amplitude and phase, tips water protons further down towards the transverse plane while tipping fat protons back up to the longitudinal axis. This pulse combination effectively reverses the initial excitation of fat and the resultant tip angle for water is the sum of the individual component pulse angles. In SSFP applications, it is critical to keep the total RF pulse duration as short as possible to avoid lengthening the repetition time. Rather than waiting for $180^\circ$ of phase evolution between component pulses, phase-modulated water-excitation employs a partial ($< 180^\circ$) off-resonance phase evolution to shorten the combined binomial pulse duration (134). The phase of the second RF pulse is set to tip the fat magnetization back up to the longitudinal axis and also provides some additional tip down of water. This
strategy of “phase-modulated water-excitation” was used to design a minimum time spatial-spectral selective binomial pulse for combination with cine-SSFP. Figure 5.1 shows a SSFP sequence utilizing a simple 1-1 binomial slice-selective RF pulse with 1.1 msec inter-pulse spacing to allow 90° of fat-water phase evolution (1-(90°)-1). This was found to be the minimum inter-pulse spacing necessary to accommodate the standard apodized-sinc RF pulses (600 μsec duration) used for cine-SSFP on our 1.5T MRI system (MAGNETOM Avanto, Siemens Healthcare, Inc., Erlangen, Germany).

Figure 5.1: Pulse sequence diagram for phase-modulated, binomial 1-(90°)-1 water-excitation cine-SSFP. The two consecutive αº flip angle, selective RF pulses with 90° phase increment results in an inter-pulse delay of τ =1.1msec for water-only excitation. Note that all gradients are fully balanced on all axes to maintain the coherent
The performance of three different binomial water-excitation pulses were investigated by numerical simulation, imaging studies of water and fat phantoms, and normal volunteer imaging. Four pulses were compared: (a) conventional slice-selective apodized-sinc RF pulse, (b) spectral-spatial binomial 1-(180°)-2-(180°)-1 WE pulse with 180° phase evolution (inter-pulse delay = 2.2 msec), (c) spectral-spatial binomial 1-(180°)-1 WE pulse with 180° phase evolution (inter-pulse delay = 2.2 msec), and (d) spectral-spatial binomial 1-(90°)-1 phase-modulated WE pulse with 90° fat-water phase evolution (inter-pulse delay = 1.1 msec), and 90° phase offset between the two pulses in the 1-1 pair. The same RF pulse envelope with duration of 600 μsec was used for all individual component excitation pulses. The effective flip angle is defined as the total flip angle for on-resonant water spins. All RF pulse design and acquisition parameters are provided in Table 5.1.

5.2.2 Numerical Simulations

Simulations were run to predict the variation of steady-state transverse magnetization with chemical shift for the SSFP sequence in combination with the four different excitation pulses. All simulations were performed with the
following simulation parameters: TR = 9.68 msec, TE = 4.8msec, Flip angle = 70° for the conventional SSFP and all WE-SSFP sequences; relaxation time constants of simulated water (T₁ = 578 msec, T₂ = 263 msec) and fat (T₁ = 252 msec, T₂ = 81 msec) were chosen to match the fat/water phantom. The TR was chosen to match that used in phantom studies of pulse sequence frequency response. Analytic expressions for the resulting rotation matrices and magnetization distributions were generated using Mathematica (Wolfram Research, Inc., Champaign, IL).

5.2.3 Pulse Sequence Implementation

WE-SSFP cine sequences using each of the four pulse designs were implemented on a 12-channel, 1.5 Tesla MR system (MAGNETOM Avanto, Siemens Healthcare, Inc. Erlangen, Germany) with 45 mT/m gradient amplitude and 200 mT/m/msec maximum slew rate. Phantom and human imaging studies were performed using twelve array coil elements.

Table 5.1 shows the MR imaging parameters used for phantom and human volunteer studies. A 2D SSFP cine with retrospective ECG-gating was used with an effective 70° total flip angle, 5-mm section thickness, a
256x192 acquisition matrix, 350x262mm FOV, one signal average, and parallel acquisition acceleration rate of 2 using "Generalized Autocalibrating Partially Parallel Acquisitions" (GRAPPA). These imaging parameters were held constant throughout all phantom and human imaging experiments. In fat/water phantom studies the TR was held constant at 8.9 msec, the TR required by the longest (1-2-1) RF pulse, in order to minimize differences in off-resonance effects among the four sequences. In human imaging experiments, the TR was set to the minimum permitted by each sequence in order to illustrate the benefits of minimizing the RF pulse duration. The shortest water-excitation pulse, 1-(90°)-1, was also tested at longer TR values to demonstrate the independence of fat suppression to choice of TR, and the loss of image quality and increased flow sensitivity were resulted of longer TR.
### TABLE 5.1

Summary of imaging parameters for phantom and *in-vivo* studies

<table>
<thead>
<tr>
<th>Sequences</th>
<th>Interpulse Phase Evolution (°)</th>
<th>Interpulse Delay (msec)</th>
<th>Total Pulse Duration (msec)</th>
<th>TR for Phantom Studies (msec)</th>
<th>TR for <em>in-vivo</em> Studies (msec)</th>
<th>Component Pulse Flip Angles (°)</th>
<th>Resultant Flip Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard SSFP</td>
<td>N/A</td>
<td>N/A</td>
<td>0.6</td>
<td>9.68</td>
<td>3.1</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>1-2-1 WE-SSFP</td>
<td>180</td>
<td>2.2</td>
<td>5.0</td>
<td>9.68</td>
<td>8.9</td>
<td>17.7 - 35.4 - 17.7</td>
<td>70</td>
</tr>
<tr>
<td>1-1 WE-SSFP</td>
<td>180</td>
<td>2.2</td>
<td>2.8</td>
<td>9.68</td>
<td>6.5</td>
<td>35.4 - 35.4</td>
<td>70</td>
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<tr>
<td>1-1 WE-SSFP</td>
<td>90</td>
<td>1.1</td>
<td>1.7</td>
<td>9.68</td>
<td>4.0</td>
<td>56.4 - 56.4</td>
<td>70</td>
</tr>
</tbody>
</table>

* NA: not applicable
5.2.4 Phantom Imaging Studies

The first phantom study was performed on a uniform spherical water phantom doped with 1.25 g NiSO$_4$ + 6 H$_2$O and 5g NaCl per 1000g water. This phantom was imaged with an applied constant gradient offset of 0.0723 mT/m in the x-direction (left-right) to demonstrate the effect of each of the four excitation pulses on the frequency response of the cine-SSFP sequence. Images were acquired using all four pulse designs and signal profiles were measured in the direction of the applied field inhomogeneity to illustrate the frequency response and compare to the simulation results. TR was kept constant at 9.68 msec across the four sequences to maintain spacing of banding artifacts for comparative purposes.

The second phantom experiment was performed using water and mineral oil phantoms (T1/T2 of water = 578/263 msec and T1/T2 of oil = 252/81 msec) to measure the ratio of fat to water signal amplitude for each pulse and compare to the expected values based on simulation results. The regions of interest (ROI) measured in the phantom images were the maximum size permissible within the boundaries of the object. The SSFP sequence was tested using the shorted TR allowed by each excitation pulse scheme.
Additionally, the shortest phase modulated 1-(90°)-1 pulse was tested at a range of shorter TR’s to demonstrate the independence of fat suppression from the choice of TR.

5.2.5 Human Subject Imaging Studies

Conventional cine-SSFP and three different WE-SSFP sequences were evaluated in six healthy volunteers (1 women; aged 46 years, and 5 men; aged 22-57 years, with a mean age of 43.25±13.72) with no history of common cardiovascular disease. Vertical and horizontal long-axis views were acquired in each subject using each of the four sequences. The phase modulated 1-1 WE-SSFP and WE-EPI sequences were also tested in one 42 year-old male patient referred for CMR to characterize a cardiac mass seen on echocardiography. All images were acquired using electrocardiographic signal gating and breath-holding. Standard system shimming was used with each of the four different excitation pulses. No patient-specific or volume-localized shimming was performed. The default shim values based on field homogeneity in a uniform spherical phantom were used for all in-vivo studies. All subjects gave written informed consent to participate in this Institutional Review Board-approved protocol.
One observer measured the signal amplitude in the myocardium and fat and the in all cine series acquired in normal subjects. Measurements were made in a single, end-diastolic frame from each of the cine series acquired in the two different views using each of the four sequences. Circular ROI’s were placed within the myocardium of the left ventricular and surrounding fat to measure average signal amplitudes (SA). For consistency, similar anatomical regions were selected in all images. The signal amplitude ratio between fat and myocardium was calculated to evaluate the effect of fat suppression.

5.3 RESULTS

5.3.1 Numerical Simulations and Phantom Imaging Studies

Figure 5.2 shows the measured frequency response profiles for SSFP with each of the four different excitation pulses (Figures 5.2a-d).
Figure 5.2: A comparison of measured and simulated frequency response patterns for SSFP and WE-SSFP.

Top two rows demonstrate measured frequency response functions in a uniform water phantom for (a) conventional slice-selective RF pulse, (b) 1-(180°)-2-(180°)-1, (c) 1-(180°)-1, and (d) 1-(90°)-1. All four sequences were run with TR = 9.68msec and constant gradient offset of 0.0723 mT/m left-to-right to illustrate the signal over a range of offset frequencies. Middle row (e-h) shows the signal profile across the phantom for each of the corresponding images. The white line across (a) indicates the location of the signal profile measurement for each image. Bottom row (i-l) shows simulated frequency response functions for the same four sequences used to generate the phantom images (a-d) and signal profiles (e-h). Reasonable agreement is observed between phantom measurements and simulation results.
Signal profiles measured along the direction of intentional linear field inhomogeneity are shown (Figures 5.2e-h) along with the results of computational Bloch equation simulations (Figures 5.2i-l) for comparison. For the conventional SSFP sequence (Figures 5.2a, e and i), if TR is set exactly to 2.2 msec + n*4.4 msec (i.e., 2.2 msec, 6.6 msec, 11.0 msec, etc.), a null will be centered over the fat resonance while leaving a broad plateau over the water peak. However, this null is too narrow to suppress fat reliably. The 1-(180°)-2-(180°)-1 (Figures 5.2b, 5.2f, 5.2j), 1-(180°)-1 (Figures 5.2c, 5.2g, 5.2k) and 1-(90°)-1 (Figures 5.2d, 5.2h, 5.2l) binomial pulses all broaden the fat resonance stop-band and maintain the on-resonance pass-band. The measured frequency responses shown in Figures 5.2e-h correspond with the numerical Bloch Equation simulation results (Figures 5.2i-l) demonstrating the widened stop-band centered on the fat resonance. The higher signal seen in the center of the phantom is commonly observed and is due to uneven distribution of RF energy. The simulated frequency response profiles in Figure 5.3 demonstrates that the stop band frequency of the 1-(90°)-1 binomial pulse is centered on the fat frequency independent on the choice of TR.
Figure 5.3: A comparison of simulated frequency response patterns for 1-(90°)-1 WE-SSFP with (a) TR = 8.9ms (b) 2/3 TR and (c) ½ TR conditions. Central stopband frequency falls near the fat frequency that indicates fat suppression of 1-(90°)-1 WE-SSFP is independent of sequence TR.
Phantom fat/water images presented in Figure 5.4 show that all tested binomial WE pulse combinations suppress the fat signal and maintain the signal amplitude of water. Phantom images obtained from the conventional slice-selective RF pulse (Figure 5.4a), 1-(180°)-2-(180°)-1 (Figure 5.4b), 1-(180°)-1 (Figure 5.4c), and phase-modulated 1-(90°)-1 (Figure 5.4d-f) WE-SSFP cine sequences show successful suppression of the fat (baby oil) signal by all binomial WE pulses. The resulting phantom image signal measurements listed in Table 5.2 demonstrate that the phase-modulated 1-(90°)-1 WE pulse significantly decreased the fat to water signal ratio over a range of TR’s. (Figure 5.4 and Table 5.2).
Figure 5.4: Fat/water phantom images acquired with (a) conventional slice-selective RF pulse with TR = 8.9 msec, (b) 1-(180°)-2-(180°)-1 with TR = 8.9 msec, (c) 1-(180°)-1 with TR = 8.9 msec, and (d) 1-(90°)-1 with TR = 4.0 msec, (e) 1-(90°)-1 with TR = 5.0 msec, (f) 1-(90°)-1 with TR = 5.6 msec. WE-SSFP cine sequences show successful suppression of the fat (mineral oil) signal with maintained steady-state water signal for all binomial WE pulses.
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<th>Sequences for Fat/water Studies</th>
<th>Interpulse Phase Evolution (°)</th>
<th>Interpulse Delay (msec)</th>
<th>TR (msec)</th>
<th>Water Signal</th>
<th>Fat Signal</th>
<th>SA Ratio**</th>
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<td>Standard SSFP</td>
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<td>8.9</td>
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<tr>
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<td>40 ± 11.2</td>
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<tr>
<td></td>
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<td>5.6</td>
<td>726 ± 20.8</td>
<td>39 ± 10.4</td>
<td>0.054</td>
</tr>
</tbody>
</table>

* NA: not applicable
** SA ratio: signal amplitude between fat and water: $\frac{S_{\text{Fat}}}{S_{\text{Water}}}$
5.3.2 Human Subject Imaging Studies

A conventional cine-SSFP image is shown in Figure 5.5a along with results from the 1-(180°)-2-(180°)-1 (Figure 5.5b), 1-(180°)-1 (Figure 5.5c), and the phase-modulated 1-(90°)-1 pulse (Figure 5.5d). These images were acquired at the minimum TR permitted by each of the pulses. All binomial WE pulses show marked fat signal reduction compared to conventional cine-SSFP. The uniformity of fat suppression is best using the 1-(180°)-2-(180°)-1 pulse (Figure 5.5b), as expected since it has the broadest stopband as shown in the simulation and phantom results. However, severe field inhomogeneity artifacts and flow artifacts appear most likely because this lengthy excitation pulse requires an impractically long TR (8.9 msec). Artifacts are reduced in images acquired using the shorter TR possible with the 1-1 pulses with full (Figure 5.5c) or partial (Figure 5.5d) phase evolution. The phase-modulated 1-(90°)-1 pulse demonstrates an appreciable degree of fat suppression with only a 29% increase in TR (4.0 msec vs. 3.1 msec) without any noticeable artifacts due to flow or field inhomogeneity. Magnifications of the atrioventricular groove shown in the lower right corner of each image in Figure 5.5d demonstrate the successful suppression of epicardial fat by the phase-modulated 1-(90°)-1 excitation pulse. However, fat is not as uniformly
suppressed throughout the field-of-view as with the $1$-$\left(180^\circ\right)$-$2$-$\left(180^\circ\right)$-$1$ pulse (Figure 5.5b) due to the narrower stop-band demonstrated in Figure 5.2.
Figure 5.5: Cardiac images acquired in a normal human subject in four-chamber view using (a) conventional slice-selective RF pulse with TR = 3.1msec, (b) 1-(180°)-2-(180°)-1 with TR = 8.9msec, (c) 1-(180°)-1 with TR = 6.5msec, and (d) 1-(90°)-1 WE-SSFP sequences with TR = 4.0msec. Flip Angle/Slice Thickness/Matrix =70°/5mm/256x192 for all images. A magnified region is shown in the lower right corner of each image to illustrate the signal in epicardial fat surrounding the right coronary artery in the atrioventricular groove. Significant fat signal attenuation is demonstrated by all binomial WE pulses, and no perceptible artifacts are observed in the 1-(90°)-1 WE-SSFP images.
Figure 5.6 shows the lipid signal is well attenuated in all of the WE methods and artifact free images were generated by the phase-modulated 1-(90°)-1 cine-SSFP sequence in a vertical long-axis view of the heart of a second normal subject. Signal measurements of *in-vivo* studies demonstrated that phase-modulated 1-(90°)-1 WE-SSFP significantly reduces the fat-myocardium signal amplitude ratio from 6.92 ± 2.9 to 0.8 ± 0.13 with minimal increase in TR without inducing any perceptible artifacts.

In Figure 5.7, conventional cine-SSFP, 1-2-1, 1-1 and phase modulated 1-1 with a variety of TR’s from 4.0 to 5.6 msec are shown in a vertical long-axis view in a normal human subject. The consistency of fat signal attenuation demonstrates that fat suppressions with phase-modulated 1-(90°)-1 water-excitation is independent of TR.
Figure 5.6: Cardiac images acquired in a normal human subject in vertical long-axis view using (a) conventional slice-selective RF pulse with TR = 3.1msec, (b) 1-(180°)-2-(180°)-1 with TR = 8.9msec, (c) 1-(180°)-1 with TR = 6.5msec, and (d) 1-(90°)-1 WE-SSFP sequences with TR = 4.0msec. A magnified region is shown in the lower right corner of each image to illustrate the signal in epicardial fat surrounding the apex of the left ventricle. The phase-modulated 1-(90°)-1 WE-SSFP sequence decreases the fat to myocardium signal ratio and provides a valuable method of differentiating fluid from adipose tissue.
Figure 5.7: Cardiac images acquired in a normal human subject in horizontal long-axis view using (a) conventional slice-selective RF pulse, (b) 1-(180°)-2-(180°)-1, (c) 1-(180°)-1, (d) 1-(90°)-1 and TR = 4.0 msec. (e) 1-(90°)-1 and TR = 5.0 msec. (f) 1-(90°)-1 and TR = 5.6 msec. A magnified region is shown in the lower right corner of each image to illustrate the signal in epicardial fat surrounding the apex of the left ventricle. Fat suppression characteristics are seen to be independent of sequence T1.
Figure 5.8 shows images acquired in a 42 year-old male referred for cardiovascular MRI to characterize a large inter-atrial mass seen by echocardiography. The phase-modulated 1-(90°)-1 WE-SSFP suppressed signal in the mass (Figure 5.8b), which had a high signal in conventional cine-SSFP (Figure 5.8a), providing evidence supporting that the mass was a lipoma, precluding the need for further invasive diagnostic procedures.

In Figure 5.9, cardiac images were acquired in the same lipoma patient by EPI cine sequence. A single set of cine loop data appropriately covered the entire cardiac cycle. Consistent fat suppression with lipomatous tumor demonstrates the capability of rapid phase-modulated water-excitation technique in EPI cine sequence.
Figure 5.8: Single end-systolic frame from cine-SSFP series acquired without (a) and with (b) phase-modulated binomial water-excitation in a patient with large intracardiac lipoma. Note the significant suppression of signal in the mass in the WE-SSFP image (b), clearly indicating this as adipose tissue.
Figure 5.9: A loop of cardiac cine images using EPI cine sequence with phase-modulated binomial water-excitation in a patient with large intracardiac lipoma
5.4 DISCUSSION

We have shown that the simple combination of a phase-modulated 1-(90°)-1 water-excitation pulse together with cine-SSFP results in a fat-suppressed steady-state with only minimal increase in TR and overall scan time. This technique utilizes the frequency offset between fat and water spins and a binomial pulse design to effectively suppress the normally bright fat signal in cine-SSFP. As shown by Thomasson (134), the component pulse spacing in binomial water-excitation need not be restricted to the time necessary to allow 180 degrees of phase evolution between fat and water. By appropriate RF phase modulation, component pulse spacing can be shortened while maintaining sufficient fat-suppression. The resultant rapid water-excitation pulses incur only a minimal increase in TR, critical in cine-SSFP to avoid off-resonance banding and blood flow artifacts. Results in phantoms showed that the fat suppression achieved is similar to that predicted by the Bloch equation simulations (Figures 5.2 and 5.4). In-vivo results showed that this technique significantly reduced bright fat signal while maintaining SSFP (Figures 5.5, 5.6, 5.7 and 5.8) and EPI (Figure 5.9) image quality. Furthermore, Figures 5.2d and h shows a single-sided stop-band for the 1-(90°)-1 pulse at -220 Hz (i.e. the fat frequency) instead of the
double-sided stop bands at ±220 Hz (Figures 5.2b, f, j and 5.2c, g, k) demonstrated by the other WE pulses. The single-sided stop band may be an advantage as it is less likely to lead to suppression of water signal in case of field inhomogeneity. The frequency response profiles in Figure 5.3 demonstrated that the stopband frequency of the 1-(90°)-1 binomial pulse is independent on the choice of TR. Moreover, the 1-(90°)-1 pulse demonstrated consistent fat suppression ability of the different TR’s in water and mineral oil phantoms (Figure 5.4d-f). Phantom signal measurements showed consistent fat signal attenuation was achieved without restriction of TR.

Existing fat suppression methods that have been described for SSFP applications (120,121,123-126) are generally of limited use in breath-hold SSFP cine imaging because they entail prolonged acquisition time, increased TR, or disruption of the steady-state. WE-SSFP has significant similarities with the fat-suppressed alternating repetition time (FS-ATR) technique described by Leupold et al.(122). The difference between the techniques is primarily conceptual, and both have shown that fat suppression can be achieved while maintaining the steady-state with only a minimal (~ 30%) increase in TR.
Leupold describes a frequency response and fat suppression in terms of a new steady-state defined by the alternation of TR between excitation pulses that places certain restrictions on the relationship between the two TR’s. Specifically, Leupold states that a TR = 4.3 msec is necessary for fat suppression at 1.5T. However, he goes on to show that fat suppression can still be achieved to some degree while allowing TR to vary. Our approach instead recognizes that the water-excitation pulse can be defined as a phase-modulated 1-(90°)-1 binomial pulse pair independent of other imaging sequence parameters. Based on this, we provide a simplified description of the method that avoids unnecessary restrictions on the sequence design. The WE-SSFP technique described here imposes no specific restrictions on TR other than the usual SSFP requirement that TR<<T2, and no fixed relationship between TR and binomial pulse spacing. While TR must be increased to accommodate the binomial pulse length, the flexibility of choice in binomial WE pulse design and selection of imaging TR was demonstrated in the phantom and in-vivo results. Three different configurations of WE pulses and TR values ranging from 4.0 msec to 5.6 msec were shown. The time between the component pulses of the binomial pulse series can be flexibly chosen based on slice profile and gradient constraints, with the understanding...
that lengthening the overall TR can have adverse effects on SSFP image quality. Any increase in TR in SSFP increases sensitivity to field inhomogeneity and flow.

One important limitation of this phase-modulated 1-(90°)-1 WE method is that field inhomogeneities can cause non-uniform fat suppression. However, this is true of any frequency-selective fat suppression scheme. Our initial results in human subjects show sufficient homogeneity that these effects are not severe at 1.5T. The variability in fat suppression throughout the field-of-view observed in the in-vivo images acquired with different pulses may be due to a variety of factors. As shown in Figure 5.2, the frequency response pattern varies from pulse to pulse and also with TR. Since these are breath-hold images of a beating heart, there can be variation in position causing variation in local homogeneity from one scan to the next. All of these factors may contribute to the observed differences.

Another consideration is that phase-modulated 1-(90°)-1 WE increases specific absorption rate (SAR) at a given effective flip angle when compared to standard SSFP or binomial WE with 180° phase evolution. When 180° of
phase evolution is allowed, each component pulse fully serves to further tip the water signal towards the transverse plane. The total resultant flip angle is divided evenly between the two $\alpha^\circ$ pulses in a 1-(180°)-1 binomial pulse. However, in phase-modulated 1-(90°)-1 binomial WE, the tipping of water into the transverse plane is accomplished almost entirely by the first pulse, while the second pulse serves primarily to tip fat back up to the longitudinal axis. This is illustrated in Figure 5.10, which shows the resultant flip angle as a function of the individual component pulse flip angles for the 1-(90°)-1 pulse; the resultant flip angle is less than the sum of the flip angles of the component pulses. As a result, the SAR is increased relative to the conventional single pulse selective excitation. The ratio of SAR for the 1-(90°)-1 WE pulse to the SAR for the conventional single pulse is plotted in Figure 5.11. For example, the SAR is increased by about 20% (SAR ratio = 1.2) compared to the conventional pulse at an effective flip angle of 70°. This could be a significant limitation in the application of this technique at higher field strengths, although it could potentially be overcome by allowing longer phase evolution (greater delay time) between the component pulses. It would also be possible to lengthen the component RF pulses to reduce SAR without extending the total binomial pulse duration by using a bi-polar rather than mono-polar
slice-selective gradient waveform. By alternating the polarity of slice selection gradient pulses from one component pulse to the next, the additional gradient lobes required for refocusing can be eliminated. However, the gradient first moment and therefore velocity sensitivity are greatly increased, and preliminary testing of this type of pulse design resulted in increased flow artifacts.
Figure 5.10: (a) The on-resonance (water) flip angle that results from a given component pulse flip angle is shown for the 1-(90°)-1 WE pulse. (b) The SAR ratio of 1-(90°)-1 WE pulse compared to a conventional RF excitation of the same resultant on-resonance flip angle.

In conclusion, our results show fat suppression is feasible by the combination of phase modulated binomial water-excitation with cine-SSFP. It was found that a phase-modulated RF slice-selective pulse with phase evolution equal to 90° (1.1 msec interpulse delay) is sufficient to null fat signal while maintaining steady-state equilibrium for high SNR, insensitivity to off-resonance artifacts, and time-efficiency. Further testing is warranted to evaluate the effectiveness of this technique in clinical imaging.
With the development of rapid fat-suppression cine technique in this chapter and the shared velocity encoding reconstruction in Chapter 4, we will change our topic to the major goal of this dissertation, i.e. real-time velocity measurement, by implementing our proposed methods in next chapter.
CHAPTER 6

REAL-TIME MR VELOCITY MEASUREMENT USING A MULTI-SHOT
GRADIENT-ECHO PLANAR IMAGING SEQUENCE COMBINED WITH
SHARED VELOCITY ENCODING RECONSTRUCTION

We previously described the theory of the shared velocity encoding (SVE) method and demonstrated the improvement of the effective temporal resolution in phase-contrast magnetic resonance imaging (PC-MRI) using the SVE reconstruction in the application of the pulse wave velocity (PWV) measurement in Chapter 4. As previously mentioned in Chapter 2, real-time velocity measurement is an essential application that is currently restricted by its insufficient temporal sampling rate. Even with the use of current MRI gradient hardware and parallel acceleration methods, the requirement of PC-MRI for twice the data of standard cine acquisitions results in insufficient
temporal resolution in real-time applications. In this chapter, we demonstrate the potential capability of using the SVE technique for real-time velocity mapping by improving temporal resolution through the combination of segmented EPI readout and SVE reconstruction. In-vivo volunteer validations are provided to support the use of the proposed real-time PC-MRI method in cardiovascular applications.

6.1 CONVENTIONAL ECG-TRIGGERED SEGMENTED K-SPACE VS. REAL-TIME VELOCITY MEASUREMENT IN PHASE-CONTRAST MRI

Over the past two decades, cardiac MRI has been shown to successfully evaluate hemodynamics in the major vessels by means of electrocardiogram (ECG) triggered segmented k-space acquisition PC-MRI (135-137). Blood flow velocity data are acquired over several cardiac and respiratory cycles, resulting in time-averaged velocity waveforms representing a single composite cardiac cycle. Recently, attention has turned to monitoring blood-flow in real time to more accurately assess the short-term hemodynamic variations in flow (21,138). The major benefits of the real-time velocity measurement technique relative to the conventional ECG-triggered segmented acquisition method are that the real-time velocity technique is able to not only monitor
beat-to-beat variations in blood-flow in real-time, but perhaps even more importantly it enables acquisition of images that are insensitive to respiratory and cardiac motions. In a two-month retrospective study at our hospital, approximately 39% (75/190) of the breath-hold segmented cine studies could not be successfully completed because of arrhythmia or breath-hold inability and the acquisition was switched to real-time cine scan. A real-time PC-MRI technique with sufficient spatial and temporal resolution to accurately measure physiological blood flow velocity not limited by the cooperation of the patient’s breath-holding or regular cardiac rhythm would fill an important clinical role in the diagnosis and evaluation of patients with a broad range of cardiovascular diseases.

6.2 INTRODUCTION

The phase sensitivity of moving spins in a magnetic field was discovered and used in measuring blood-flow velocity for over two decades (58-60). At present, quantitative assessment of blood-flow velocity in the major vessels is commonly performed by ECG-triggered, segmented k-space phase-contrast magnetic resonance imaging (PC-MRI) (97,139,140). However, this method requires reliable cardiac gating, regular cardiac rhythm, and either
signal-averaging, respiratory gating, or breath-holding to suppress respiratory motion artifacts. Furthermore, the resulting velocity information is a weighted temporal average of MR signal acquired over multiple cardiac and respiratory cycles; short-term hemodynamic variations are lost, such as those that occur under pharmacological stress (139,140) or during physical exercise examinations (141,142).

Real-time PC-MRI has been previously proposed using gradient-echo planar imaging (GRE-EPI) (46,143-145) and spiral sequences (22,47,146), but limited performance has precluded the routine clinical applications. These rapid k-space sampling strategies have demonstrated the MRI hardware capability of evaluating blood-flow velocity in real time; however, existing PC-MRI methods still suffer from an issue of insufficient spatial and/or temporal resolution which can lead to inaccurate velocity measurements (21,138). Conventional PC-MRI requires either a pair of velocity-encoded and velocity-compensated k-space datasets (70), or a pair of equal and opposite polarity velocity-sensitized k-space datasets (113). Phase-difference reconstruction is performed on each complex data pair to eliminate any residual non-zero phase variations due to effects other than
velocity. Thus, conventional MRI velocity measurements require twice as much data as standard MRI scans; this requirement either degrades temporal sampling rate by a factor of two, or doubles the acquisition time to maintain sufficient temporal resolution. As the result, the temporal resolution requirements for real-time velocity measurements are still beyond those achievable using the current existing PC-MRI acquisition.

In this chapter, we propose a simple, practical shared velocity encoding (SVE) method specifically for real-time velocity measurements. With the SVE method, the effective temporal resolution of real-time PC-MRI is improved by a factor of two without an increase in scan time or additional hardware requirements. The aim of the present work is to design and demonstrate a novel method for rapid real-time velocity measurement with sufficient effective temporal resolution to eliminate the need for ECG synchronization and breath-holding, and to provide beat-to-beat hemodynamic information.
6.3 MATERIALS AND METHODS

6.3.1 Shared Velocity Encoding Reconstruction

In the conventional PC-MRI method, slice-selective gradients are followed by either velocity-encoding or velocity-compensating gradients, or a pair of equal and opposite velocity sensitivity gradients, single k-space line readout, and finally a spoiler gradient before the next slice-select RF pulse, as shown in Figure 6.1.

![Figure 6.1: Conventional gradient-echo PC-MRI sequence with a pair of velocity-compensated and velocity-encoded bipolar gradients](image)

With the strategy of echo-planar readout, multiple phase-encoded echoes are acquired by using gradient reversals to form multiple gradient echoes.
before the next RF excitation within a range of 30~150 msec of TR (74). EPI thus offers a significant gain in sampling efficiency compared to the standard single-echo MR sequences. Thus, the major difference between echo-planar sequence and the conventional single-readout GRE sequences is that the former technique collects multiple k-space lines by oscillating the readout gradient to form a series of gradient-echoes within each repetition time, as illustrated in Figure 6.2.

A conventional phase-velocity measurement requires the acquisition of two
separate and complete k-space datasets with different velocity sensitivities. The purpose of acquiring velocity-compensated data, in addition to velocity-encoded data, is to eliminate background phase variations that are caused by gradient imperfection, eddy currents, field inhomogeneity, etc. Thus, the velocity-compensated technique acquires a k-space that balances the zero and the first order gradient moments by incorporating additional bipolar gradients. As a result, a reference scan generates a background phase mapping that merely consists of non velocity-related phase variations for background phase cancellation. The similar phase subtraction mechanism also adapts to a pair of datasets with equal and opposite velocity sensitivity for residual phase compensation in Figure 6.3.
In Chapter 3, we presented an alternative method to accelerate the acquisition of reference scan data by reducing the spatial resolution of the phase-reference or temporal view-sharing of the phase-reference. However, the SVE reconstruction proposed in Chapter 4 achieves the highest possible acquisition efficiency because no additional reference data are required. As described in chapter 4, SVE reconstruction works with the bipolar velocity encoding technique by using alternating polarity velocity encoding gradients for background phase elimination. In this chapter, the combination of segmented EPI readout and SVE reconstruction is used to achieve high temporal resolution real-time velocity mapping.
6.3.2 Sequence Implementation and Study Design

Real-time GRE-EPI with SVE reconstruction was implemented on a 1.5T MR scanner (MAGNETOM Avanto, Siemens Medical Systems, Inc. Malvern, PA) with 12-channel surface phased-array coils. Twelve healthy volunteers (mean age 32.5 ± 11.5 years, range 19 to 56; 3 females) with no history of cardiovascular disease were scanned. For each volunteer study, MR flow measurements began with the acquisition of a conventional ECG-triggered, segmented k-space, spoiled gradient echo PC-MRI measurement. In
real-time flow measurement studies, we evaluated equivalent imaging parameters similar to the clinical segmented PC-MRI protocol used in our institution (i.e. effective temporal resolution of 55ms and matrix = 160x120). Furthermore, identical segmented PC-MRI acquisition before and after real-time measurements at each anatomical slice location. We calculated the mean value of flow volumes and the value of peak flow from both of these segmented PC-MRI measurements as a reference and compared with the proposed real-time GRE-EPI with SVE reconstruction. Averaging of the segmented scans acquired before and after each real-time measurement was done to ensure that any changes in the physiological state of the subject (heart rate, blood pressure, etc.) would not adversely affect the comparison of the two techniques.

Through-plane flow measurements using segmented, spoiled gradient echo PC-MRI and the proposed real-time GRE-EPI with echo train length = 15 and SVE reconstruction were performed for quantification of flow in two separate slices: (i) cutting the main pulmonary artery (PA) between pulmonary valve and PA bifurcation and (ii) perpendicular to the aorta just above the aortic valve, avoiding the aortic valve itself. Common acquisition parameters
were: flip angle = 25°, FOV = 300 x 400 mm², spatial resolution = 2.5 x 2.5 mm², parallel acceleration rate = 2, and venc = 150 cm/s. The effective temporal resolution / TE of the conventional gradient-echo and real-time GRE-EPI sequences were 55 / 1.97 ms and 55 / 2.5 ms, respectively.

| TABLE 6.1 |
| Summary of imaging parameters for in-vivo and phantom studies |

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<tr>
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<td>25°</td>
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</tbody>
</table>

6.3.3 In-Vitro Flow Phantom Validation

For the purpose of acquiring the consistent flow data without any physiological effect (ex. change of breathing pattern), we utilized the pulsatile flow phantom described in Chapter 4 to conduct the accuracy assessment of the different PC-MRI methods. Two through-plan flow measurements were performed by using (i) conventional segmented GRE PC-MRI and (ii) the
proposed real-time GRE-EPI PC-MRI, respectively. Detailed MR scan parameters, which were chosen similar to in vivo studies, are summarized in Table 6.1. Peak and mean flow volumes are analyzed and Root-Mean-Square bias also calculated comparing conventional segmented and real-time PC-MRI methods.

### 6.3.4 Data Analysis

A quantitative evaluation of the flow measurements was performed by calculating peak flow volumes and pulmonary-to-systemic flow ratio (Qp/Qs) using the conventional segmented and the proposed real-time PC-MRI approaches. The value of flow in the flow-vs-time curve was determined by the averaged velocity within the region of interests (ROIs). Peak flow measurements were compared, and Root-Mean-Square Error (RMSE) was calculated between flow curves obtained by means of each phase-contrast velocity measurement method.

### 6.3.5 Statistical Analysis

Paired Students t-tests were used to compare pulmonary-to-systemic flow ratio and peak flow volume differences between conventional PC-MRI and
real-time GRE-EPI with SVE reconstruction in the group of healthy volunteers. A value of $p < 0.05$ was considered to indicate a statistically significant difference. All parameters were expressed as the mean ± SD. The analysis of Bland-Altman method was used to evaluate the agreement between different PC-MRI techniques. The agreement between the methods was assessed by calculating the paired difference between the two methods for each measurement and by estimating the bias and 95% limits of agreement relative to the mean measurement of both methods.

6.4 RESULTS

6.4.1 In-Vivo Human Study Results

The magnitude and phase-contrast images of a plane cutting through the aorta just above the aortic valve from one healthy volunteer are shown in Figure 6.4. Magnitude images clearly illustrate vascular anatomy with a capability of ROI placement by using both the segmented (Figure 6.5a) and the real-time PC-MRI methods (Figure 6.5b).
Phase-contrast images (Figure 6.5c and d) and corresponding aortic flow curves (Figure 6.6a and b) exhibit great similarity between the two methods.

Two flow measurements comparing conventional segmented PC-MRI (Figure 6.6a) and real-time SVE PC-MRI (Figure 6.6b) are shown in Figure 6.6 to illustrate the similarities and differences between real-time beat-to-beat flow
versus segmented acquisition. For comparison purposes, the non-averaged real-time aortic flow curve in eight consecutive cardiac cycles (Figure 6.6c) were averaged and displayed as averaged aortic flow curve (Figure 6.6d), which agrees qualitatively with the averaged segmented k-space PC-MRI curve.

Figure 6.6: Sample aortic volume flow-time curves from one healthy volunteer. (a) Beat-to-beat quantitative flow measurement obtained using real-time SVE method and (b) conventional time-averaged PC-MRI. (c) For comparison purposes, the non-averaged real-time aortic flow volume in consecutive eight cardiac cycles are averaged and displayed as averaged aortic flow curve.
RMS error was calculated between the segmented and the averaged real-time flow curve obtained from measurement over 8 cardiac cycles suggesting an insignificant difference of 15.56 ml/sec between peak flows generated by conventional and real-time SVE techniques. The RMSE difference is equivalent to 4.9% of peak flow measured using the conventional segmented PC-MRI method. The Qp/Qs ratios determined by conventional segmented and real-time SVE PC-MRI were 1.04 ± 0.077 (range 0.96 to 1.14) and 1.07 ± 0.094 (range 0.98 to 1.22), respectively. The difference is insignificant. Figure 6.7 shows magnitude and velocity mapping images from a slice cutting through the main pulmonary artery between pulmonary valve and PA bifurcation. The peak flow demonstrated negligible differences of 3.3% in the aorta and 6.4% in the pulmonary artery between the two techniques.
Cardiac output, which is expressed as L/min, obtained from pulmonary (right ventricle output) and aortic (left ventricle output) flow measurements show excellent correlation between conventional segmented PC-MRI and real-time PC-MRI with SVE reconstruction ($y=0.913x+1.09$, $r = 0.969$) and ($y=0.936x+0.68$, $r = 0.975$), respectively. The Students’ t test results for the Qp/Qs shunt ratio measurements show a mean difference of 0.012 (95% confidence interval, -0.068 to 0.094). The agreement between the two
methods was assessed by comparing the difference between the results of the two methods with the mean result (Figure 6.8). No statistically significant difference was found between the conventional and real-time PC-MRI methods.

![Figure 6.8: Bland-Altman analysis of agreement for flow volume in the aorta. Plot of difference against mean for aortic flow volumes by conventional segmented PC-MRI vs. real-time SVE method. Upper and lower limits of agreement, mean±2SD](image)

### 6.4.2 In-Vitro Results

In the pulsatile flow phantom study, the flow measurement results show a mean deviation of 4.69% in peak flow volumes and 3.42% in mean flow volumes; these results are similar to those obtained in vivo. The RMSE of the peak flow measurement revealed an insignificant RMSE of 4.73 ml/sec.
between conventional segmented and GRE-EPI SVE methods.

6.5 DISCUSSIONS

We have illustrated that SVE results in a factor of two improvement in the effective temporal resolution with maintained spatial resolution and no increase in scan time. With the SVE reconstruction, beat-to-beat real-time flow quantification becomes practical and clinically valuable without the need for cardiac ECG-gating and insensitive to respiratory motion. In-vivo volunteer studies demonstrated good agreement between flow measurements using conventional ECG-triggered, segmented k-space PC-MRI and real-time PC-MRI with SVE reconstruction. Real-time velocity and flow measurements obtained using the proposed SVE method were demonstrated to be equivalent to the conventional segmented breath-hold acquisitions. Furthermore, volunteer studies illustrated that GRE-EPI PC-MRI with SVE reconstruction provides sufficient effective temporal resolution to evaluate hemodynamics on the major vessels in real time, and suggests that real-time MR velocity measurement is now a feasible method to assess blood-flow characteristics.
The pulmonary-to-systemic flow ratios obtained from both conventional segmented and real-time SVE PC-MRI revealed slightly elevated pulmonary flow volumes compared to aortic flow volumes. In a healthy human body, the coronary circulation comprises on average 4 to 5 percent of total cardiac output from the systemic circulation (147); this might explain the small offset of flow ratios in both methods. The major benefit of the real-time velocity measurement technique is the capability of consecutively monitoring blood-flow and cardiac function insensitive to cardiac and respiratory motion. As previously mentioned, in the OSU clinical CMR lab approximately 39% (75/190) of the time breath-hold segmented k-space cine studies fail because of patients’ arrhythmia or breath-hold inability and the acquisition was switched to real-time cine. It is expected that, after sufficient validation testing in patients, real-time velocity mapping will be used clinically in a similar fashion in patients unable to breath-hold or with severe arrhythmias.

Parallel imaging reconstruction accelerates MRI acquisition by undersampling of k-space lines while taking a penalty of decreased signal-to-noise ratio (10). However, when using an EPI readout, the signal loss can be compensated by utilizing shorter echo train length to achieve
equivalent number of total k-space lines. Shortening the echo train allows the MRI signal to be collected prior to severe signal loss caused by T2* decay and off-resonance effects. Moreover, real-time PC-MRI scans typically are performed with a limited spatial resolution in order to preserve sufficient temporal resolution. Low spatial resolution introduces another potential phase-velocity error caused by the partial-volume effect from a mixing of moving and static spins within a pixel. Parallel imaging acceleration may be used to preserve sufficient in-plane spatial resolution and minimize partial-volume effects in medium and small vessel applications. While the current implementation did utilize the TGRAPPA parallel acquisition method, it is expected that further gains in acceleration rate will be achieved in the future using coils with additional array elements (148).

The major advantage of SVE reconstruction is to utilize the equal and opposite velocity sensitivities of PC-MRI to extract unique velocity information from every velocity-sensitized datasets instead of data pairs. However, one potential drawback of the present SVE reconstruction is the lack of velocity-compensated magnitude images that might serve as a reference marker for placing ROIs in standard post-processing software. In fact, a
negligible flow artifact in velocity-encoding magnitude images is still capable of locating appropriate ROIs within the major vessels and other purposes for post-processing procedure (Figure 6.8b and d).

In real-time PC-MRI methods for quantifying beat-to-beat hemodynamics, trade-offs of MRI acquisition parameters should be considered between spatial resolution, temporal resolution, and accuracy of velocity measurement. With rapid k-space sampling trajectories including spiral PC-MRI (22,146) and echo-planar imaging PC-MRI (143-145), sufficient temporal resolution have been achieved, however, rapid gradient oscillations can induce eddy currents that cause phase errors and spatial distortion in the phase-contrast images. Advanced phase correction algorithms are required to compensate undesired phase variations that are not induced by motion (149,150).

This study suggests that the additional temporal-phase images provided by the proposed SVE method enable real-time acquisition of velocity data with temporal and spatial resolution comparable to conventional segmented breath-hold methods. This technique is beneficial to provide high temporal resolution not only for real-time velocity imaging but also for velocity jet
quantification or for differentiating pulse wave arrival times for accurate PWV measurement. Further research can combine non-segmented SVE techniques to explore local PWV in a carotid artery with ultra-high temporal and spatial resolution (i.e. Chapter 3), and three-dimensional velocity mapping MRI.
CHAPTER 7

THEORETICAL ASPECTS OF IN-PLANE VELOCITY MEASUREMENT
USING ECHO-PLANAR IMAGING WITH SHARED VELOCITY ENCODING
RECONSTRUCTION

It has been implicitly assumed that MR velocity measurement is based on an imaging plane oriented perpendicular to the flow direction throughout the major portion of this dissertation. Under this assumption, a standard through-plane phase-velocity measurement which utilizes a pair of velocity-encoded and velocity-compensated gradients or bipolar velocity-encoded gradients is performed along the slice-selective axis while velocity-compensated gradients are applied along both the frequency-encoding and the phase-encoding axes.
In this chapter, we present a brief feasibility study including theoretical analysis and numerical simulation of in-plane velocity measurement using a multi-echo readout sequence combined with shared velocity encoding (SVE) reconstruction. Finally, the concept of three-directional velocity quantification using echo-planar imaging (EPI) and SVE reconstruction is addressed in this chapter.

7.1 INTRODUCTION

Carr and Purcell first recognized in 1954 the phase shift that occurs when spins move along a magnetic gradient field (57). In the past two decades, investigators within the MRI research community have continued to evaluate the phase evolution that originates from motion of moving spins (58-60,97). The phase-velocity imaging technique has offered a method of non-invasive velocity measurement by utilizing this MR phenomenon. To date, most of the velocity mapping techniques have been developed and implemented using the spoiled gradient-echo (GRE) sequence and its derivatives (111,151,152). The standard GRE sequence acquires one k-space line after each slice-selective RF excitation and phase-encoding gradient. As a result, the scan time of the GRE technique is the product of the imaging repetition time
and the number of the total phase-encoding lines. With the advent of MRI in the 1970s, Sir Peter Mansfield proposed a novel echo-planar acquisition strategy that still today is one of the most efficient MRI data acquisition methods (153). Recently, the EPI technique has found clinical applications in first-pass perfusion MRI (154) and cardiac real-time imaging (155). With the EPI technique, multiple phase-encoded echoes are acquired following each slice-selective excitation (74), as opposed to a conventional GRE MRI acquisition that repeatedly collects single echoes until the entire k-space is filled. The scan time of single-shot EPI is simply the interval between the beginning of the excitation and the end of data collection, typically on the order of tens of milliseconds, making EPI one of the fastest acquisition strategies available. To our knowledge, in-plane velocity measurement in human subjects using PC-MRI with echo-planar readout has not been implemented successfully although its theoretical aspects have been described.

The aim of this chapter is to investigate the feasibility of in-plane velocity measurement by using theoretic analysis and numerical simulations. The goal is to determine the practicality of EPI-based PC-MRI and SVE for multi-directional and multi-dimensional velocity encoding.
7.2 THEORY AND NUMERICAL ANALYSIS

In this analysis, phase-velocity analysis is discussed separately along the three orthogonal directions (i.e. slice-selective, phase-encoding and frequency-encoding) of the MRI system. For the purpose of simplicity, constant plug-like flow is assumed and considered in this work. However, the result can be easily extended to the more general laminar flow or pulsatile flow. Simulations were run to analyze the zeroth and the first gradient moments with different velocity-dependent gradient waveforms. The maximum gradient amplitude and minimum gradient ramp time of this study are assumed to be 28 mT/m and 10 usec/(mT/m), respectively. All simulations were performed using Mathematica software (Wolfram Research, Inc., Champaign, IL.).

7.2.1 Motion along the Slice-Selective Direction

As we mentioned in Chapter 2, motion of moving spins induces a signal loss and ghosting artifacts in MR images because of the velocity-dependent phase accumulation of moving spins. To avoid this problem, gradient moment nulling (GMN) was developed to bring spins moving with a constant velocity back to zero phase at the echo time (156-158). The GMN technique can be implemented in the phase-velocity PC-MRI sequence to compensate
periodic flow and avoid ghosting artifacts. The main goal of velocity compensation is to compensate the residual phase that is accumulated before data acquisition by adjusting the gradient amplitude and timing.

Figure 7.1a shows a standard slice-selective gradient used for slice excitation in a two-dimensional MRI scan. Figures 7.1b demonstrates that a standard slice-selective gradient waveform accumulates a zero net area (i.e. the zeroth gradient moment), these by refocusing the phase of stationary spins. However, the first gradient moment has not vanished after the standard slice-selective gradient as shown in Figure 7.1c. Therefore, the residual phase accumulation could cause velocity-dependent phase shift and ghosting artifacts in the MR image.
Figure 7.1: Slice-selective gradient configuration for a standard 2D MRI sequence without additional velocity-compensation gradients. (a) slice-selective gradient waveform, (b) the zeroth gradient moment vanishes at the end of refocused gradient, (c) the first gradient moment is not compensated but proportional to the phase accumulation after the slice-selective gradient
The GMN technique can be implemented in the slice-selective axis in order to bring the phase of constant velocity spins back to zero status. Figure 7.2a shows a typical velocity-compensation waveform that balances both the zeroth and the first gradient moments by adding a third lobe in the slice-selective gradient pattern. However, additional time is necessary to accommodate the third gradient lobe compared to the standard two-lobe slice-selective excitation waveform. The velocity compensation technique can be used to balance the zeroth and the first gradient moments not only in the GRE but also in the EPI sequence because both sequences use equivalent gradient waveforms for slice-selective excitation.
Figure 7.2: Slice-selective gradient configuration for a standard 2D MRI sequence with additional velocity-compensation gradients. (a) slice-selective gradient waveform, (b) the zeroth gradient moment vanishes at the end of refocused gradient, (c) the first gradient moment is also compensated after the slice-selective gradient.
7.2.2 Motion along the Frequency-Encoding Direction

This section examines the phase accumulation resulting from spins moving along the frequency-encoding direction. The echo-planar readout strategy collects k-space data using a markedly distinct approach compared to the standard MRI k-space trajectory. EPI employs rapidly oscillating gradients along the frequency-encoding axis with serial blipped gradients along the phase-encoding axis. As a result, a train of gradient-echoes are generated by multiple reversals of the frequency-encoding gradient polarity from positive to negative and vice versa. This k-space trajectory provides very high sampling efficiency because rf pulses and rewinder gradient lobes between echoes are not required. However, this echo-planar readout creates two types of phase modulation corresponding to the odd and even k-space lines because they are acquired with an opposite readout gradient polarity. It has been shown that every even echo is exactly nulled for the zeroth and the first gradient moment at the center of echo, as shown in Figure 7.3 (54). However, every odd echo has an increasing accumulation of the first gradient moment and therefore an increasing phase proportional to velocity.
Figure 7.3: (a) Normalized phase accumulation during echo-planar readout gradient and (b) the enlargement of the central portion of (a) illustrates the relationship between normalized phase accumulation versus kx with flow along the frequency-encoding axis. Note that the residual phase is nulled at the center of every even echo, while accumulated phase at the center of every odd echo.

A flyback trajectory has been proposed that allows velocity compensation to be performed on each echo of the echo-planar readout (54,159). In the flyback trajectory, all echoes are acquired using the same polarity gradient lobes. The phase is rewound as rapidly as possible but without data sampling. Efficiency loss is minimized by rewinding the phase a rapidly as
possible. Duerk and Simonetti (159) provided a theoretical description of motion compensation in the echo-planar readout based on the hardware performance in the early 1990s. Results in reference (159) present the phase evolution based on the standard echo-planar readout (Figure 7.4a) that induces a velocity-dependent phase shift at odd echoes. With flyback trajectory implementation, the velocity-dependent phase of a spin moving along the frequency-encoding axis has zero net accumulated phases at every echo.
The same concept presented in reference (159) was simulated based on modern gradient system specifications of maximum gradient strength of 28 mT/m, a minimum gradient ramp time of 10 usec/(mT/m) and an EPI echo train length of four. In contrast to the previous report (159), our results suggest
that the imaging repetition time will be prolonged by only 41% by utilizing a flyback trajectory compared to every echo readout because modern gradient amplifiers produce shorter gradient ramp times and larger gradient amplitudes. Based on the simulation of a four-echo readout EPI sequence, the flyback trajectory prolongs the imaging repetition time from 7.1msec to 10.1msec in order to acquire all echoes with consistent polarity. A schematic diagram of velocity-encoding in the frequency direction by using equal and opposite velocity-sensitive gradients is shown in Figure 7.5.
In order to implement SVE velocity measurement along the frequency-encoding axis, a velocity-dependent bipolar gradient is applied to create positive velocity sensitivities for moving spins and followed by another acquisition using the same waveform but opposite polarity bipolar velocity encoding gradients. Similar phase-contrast subtraction method is performed.
to extract the velocity information along the frequency-encoding axis in echo-planar readout.

7.2.3 Motion along the Phase-Encoding Direction

Although GMN has been widely implemented in slice-selective and frequency-encoding directions, motion compensation along the phase-encoding axis in the EPI sequence is complicated and was impractical using the gradient hardware systems of the 1990s. In this section, we briefly address the feasibility of implementing the GMN technique along the phase-encoding axis of an EPI sequence using current MRI hardware performance characteristics.

When using a conventional, uni-polar, blipped phase-encoding waveform the velocity sensitivity changes from echo to echo. Thus, k-space consists of several velocity-encoding k-space segments equal to the echo train length of the segmented EPI sequence. The basic idea for velocity compensation along the phase-encoding axis is to convert each phase-encoding blip waveform to a bipolar waveform with zero first moment that still provides the net zeroth gradient moment needed to encode a specific line of k-space.
Additionally, the first gradient moment of the bipolar phase-encoded gradient should have a constant value for every blip because that corresponds to the velocity sensitivity of each echo, and hence each line of k-space. Figure 7.6 shows gradient conventional train of unipolar phase-encoding blips and the first gradient moment graph, which corresponds to velocity sensitivity of each k-space line.
Figure 7.6: Phase-encoding gradient configuration for a standard 2D MRI sequence without additional velocity-compensation gradients. (a) phase-encoding gradient waveform, (b) the zeroth moment, (c) the first moment during the phase-encoding gradient
To avoid this specific issue in echo-planar sequences, a method of velocity compensation or consistent velocity encoding between echoes (k-space lines) must be implemented along the phase-encoding axis. Taking advantage of modern gradient amplifier specifications, the bipolar velocity compensated gradient blip can fit into the ramp time or the negative dephasing lobes of the fly-back readout gradient waveform. In Figure 7.7, the velocity-compensated bipolar blip technique that we described in the previous section is shown in an example 4-echo, echo-planar readout sequence. The desirable values of zeroth gradient (i.e. the distance from the origin of k-space) are encoded by using the bipolar two-lobe design instead of blips. Furthermore, first gradient moment of this design shows each echo has the same velocity-sensitivity within echo-train. In the variety of clinical velocity measurement applications, the appropriate velocity-phase sensitivity can be adjusted by additional pre-dephasing lobe of EPI sequence.
Figure 7.7: Phase-encoding gradient configuration for a standard 2D MRI sequence with additional velocity-compensation gradients. (a) phase-encoding gradient waveform, (b) the zeroth moment, (c) the first moment during the phase-encoding gradient
In order to implement SVE velocity encoding along the phase-encoding axis, a similar approach that employs two bipolar gradients with the same waveform but opposite polarity is applied along the phase-encoding axis. To minimize gradient amplitude requirements of gradient moment compensation, the time origin of gradient moment calculation might be chosen in the center of echo train to reduce the gradient amplitude of the first and last echoes. According to this feasibility investigation, the maximum echo train length of the EPI sequence with in-plane velocity encoding should be less than six to avoid excessively long echo train durations, which would lead to sensitivity to T2* and off-resonance artifacts. The schematic sequence diagram which combines the bipolar velocity-encoded lobes along the phase-encoding axis and flyback trajectory along the frequency-encoding axis is displayed in Figure 7.8.
Three Directional (+) Velocity Encoding

Figure 7.8: Schematic sequence diagram of bipolar velocity-encoded gradients along the phase-encoding axis combined with fly-back gradient lobes along the frequency-encoding axis.

7.3 MULTI-DIRECTIONAL VELOCITY MEASUREMENTS

7.3.1 2D MRI Velocity Measurement

As we described in Chapter 2, PC-MRI has been primarily used for blood flow measurements based on the phase shift of moving spins through a magnetic field gradient. Most of the velocity mapping techniques fall into the two categories of through-plane and in-plane velocity measurements, as shown in Figure 7.9 (160).
7.3.2 2D In-Plane MRI Velocity Measurement

Through-plane velocity measurements have been implemented and evaluated using the GRE (42,97,161) and EPI (21,46,138,142) techniques. However, there are only limited studies that focused on in-plane velocity mapping techniques using the GRE sequence (162-164). Phase-velocity MR phenomenon can also be applied in all three spatial directions by using a pair of velocity-compensated or bipolar velocity-sanitized gradients in the frequency-encoding axis in order to encode in-plane blood flow. The conventional in-plane encoding approach is similar to through-plane velocity encoding as previously mentioned in Chapter 2 and 4. The major difference is to apply bipolar gradients along the frequency-encoding and/or phase
encoded axis instead of slice-selective axis, as shown in Figures 7.10 and 7.11.

Figure 7.10: Spoiled gradient-echo phase-contrast pulse sequence for one-directional velocity encoding along the frequency-encoding direction using a pair of velocity-compensated and velocity-encoded gradients.

Figure 7.11: Spoiled gradient-echo phase-contrast pulse sequence for one-directional velocity encoding along the frequency-encoding direction using a pair of equal and opposite polarity velocity-sensitized gradients.
Figure 7.12 shows one example of in-plane velocity measurement using PC-MRI. Velocity-encoding was applied from bottom to top direction in order to encode the blood flow velocity from left atrium to left ventricle and through the aortic outflow tract.

Figure 7.12: In-plane velocity measurement using PC-MRI (a) magnitude image and (b) phase-contrast image. Please note the velocity encoding direction is applied from bottom to top in the image.

### 7.3.3 Three-Dimensional Through-Plane MRI Velocity Measurement

Three-dimensional through-plane PC-MRI has several unique advantages compared to two-dimensional through-plane PC-MRI scan, in terms of high
signal-to-noise, spatial resolution and object visualization. Three-dimensional MRI is accomplished by the addition of a phase-encoding step in the slice-selective direction. However, the long acquisition time of three-dimensional PC-MRI is the major problem that has prevented widespread use in clinical applications.

The purpose of this section is to estimate the improvement in total scan time of 3D through-plane velocity measurement that could be expected with the implementation of EPI and SVE methods. For a fifteen-echoes echo-planar readout sequence, acquisition matrix of 120 k-space lines, segmentation of 4, parallel imaging factor of 2, and 8 partitions in a 3D volume the total imaging acquisition requires $2 \times 8 = 16$ heart beats. A comparable single-slice 2D PC-MRI scan with SVE is completed within 2 heart beats.

### 7.3.4 Two-Dimensional Three-Directional Encoding MRI Velocity Measurement

With the advent of modern MR hardware and imaging technique achievements, 2D three-directional velocity-encoding PC-MRI offers the possibility of acquiring velocity information in all three orthogonal directions.
within a single MR scan. As we mentioned in early chapters in this dissertation, for a conventional one-directional velocity measurement using bipolar velocity encoding PC-MRI, a pair of k-space datasets with different velocity sensitivities is necessary for background phase subtraction (68,158). Each pair of velocity-sensitized datasets is acquired along one Cartesian axis while maintaining the same velocity sensitivity in the other two Cartesian directions. To encode velocity along three orthogonal directions, three pairs of measurements (i.e. six measurements in total) are required to separately encode each velocity component in each direction by using conventional bipolar velocity encoding PC-MRI.

The three-directional PC-MRI method can be performed in a series of velocity-compensated and velocity-encoded MR scans on the three orthogonal axes, as shown in the Table 7.1.
### TABLE 7.1

**Velocity-compensated and encoded table for three-directional PC-MRI**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Slice-selective axis</th>
<th>Frequency-encoding axis</th>
<th>Phase-encoding axis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>VC</td>
<td>VC</td>
<td>VC</td>
</tr>
<tr>
<td>2</td>
<td>Venc (+)</td>
<td>VC</td>
<td>VC</td>
</tr>
<tr>
<td>3</td>
<td>VC</td>
<td>Venc (+)</td>
<td>VC</td>
</tr>
<tr>
<td>4</td>
<td>VC</td>
<td>VC</td>
<td>Venc (+)</td>
</tr>
</tbody>
</table>

Note: Venc(+) and VC represent the positive velocity-encoding and velocity-compensated bipolar gradients

The purpose of measurement #1 is to acquire a background phase map without any influence of motion of blood flow. Measurements #2, #3 and #4 acquire the velocity information along each Cartesian axis while velocity compensation is applied along other axes. Therefore, each velocity component along in corresponding Cartesian axis is estimated by phase-subtraction between a velocity-encoding scan and a phase reference scan. The major limitation of the multiple-directional velocity measurement is the long scan time that restricts its clinical applications. The maximum achievable spatial and/or temporal resolution must be compromised in order to keep the total scan time tolerable for patients.
Pelc et al proposed the balanced four-point encoding strategy for multi-directional velocity measurement using bipolar velocity encoding PC-MRI in 1991 (53). With the implementation of balanced four-point encoding strategy, bipolar velocity encoding PC-MRI can generate a three-directional velocity map using four phase-velocity MRI scans. Table 7.2 summarizes the four-point velocity encoding strategy in slice-select, frequency-encoding and phase-encoding axes by using bipolar velocity encoding PC-MRI.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Slice-select axis</th>
<th>Frequency-encoding axis</th>
<th>Phase-encoding axis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Venc (-)</td>
<td>Venc (-)</td>
<td>Venc (-)</td>
</tr>
<tr>
<td>2</td>
<td>Venc (+)</td>
<td>Venc (+)</td>
<td>Venc (-)</td>
</tr>
<tr>
<td>3</td>
<td>Venc (+)</td>
<td>Venc (-)</td>
<td>Venc (+)</td>
</tr>
<tr>
<td>4</td>
<td>Venc (-)</td>
<td>Venc (+)</td>
<td>Venc (+)</td>
</tr>
</tbody>
</table>

Note: Venc(+) or Venc(-) represent the positive and negative velocity-encoding bipolar gradients

The proposed EPI sequence combined with SVE reconstruction can be extended to three-directional velocity measurements by using the balanced
four-point velocity encoding strategy as shown in Table 7.2. The simplest example for illustration purpose is to use a single-shot EPI sequence with SVE reconstruction for three-directional velocity measurement, as shown in Figure 7.13. The opposite polarity of velocity encoding (Venc) in each Cartesian axis is created by flipping the entire gradient waveform. Flipping the sign or polarity of the gradient waveform serves to flip the polarity of velocity sensitivity as well.
The intermediate phase-contrast information in the single-shot EPI technique is reconstructed by combining a group of four velocity measurements with different velocity sensitivities. SVE reconstruction combines the velocity-encoding data from the prior and next
velocity-sensitized datasets.

To estimate the feasibility of a three-directional velocity mapping EPI sequence that utilizes the SVE technique, the following assumptions and estimations are considered. Assume that the slice of interest is to be imaged with 128 k-space lines. Parallel acceleration rate of 2 is used to halve the total number of phase-encoding lines in the given k-space matrix. Assume that a conventional EPI sequence with echo-train-length of 4 is used. A repetition time of 10.1 msec is required based on the current MRI hardware and software performance.

For three-directional velocity encoding using the balanced four-point encoding strategy, the temporal resolution is equal to four times the repetition time \((10.1 \times 4 = 40.4 \text{ msec})\). Therefore, one slice with three-directional velocity mapping requires 16 heartbeats; a reasonable breath-hold duration with sufficient temporal and spatial resolution for clinical applications.
7.4 CONCLUSION

We have illustrated that constant velocity encoding in three orthogonal axes can be achieved using methods proposed earlier for EPI trajectories. With the advent of modern MRI hardware and software developments, the segmented EPI PC-MRI sequence with in-plane velocity encoding becomes practical with current clinical MRI scanners. The advantage of the high acquisition speed of the EPI method provides a time-efficient velocity measurement 2D three-directional velocity mapping and 3D one-directional or multi-directional velocity measurement for cardiovascular applications.

In this chapter, we have investigated the feasibility of a fast PC-MRI method that combines aspects of echo-planar readout and SVE reconstruction, such that the technique has the potential to significantly accelerate the acquisition of three-directional and three-dimensional PC-MRI data.
The new methods developed and presented in this dissertation have focused primarily on addressing the need for improved temporal resolution in phase-contrast magnetic resonance imaging (PC-MRI). In addition, a rapid fat-suppression method was described that enabled the use of longer echo trains, further improving the time-efficiency of segmented-EPI PC-MRI. Finally, the potential extension of these concepts to multi-directional and multi-dimensional flow quantification was evaluated in theory and simulation.

These works demonstrated the spatial and/or temporal resolution in PC-MRI could be improved using partial coverage of the phase-reference
dataset while maintaining the original form of the velocity-encoded dataset with minimum loss of accuracy in the velocity measurement. Furthermore, shared velocity encoding (SVE) reconstruction was proposed and shown to provide a factor of two improvement in the effective temporal resolution of PC-MRI without increasing the scan time. Moreover, the chemical shift artifacts resulting from off-resonance fat signal were suppressed by the proposed phase-modulated water-excitation method in Chapter 5. The combination of these techniques resulted in a method to quantitatively measure beat-to-beat hemodynamic characteristics in the major vessels. We concluded with a brief discussion of the potential capability of multi-directional velocity mapping using the EPI and SVE methods.

While several new techniques have been presented and shown to provide accurate real-time measurement of blood flow velocity, there is room for additional improvement in imaging performance, and more importantly, there is a need for validation of these techniques and investigation of their role in clinical diagnostic imaging. Several advanced parallel reconstruction algorithms have been proposed to improve acquisition efficiency in a variety of MRI applications (165-170) with the combination and advantages of these
methods in combination with EPI and SVE reconstruction should be explored.

Carefully designed, prospective clinical investigations should be performed to assess the accuracy of velocity measurements in clinical applications such as the evaluation of patients with valvular stenoses and insufficiencies. Furthermore, the accuracy of real-time velocity measurements in smaller arteries requiring higher spatial resolution must be investigated to understand the limitations and applications of this technique. Further technical developments and clinical validations will extend and popularize the application of the techniques described in this dissertation in the field of cardiovascular MRI.
Reference:

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