Fast Measurements of Blood Flow Using Magnetic Resonance

by

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A thesis submitted in conformity with the requirements for the degree of Doctor of Philosophy
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Abstract

This thesis investigates the non-invasive measurement of blood flow in large arteries using magnetic resonance (MR). Functional information can be obtained from such measurements, including stenosis grade, tissue perfusion, and vessel-wall elasticity. Unfortunately, traditional MR measurements of blood flow are relatively slow, and must combine data acquired from different cardiac cycles. Measurement errors may be introduced by this procedure if the flow is not purely periodic (e.g., due to respiration or arrhythmia). A solution to this problem is to collect an independent flow measurement each heartbeat. This thesis develops MR methods for this purpose using volume-selective excitations with reduced spatial encoding, with the goal of measuring aortic stiffness from data collected in one heartbeat.

This work is divided into three incremental stages. The first develops a method to track the one-dimensional (1D) displacement of an excited bolus of blood. Displacement is derived from the frequency of the MR signal, which changes as the bolus moves through a magnetic-field gradient. The second stage extends this work by exciting blood at multiple positions along the vessel, and recording their displacements simultaneously using rapid 1D projections. From these 1D measurements, an expression for the velocity spectrum of the blood is also derived. The influence of specific excitation profiles and velocity profiles on these measurements is explored. The final stage applies the measurement to pulsatile aortic flow. An algorithm that detects the onset of systolic flow at each vessel position is developed and used to measure the aortic pulse-wave velocity (PWV), a parameter related to vessel stiffness. Measurements of the PWV in a single heartbeat are presented.

This thesis demonstrates that volume-localization can be used to obtain independent
blood-flow measurements each heartbeat. This is significant because it enables measurement of blood motion despite potential beat-to-beat fluctuations in the flow. The research culminates in a non-invasive measurement of the pulse-wave velocity that could facilitate the study of vascular mechanics. Use of this tool could lead to a greater understanding of cardiovascular physiology, particularly the mechanism through which disease processes and therapeutic interventions affect the mechanical properties of the aortic wall.
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# Contents

Abstract ii

Acknowledgements iv

List of Tables viii

List of Figures ix

Dedication xi

## Chapter 1 Introduction

1.1 Introduction 1

1.2 Properties of the Vascular Wall 3

1.2.1 Aortic Elasticity 3

1.2.2 Quantification of Vessel Elasticity 5

1.3 Importance of Fast Blood-Flow Measurement 9

1.4 Volume-Selective Excitations 11

1.5 Thesis Hypothesis and Outline 15

References 16

## Chapter 2 Motion Measurements from Individual MR Signals 25

2.1 Introduction 25

2.2 Theory 26

2.2.1 Error Analysis 29

2.3 Materials and Methods 34

2.4 Results 39

2.5 Discussion 44
# Table of Contents

**Chapter 3  Tagging Measurement of Blood Flow**

- 3.1 Introduction ........................................... 51
- 3.2 Theory .................................................. 53
  - 3.2.1 General Description of 1D Tagging Measurements .......... 54
  - 3.2.2 Cylindrical or Gaussian Excitation Profiles & Parabolic Flow .... 57
  - 3.2.3 General Analysis of Tag Motion .......................... 59
  - 3.2.4 Calculation of Velocity Spectrum ........................ 61
- 3.3 Materials and Methods .................................. 64
- 3.4 Results .................................................. 68
- 3.5 Discussion .............................................. 73

**Chapter 4  Tagging Measurements of PWV**

- 4.1 Introduction ............................................. 83
- 4.2 Methods .................................................. 84
- 4.3 Results .................................................. 87
  - 4.3.1 Description of Position-Time Matrix ...................... 87
  - 4.3.2 Model of Tag Motion .................................... 90
  - 4.3.3 Detection of Pressure-Wave Position ....................... 92
  - 4.3.4 Reproducibility of PWV Measurement ....................... 94
  - 4.3.5 Effect of ECG Error on PWV Measurement .................. 95
  - 4.3.6 In Vivo Measurements of PWV ........................... 98
- 4.4 Discussion .............................................. 99

**Chapter 5  Summary and Conclusions**

- 5.1 Thesis Summary .......................................... 106
- 5.2 Opinions and Future Explorations ........................ 109
  - 5.2.1 Real-Time Flow Measurement ............................. 110
  - 5.2.2 Automated Tracking of Tag Motion ....................... 112
  - 5.2.3 Clinical Studies of Distensibility ...................... 114

**References**

- 47
- 78
- 101
- 106
5.2.4 Improved Calculation of the PWV ................................................................. 116
5.2.5 Extension to Pulse Pressure ................................................................. 118
5.3 Conclusions ................................................................. 120

References ................................................................. 120
List of Tables

2.1 Comparison between STEAM and 2D-selective excitation .................. 39
3.1 Comparison between tag velocity and blood velocity ....................... 70
4.1 Results of in vivo PWV measurements ........................................ 98
List of Figures

1.1 Model of pressure-wave transmission in the aorta ........................................ 7
1.2 Illustration of two volume-selective excitations .......................................... 13

2.1 Effect of random noise on instantaneous-frequency calculation .................... 31
2.2 Effect of signal contamination on blood-displacement measurement .......... 32
2.3 Effect of volume shape on instantaneous-frequency calculation ..................... 34
2.4 Pulse sequence timing diagrams for STEAM and cylindrical excitation ........ 36
2.5 Relationship between signal amplitude and echo-train length, excited-volume
   thickness, and readout-gradient amplitude ............................................. 40
2.6 Experimental validation of blood-flow measurement using STEAM ................. 42
2.7 *In vivo* measurement of blood flow in descending aorta using STEAM ........ 43

3.1 Effect of velocity profile on tagging measurements of flow .......................... 54
3.2 Simulated effect of velocity profile and excitation profile on tag evolution .... 55
3.3 Simulated dependence of signal amplitude on velocity profile and excitation
   profile .................................................................................................. 58
3.4 Simulated effect of Gaussian excitation profile on measurement of velocity
   spectrum .............................................................................................. 60
3.5 Calculation of velocity spectra from simulated tagging data .......................... 63
3.6 Pulse sequence used to measure tag motion .................................................... 65
3.7 Tagging measurements of constant flow in a straight tube ............................. 69
3.8 Measurements of excitation profile and velocity profile in a tube .................. 71
3.9 Tagging measurements of blood motion in a human aorta ............................. 72

4.1 Pulse sequence used to measure tag motion in the aorta ............................... 85
4.2 Calculation of the PWV in a human aorta from representative tagging data .. 88
4.3 Fitting function used to detect the motion of the tagged blood ......... 91
4.4 Consecutive measurements of the aortic PWV in one individual ....... 95
4.5 Variability of the onset of flow in the aorta relative to the ECG trigger ... 96

5.1 Preliminary results from an automated tag-fitting method .............. 114
To my parents.
Chapter 1

Introduction

1.1 Introduction

Dysfunction of the cardiovascular system is associated with approximately 40% of the deaths in Canada\cite{1}; as a result, the cardiovascular system is a prominent focus of medical research in this country. The work described in this thesis investigates the measurement of an important component of the cardiovascular system: blood flow in large arteries. While much can be learned from static anatomical images of a vessel, functional information can be obtained from quantitative measurements of blood flow, such as stenotic grade\cite{2} or vessel-wall stiffness\cite{3}.

The goal of this thesis is to develop fast non-invasive measurements of blood flow using a magnetic-resonance (MR) imager. One problem with traditional MR measurements of blood flow is they are slow. In order to create a single image of the flow, these methods often combine data acquired during different cardiac cycles. The acquisition of these data is
CHAPTER 1. INTRODUCTION

gated to the cardiac cycle (e.g., using the R-wave peak of an electrocardiogram), so the data are assumed to correspond to the same phase of the cardiac cycle. Therefore, measurement errors may be introduced by this procedure if the flow is not purely periodic. Possible sources of aperiodic flow include respiration, cardiac arrhythmia[4, 5], and patient motion. Section 1.3 explores this problem in more detail, and proposes a simple solution: acquire the flow data in one heartbeat and eliminate the need to combine data.

In order to measure flow more quickly, new MR methods must be developed. The blood-flow measurements developed in this thesis rely on so-called “volume-selective excitations”. This approach restricts the volume over which the flow measurements are made, which simplifies the data acquisition and reduces the measurement period. Volume-selective excitations are introduced in Section 1.4, and their ability to provide fast measurements of blood flow is explained. The novel use of these excitations to measure blood flow is a focus of this thesis.

An important application of the flow measurements in this thesis is the study of aortic-wall mechanics. Section 1.2 begins with a basic introduction to the anatomy and function of the aorta, and develops an expression for vessel elasticity based on blood-flow measurements. Disruptions of the vessel wall by specific diseases are also discussed.

Chapter 1 concludes with an outline of the remaining chapters of the thesis. The chapters refine a method for rapidly measuring blood flow, and culminate in a method able to assess the mechanical properties of the aortic wall.
CHAPTER 1.  INTRODUCTION

1.2 Properties of the Vascular Wall

1.2.1 Aortic Elasticity

The aorta is more than a conduit for distributing blood to the body. It also serves a mechanical function by reducing the pulsatility of blood flow and making the flow to peripheral tissues more continuous. A mechanism for this function was first proposed by Stephen Hales[6] in 1733. In Hales's model, the aorta distends during systole as it fills with blood ejected from the left ventricle. In diastole, the left ventricle must refill and is unable to pump blood to the body, yet blood circulation is somehow maintained. Hales reasoned that the aorta recoils back to its original diameter during diastole, and thereby supplies blood flow late into the cardiac cycle. Hales likened the function of the aorta to that of an air compression chamber from his era, which was called a "Windkessel" in its German translation. As a result, this model of the aorta continues to be called the Windkessel model. Although this is not a perfect model for the function of the aorta, it provides an intuitive description of how the aorta (and elastic arteries in general) behave.

The mechanical properties of the aorta result from the anatomy of the aortic wall. The wall is composed of three layers: a thin inner layer called the intima, a thick middle layer called the media, and an outer layer called the adventitia. The mechanical properties of the wall are determined largely by the elastin and smooth muscle in the media and by the collagen in the adventitia[7]. Elastin and collagen are both structural proteins. Elastin enables the aorta to expand like a balloon during systole, while collagen provides rigidity to the aorta and limits its expansion. Smooth muscle can actively change the mechanical
properties of the aortic wall, but tends to have a greater influence on smaller vessels like arterioles[8].

Research studies have discovered a relationship between vessel elasticity and many normal and disease processes. Aortic stiffness decreases from birth until approximately 10 years of age, after which it increases[9, 10]. Highly-trained athletes have aortas that are less stiff than normal individuals of the same age[11]. Disorders such as atherosclerosis[12, 11], diabetes mellitus[13], and the Marfan syndrome[14] also influence aortic stiffness. Diabetics have increased aortic stiffness, possibly due to early atherosclerosis[13]. The Marfan syndrome is commonly associated with an increased aortic stiffness[14], which is thought to be the source of the high aortic aneurysm and rupture rates in this population[15]. Aortic elasticity also affects left-ventricular afterload[16].

Measurements of vessel-wall mechanics may provide information about the progression of these diseases, and their response to therapy. For example, Boese et al. are attempting to characterize aortic aneurysms based on their mechanical properties[17], while Groenink et al. have assessed the response of Marfan patients to beta-adrenergic blocking agents[18] using measurements of aortic elasticity.

A non-invasive method to characterize vessel wall elasticity would be a valuable research tool to investigate the risk of developing arterial disease, and to monitor disease progression and response to therapy. The following section introduces methods for quantifying these mechanical properties.

---

1The Marfan syndrome is a genetic disorder that disrupts the normal production of a structural protein named fibrillin. A symptom of the disorder is an increased aortic stiffness.
1.2.2 Quantification of Vessel Elasticity

A common measure of the mechanical properties of the aortic wall is called the distensibility. Distensibility, $D$, is defined as the fractional change in vessel cross-sectional area, $\Delta A/A$, for a given change in blood pressure, $\Delta p$:

$$D = \frac{\Delta A/A}{\Delta p}.$$  \hspace{1cm} (1.1)

A vessel with a low distensibility is stiff, while a vessel with a high distensibility is flexible.

Distensibility calculations using Eq. 1.1 require measurements of vessel area and pressure from at least two phases of the cardiac cycle. Vessel area can be measured non-invasively with a cross-sectional imaging technique such as MR or ultrasound, but pressure measurements require a catheter-based pressure transducer to be inserted into the vessel. Aortic pressure estimates based on radial artery pressure measurements have also been developed[19], but the accuracy of these techniques, especially when applied to patients with systemic vascular disease, is currently under debate[20, 21].

Catheters can provide measurements of pressure, but such studies are costly and require a cardiologist. Furthermore, catheterization may disrupt the mechanical state of the vessel under investigation. If the device comes into contact with the vessel wall, it can change the smooth-muscle tone of the wall and the apparent distensibility of the vessel[22, 23]. For this reason, Stefanadis et al.[22] proposed that hemodynamic indices equilibrate for 20 minutes after catheterization, and at least 30 minutes after infusion of contrast media, before recording measurements of distensibility. Invasive measurement devices also alter
the blood flow in the vessel, which may affect the measurement. Tasu et al. reported[24] that flow disturbances were visible up to 10cm beyond the tip of their pressure catheter, which limited how closely two simultaneous measurements of pressure could be made in their experiments. Finally, anesthetics can affect the cardiovascular state of the patient, which indicates that distensibility measurements should be performed in conscious subjects[25, 26].

Alternatively, distensibility can be calculated from measurements of the pulse-wave velocity (PWV). This parameter refers to the speed at which a pressure wave propagates down a vessel, and is related to the distensibility by the Moens-Korteweg equation and its variants[27]. Use of this relationship leads to the following expression for distensibility:

\[
D = \frac{1}{\rho \cdot (\text{PWV})^2},
\]

where \(\rho\) is the density of blood. Equation 1.2 shows that the PWV will be higher in a less distensible vessel. Values for the aortic PWV normally exceed 3m/s, depending on the age of the subject and the site of the measurement[28]. Diseases that affect the aortic distensibility also change the aortic PWV. For example, patients with the Marfan syndrome have an approximately 20\% higher PWV than normal for their age[29]. An aortic PWV greater than 13m/s appears to be a predictor of cardiovascular mortality[30].

Equation 1.2 provides an indirect calculation of distensibility from measurements of the PWV and \(\rho\) only. The advantage of this expression over Eq. 1.1 is that the PWV can be determined non-invasively from measurements of blood flow. A description of how the propagating pressure wave initiates blood flow is presented in the following model.
A simple model of pressure-wave transmission in the aorta was developed, and is depicted in Fig. 1.1. This model is the basis of the PWV measurements presented later in Chapter 4. The model assumes that the pressure in the left ventricle increases linearly with time during contraction, and that the resulting pressure wave travels without attenuation at a constant velocity over the measured segment of the aorta. These conditions create a constant pressure gradient with respect to position along the vessel. Assuming that the effect of blood viscosity is small, this spatial pressure gradient will accelerate the blood at a constant rate until the end of systole, as described by the Navier-Stokes equation[31].

Figure 1.1: Simple model of pressure-wave transmission in the aorta. The figure depicts the pressure in the aorta as a function of position down the vessel and time. The thick dashed line represents the wavefront, or “foot”, of the pressure wave traveling at a constant velocity of 5m/s. In this model, the pressure at each position is initially equal to the diastolic pressure of 80mmHg. During systole, the pressure increases linearly with time until it plateaus at the systolic pressure of 118mmHg, 50ms later. This pattern is the same at all positions, except for a delay in the onset of the pressure rise. This delay corresponds to the transit time of the pressure wave down the aorta. According to this model, a linear rise in pressure with respect to time, combined with a constant PWV, produces a constant pressure gradient with respect to position, until the end of systole. The thick solid lines depict the pressure at a fixed position (z') as a function of time, and the pressure at a fixed time (t') as a function of position.
similar relationship between flow and pressure was derived from the Navier-Stokes equation by Fry[32]. The prediction of constant acceleration derived from this model is corroborated by MR measurements of flow in the literature, which show that the aortic blood velocity increases at an approximately linear rate for over 30ms following the start of systole[17].

The onset of acceleration coincides with the leading edge, or “foot”, of the pressure wave (see Fig. 1.1). It is therefore possible to measure the PWV by detecting the onset of systolic blood flow at different positions along the vessel. The equation for the PWV is given by:

\[ \text{PWV} = \frac{\Delta z}{\Delta t}, \]  

where \( \Delta z \) is the distance between two blood-flow measurements in the aorta, and \( \Delta t \) is the time between the onset of flow at those two sites.

Non-invasive measurements of the PWV have been performed using such methods as Doppler ultrasound[3] and phase-contrast MR[33] to detect blood flow. Doppler ultrasound is able to provide measurements of flow with high temporal resolution, but it is limited by the need for an acoustic window to the aorta and hardware to record flow at two sites[34]. Phase-contrast MR can provide detailed images of velocity, but it is relatively slow and requires data to be collected across multiple heartbeats and later combined[35]. Advanced MR measurements of flow have been developed that reduce the acquisition time[36], but data from multiple heartbeats must still be amalgamated in order to calculate the PWV with these methods[37]. In the next two sections, the consequences of combining data from
multiple heartbeats are discussed, and a strategy for obtaining faster MR measurements of blood flow is described.

1.3 Importance of Fast Blood-Flow Measurement

Magnetic-resonance imaging measurements of flow are relatively slow. On a modern clinical MR scanner, for example, approximately 50ms are required to acquire an image with a spatial resolution of 1.5mm×3mm and a field of view of 20cm×40cm using a method called echo-planar imaging[38]. This temporal resolution may be sufficient to capture the physiological motion of most structures, including the systolic motion of the heart. However, a pressure wave moving at 5m/s would travel 25cm in this time, making its measurement difficult (if not impossible) at such low temporal resolution.

In order to increase the effective temporal resolution of flow measurements, cardiac triggering is often used to combine data collected from different heartbeats. If the pattern of flow is not exactly the same following each cardiac contraction, this procedure can introduce errors to the flow measurement. These beat-to-beat changes can result from cardiac arrhythmia and changes in cardiac contraction due to respiration[4]. Errors in the electrocardiogram triggering of the data acquisition also affect the accuracy of the data amalgamation. Triggering errors are enhanced by respiration, which moves the heart and alters the received electrocardiogram signal[5].

These effects can introduce systematic errors to blood flow measurements that span multiple heartbeats. For example, consider that blood flow is measured at two levels of the
aorta 20cm apart in order to calculate the PWV. If the acquisition of the distal blood-flow measurement is erroneously delayed by only 10ms relative to the other, and the PWV is 5m/s, the measurement will underestimate the PWV by 1m/s (20%). According to Eq. 1.2, this error translates to a 40% error in the calculated distensibility. The PWV error produced by this delay would increase if the distance between the measurement locations was smaller or the PWV was higher. The accuracy needed for PWV measures will depend on the specific application. Given the large biological variability of the PWV[10], an accuracy of 1m/s may be sufficient to distinguish population differences. For longitudinal studies of individual subjects, however, a greater accuracy may be needed.

A straight-forward approach to eliminate this trigger error is to collect all the flow data in one heartbeat. Data from consecutive heartbeats would then provide independent flow measurements, which could be averaged together later. This approach was adopted by Gary McVeigh et al. using Doppler ultrasound to measure flow in the aorta[39]. In their study, flow data were collected each heartbeat, temporally aligned, and averaged. Each flow measurement was statistically compared with the measured average, and either included in the average or discarded. Magnetic resonance measurements of flow generally assume that the data is acquired under exactly the same conditions each heartbeat, or that beat-to-beat fluctuations will average to zero when the data are combined, which is not strictly true[40]. This argues for a flow measurement that can be completed in a single heartbeat. Such a measurement could also be used to quantify beat-to-beat changes in the flow, as will be shown in Chapter 4.

There are also immediate clinical benefits to fast MR measurements of blood flow.
By reducing the total scan time of the study, patients may spend less time in the magnet. The risk of corrupted data due to patient motion is also reduced. Fast measurements reduce or eliminate the need for breath holding\(^2\), which can be difficult for cardiovascular or disoriented patients. Finally, measurements with high temporal resolution would allow flow under changing physiological conditions to be investigated (e.g., during stress testing or pharmaceutical treatment).

There is a limit, however, to how quickly a flow-sensitive MR image can be acquired. This limit is due primarily to the speed with which the spatial distribution of the MR signals can be resolved, or "spatially encoded". The next section explains this limitation in greater detail, and introduces a strategy to compensate for it using volume-selective excitations.

### 1.4 Volume-Selective Excitations

The formation of an MR image can be divided into two general steps: excitation and readout. Excitation refers to the generation of an MR signal, while readout refers to the acquisition of that signal.

The spatial distribution of signal produced by an excitation can be tailored to the specific imaging needs. Excitations are most often used to generate signal from thin cross-sectional slices through the anatomy. These excitations are called "slice-selective" excitations, and are used to create two-dimensional (2D) images. Alternatively, a "non-selective" excitation can be used to generate signal from throughout a large volume and obtain 3D

\(^2\)Breath holding refers to the practice of collecting MR data while the patient suspends respiration. The purpose of breath holding is to eliminate respiratory motion during data acquisition, which would otherwise corrupt the data.
CHAPTER 1. INTRODUCTION

images.

A drawback of 2D and 3D MR imaging methods is that they are relatively slow. This limitation results primarily from the need to spatially encode each dimension of the image using magnetic-field gradients. The maximum amplitude and slew-rate of these gradients limits the speed with which the MR signals can be spatially encoded. Increasing the number of spatially-encoded dimensions generally lengthens the acquisition (e.g., a 3D acquisition is often longer than a 2D acquisition).

This suggests that the acquisition time can be reduced by spatially encoding fewer dimensions. However, the MR signals distributed along any unresolved dimension of the excited volume will be combined by such an acquisition (i.e., projected onto the spatially-encoded dimensions). For example, an excited volume that is spatially encoded along only two dimensions results in a 2D projection of the volume. A familiar example of 2D-projection imaging is standard X-ray imaging. Projections cause anatomical structures to overlap, which may obscure the signal of interest. For this reason, excitations are used that reduce the thickness of the excited volume along the unresolved dimensions. Volume-selective excitations are a general class of excitations that can restrict the excited volume along one or more spatial dimensions, and so can be applied to this problem.

In this thesis, 3D volume-selective excitations are used to excite volumes of blood within the lumen of the aorta. One-dimensional spatial encoding is then used to record the motion of the excited blood at high temporal resolution. Such a measurement relies on the fact that blood in large vessels moves primarily along one direction (i.e., along the length of the vessel). Therefore, only that spatial dimension needs to be encoded in order to measure
the bulk motion of blood in the vessel.

A variety of volume-selective excitations are used in the following chapters. The first is named STimulated Echo Acquisition Mode (STEAM)[41], which is used to excite a box-shaped volume. The volume is selected by consecutively exciting three orthogonal slices such that only the volume of their intersection produces a measured MR signal (see Fig. 1.2a). The STEAM excitation is selected for its ability to excite small volumes quickly (e.g., $(3\text{mm})^3$ in less than 15ms). The second method combines two separate excitations.

![Illustration of volume-selective excitations](image)

Figure 1.2: Illustration of volume-selective excitations used in this thesis. (a) The STEAM sequence excites three orthogonal slices, and generates a measured MR signal from the volume of their intersection. (b) A combination of a SPAMM excitation with a cylindrical excitation generates MR signals from a column of evenly-spaced discs. In both (a) and (b), the vertical direction corresponds to the long axis of the vessel, which is the only spatially-encoded dimension in these measurements.
One is called SPAtial Modulation of Magnetization (SPAMM)\cite{42}, which is used to excite a series of evenly-separated parallel planes. The SPAMM excitation is chosen for its ease of implementation and short duration (e.g., less than 2ms). The other is called a cylindrical or 2D-selective excitation\cite{43, 44}, which is used to excite a cylindrical volume perpendicular to the parallel planes of the SPAMM excitation. A cylindrical volume is used because it is similar to the expected shape of the aortic lumen. The combination of the SPAMM and cylindrical excitations produces a column of evenly-spaced discs, or "tags", as shown in Fig. 1.2b. The manner in which these excitations are used to measure blood flow is detailed in later chapters.

The concept of using volume-selective excitations to improve the temporal resolution of MR motion measurements is not new. Pearlman et al. used such an approach to measure myocardial and heart-valve motion\cite{45}, while Korin et al. made quantitative measurements of the respiratory kinematics of the upper-abdominal organs\cite{46}. Measurements were later developed of the velocity spectrum of blood\cite{36, 47}, the motion of the brain and cerebrospinal fluid (CSF)\cite{48}, and the diffusion of water in the brain\cite{49}. Vasanawala et al. used volume-selective excitations with a velocity-encoding acquisition to detect the onset of flow in the aorta, which could be used as a wireless method for triggering an acquisition to the cardiac cycle\cite{50}.

One-dimensional MR measurements have also been used to measure the PWV in the aorta. Hardy et al. used 1D measurements of velocity spectra to track pressure waves in the aorta of human volunteers\cite{51}. However, in order to obtain velocity spectra at high temporal resolution, this method required data to be collected over a period of one to
four minutes. A goal of this thesis is to measure blood flow in a single heartbeat. This is accomplished by combining 3D-selective excitations with novel processing algorithms. It will be shown that independent flow measurements can be obtained each heartbeat by using appropriate volume shapes and processing algorithms. The following chapters develop such measurements, as outlined in the next section.

1.5 Thesis Hypothesis and Outline

The novel use of volume-selective excitations in the MR measurement of blood flow is investigated in this thesis. The hypothesis of this thesis is that volume-selective excitations can be used to obtain an independent MR measurement of blood flow each cardiac cycle. The following three chapters present incremental advances in a method for measuring the motion of blood in the aorta.

Chapter 2 introduces an MR method for measuring the motion of a bolus of blood traveling down the aorta. An analysis of several effects that could confound the measurement is presented, along with a demonstration of the method in both an experimental apparatus and a human subject. This work has been published in the Journal of Magnetic Resonance Imaging[52].

Chapter 3 extends this work by developing a method able to measure blood flow at multiple positions along a vessel simultaneously. The effect of the velocity profile of the flow is included in the analysis of the 1D measurements. Validations of this method in both an experimental apparatus and a human subject are presented. This work has been accepted
for publication in Magnetic Resonance in Medicine.

Chapter 4 applies the method developed in Chapter 3 to the measurement of the aortic PWV. A method for detecting the systolic pressure wave from the 1D measurements of blood flow is developed, and used to calculate the PWV in human volunteers. The method is also used to measure beat-to-beat changes of the flow. This work is being prepared for submission to the Journal of Magnetic Resonance Imaging.

In Chapter 5, a summary of the thesis is presented. A description of future research and potential applications of this work is also included, along with speculations on the clinical relevance of measurements of aortic distensibility.
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Chapter 2

Motion Measurements from Individual MR Signals Using Volume-Selective Excitations

2.1 Introduction

The motion sensitivity of magnetic resonance (MR) is exploited by numerous techniques to measure organ displacement and blood flow. Some MR techniques for measuring motion rely on changes in the phase of the MR signal due to motion through a magnetic-field gradient[2, 3]. The most common phase-sensitive methods are phase-contrast (PC)[4, 5] and Fourier velocity encoding (FVE)[4, 6, 7]. These methods produce images of velocity, which are useful for detecting regional variations of motion (e.g., blood flow through stationary tissue). Creating images requires spatial encoding, which leads to a relatively low temporal resolution and a long collection time. As a result, these methods may not accurately measure motions that change rapidly in time. When investigating the bulk motion of a single organ

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1This chapter is published in the Journal of Magnetic Resonance Imaging[1].
or flow through one vessel, motion measurements across an entire slice are superfluous. This suggests that measurements of motion can be performed with reduced spatial encoding to increase the temporal resolution\cite{8,9,10,11}.

This chapter presents a novel MR method for measuring the trajectory of a designated structure, based on changes in the frequency of an MR signal from the structure as it moves. The hypothesis is that blood position can be measured every few milliseconds using volume-selective excitations and reduced spatial encoding. This chapter describes the basic principles of the method, including sources of error, and demonstrates the method on a commercial MR imaging system through experiments with a moving phantom and a human subject. Measurements of the displacement of blood in the aorta are presented.

2.2 Theory

The approach developed to measure motion begins by exciting a small volume of flowing blood, and then applies a magnetic-field gradient along the direction of motion. As the excited volume of interest (VOI) moves, the precessional frequency of its transverse magnetization changes. This time-dependent frequency, \( f(t) \), is given by:

\[
f(t) = \frac{\gamma}{2\pi} \hat{r}(t) \cdot \vec{G}(t),
\]

where \( \hat{r} \) is the position of the VOI with respect to the gradient \( \vec{G} \), both of which depend on time, \( t \), and \( \gamma \) is the gyromagnetic ratio. Since \( G(t) \) is known, calculating position requires the measurement of \( f(t) \) from the MR signal.
CHAPTER 2. MOTION MEASUREMENTS FROM INDIVIDUAL MR SIGNALS

The frequency of a signal at a point in time, also called the instantaneous frequency (IF), can be calculated in many ways[12]. The IF is defined here as the rate at which the phase of the transverse magnetization changes, expressed here as a discrete forward difference:

\[ \dot{f}_n = \frac{\phi_{n+1} - \phi_n}{2\pi \Delta t}, \]  

where \( \dot{f} \) is the estimated IF of the signal, \( n \) denotes the sample number of the signal, and \( \Delta t \) is the sampling interval between the phase measurements \( \phi_{n+1} \) and \( \phi_n \). Combining Eqs. 2.1 and 2.2 leads to the following expression:

\[ r_n = \frac{\phi_{n+1} - \phi_n}{\gamma G_n \Delta t}, \]  

where \( r_n \) and \( G_n \) are the discrete position and gradient values, respectively. The gradient used to encode displacement can be an arbitrary shape, but an oscillating gradient is used because it also refocuses the signal periodically. In this chapter, the data collected following one excitation is considered to constitute a single MR signal.

Several factors other than motion affect the phase evolution of the signal and can confound the IF calculation. To understand the origin and magnitude of these effects, it is useful to represent the measured signal, \( s(t) \), by the following equation:

\[ s(t) \propto e^{-t/T_2^\ast} \int \int _{-\infty}^{+\infty} M(\tau_o) e^{-i\gamma \int_0^t G(\tau') r(\tau') d\tau'} d\tau_o, \]  

(2.4)
CHAPTER 2. MOTION MEASUREMENTS FROM INDIVIDUAL MR SIGNALS

where $M(\vec{r}_0)$ is the distribution of magnetization immediately following excitation, which decays with a time constant $T2^*$. 

Assuming that a gradient $G_z(t)$ is applied in the z-direction only, Eq. 2.4 can be decomposed into three factors. These factors represent the effects of signal decay, excitation profile, and displacement, as delimited by square brackets in the following equation:

$$s(t) \propto \left[ e^{-t/T2^*} \right] \left[ \int \int_{-\infty}^{+\infty} \text{FT}_z \{M(\vec{r}_0)\} \, dx_0 \, dy_0 \right] \left[ e^{-i\gamma \int_0^t G_z(t') \cdot \Delta z(t') \, dt'} \right], \quad (2.5)$$

where $\text{FT}_z\{\cdot\}$ denotes the Fourier Transform (FT) along the z dimension. Given $s(t)$, the goal is to extract from Eq. 2.5 the displacement of the VOI in the z-direction, $\Delta z(t')$.

The phase of the signal, $\phi(t)$, is the sum of the phases contributed by each time-dependent factor in Eq. 2.5. The phase from the first factor is identically zero because the exponential function is purely real. Phase contributions from the second factor are zero if the slice profile is symmetric in the z-direction (since the FT of a symmetric function is purely real). If the third factor is the only significant contributor to $\phi(t)$, the phase of the measured signal is given by the following expression:

$$\phi(t) = \gamma \int_0^t G_z(t') \cdot \Delta z(t') \, dt',$$ \quad (2.6)

which is the integral form of Eq. 2.1. The displacement accuracy of this method is analyzed in the following section.
2.2.1 Error Analysis

Effect of SNR

Given the relationship between position and frequency expressed in Eq. 2.1, the random error (standard deviation) of a position measurement made with this method, \( \sigma_r \), is given by:

\[
\sigma_r = \frac{2\pi}{\gamma|G|} \sigma_f,
\]

(2.7)

where \( \sigma_f \) is the error in the frequency calculation and \( |\cdot| \) denotes the absolute value.

From Eq. 2.2, an expression for \( \sigma_f \) can be derived in terms of errors in the phase measurements, \( \sigma_\phi \):

\[
\sigma_f \approx \frac{\sqrt{2}}{2\pi \Delta t} \sigma_\phi,
\]

(2.8)

assuming that the noise is uncorrelated and of similar magnitude between successive phase measurements.

The phase of an MR signal has an uncertainty which is well approximated for high SNR by [13]:

\[
\sigma_\phi = \frac{\sigma_M}{M} = \frac{1}{\text{SNR}},
\]

(2.9)

where \( M \) is the amplitude of the signal, with uncertainty \( \sigma_M \).
Combining Eqs. 2.7, 2.8, and 2.9 results in the following expression for $\sigma_r$ in terms of the gradient strength, sampling interval, and SNR:

$$\sigma_r \approx \frac{\sqrt{2}}{\gamma |G| \Delta t \text{SNR}}.$$  \hspace{1cm} (2.10)

For example, an uncertainty on the order of 0.5mm results from a time resolution of 1ms, a gradient strength of 1mT/m, and an SNR of 10. Since the SNR of a signal changes over its lifetime (e.g., due to decay), $\sigma_r$ also changes with time. A demonstration of this effect is presented in Fig. 2.1.

As Eq. 2.10 shows, one way to reduce $\sigma_r$ is to increase the strength of the readout gradient. However, this increases the bandwidth (i.e., the range of frequencies) of the signal and leads to more rapid dephasing across the excited volume and, hence, signal decay. One way to reduce dephasing is to reduce the slice thickness, which also reduces the maximum amplitude of the signal. A better solution is to use an oscillating readout gradient to rephase the signal periodically, similar to echo-planar imaging but without phase encoding.

It is advantageous to preserve the strength of the signal for as long as possible, so that motion can be measured for a longer time following a single excitation. Ideally, $T2^*$ decay limits the total time over which accurate calculations of $\bar{\tau}(t)$ can be made. If an adequate SNR cannot be maintained over an entire readout, it is possible to average adjacent samples within one signal, which reduces the effective temporal resolution. Averaging $N$ independent phase measurements of one signal increases $\Delta t$ by a factor of $N$ and increases SNR by a factor of $\sqrt{N}$, thereby reducing $\sigma_r$ by a factor $N\sqrt{N}$. Such smoothing is an effective means
Figure 2.1: Effect of random noise on the calculation of the IF. The data were simulated to represent magnetization moving at a constant velocity of 10mm/s through a linear magnetic-field gradient of 1mT/m. The signal was given a Gaussian envelope to mimic the effect of signal refocusing. (a) Real part of a signal sampled every 100µs with a peak SNR of 10, (b) unwrapped phase of the signal, and (c) frequency and displacement calculated from the forward difference of the phase, including a linear fit to the data (solid line). The signal was created with a linearly increasing frequency, and had zero-mean Gaussian white-noise added separately to the real and imaginary components. The quoted SNR was calculated from the maximum signal amplitude relative to the standard deviation of the noise. The error bars in (c) were derived using Eq. 2.10, and show how the displacement accuracy varies with the signal strength. Systematic sources of error were not included in this simulation. The effective time resolution of the displacement calculations was 3.3ms.
Effect of Signal Contamination

In practice, tissues surrounding the VOI are also excited and contaminate the MR signal. This signal contamination biases displacement measurements if the position of the contaminant differs from that of the VOI. The mechanism of this error is illustrated in Fig. 2.2a. Such a source of error is similar to partial-volume effects in PC imaging[14].

![Figure 2.2: (a) Vector diagram illustrating the effect of signal contamination from stationary tissue on displacement calculations. \( \tilde{S}_C \) and \( \tilde{S}_V \) represent the transverse magnetization from stationary contamination and the moving VOI, respectively. \( \tilde{S}_V \) precesses at frequency \( f_V \), determined by the displacement of the VOI, while \( \tilde{S}_C \) remains fixed in the rotating frame of reference. The measured magnetization, \( \tilde{S}_T \), precesses at a frequency \( \hat{f}_T \) which differs from \( f_V \) and leads to an incorrect displacement calculation. (b) Fluctuation in apparent frequency in the presence of 5% contamination. The rate at which \( \hat{f}_T \) oscillates depends on \( f_V \), while the magnitude of the oscillations is proportional to the relative contamination.](image)

Assuming that the major contribution to signal contamination is from stationary tissue, the measured frequency, \( \hat{f}_T \), varies over a range of frequencies specified by:

\[
f_V \cdot \left( 1 + \frac{S_C}{S_V} \right)^{-1} \leq \hat{f}_T \leq f_V \cdot \left( 1 - \frac{S_C}{S_V} \right)^{-1},
\]  

(2.11)
where \( f_V \) is the desired frequency of the signal from the VOI, and \( S_V \) and \( S_C \) represent the signal magnitude from the VOI and contaminant, respectively. Interference between these two signals creates a beat pattern with a time-varying frequency. If \( S_C \) is small relative to \( S_V \), then the measured frequency varies sinusoidally as shown in Fig. 2.2b, with the following root-mean-squared (RMS) error, \( \sigma_{fc} \):

\[
\sigma_{fc} \approx \frac{f_V}{2} \cdot \frac{S_C}{S_V} \quad \text{for } S_V \gg S_C. \tag{2.12}
\]

For small contamination, \( \sigma_{fc} \) (and \( \sigma_r \)) are proportional to the relative amount of signal contamination.

**Effect of Excitation Profile**

The shape of the excited volume affects the frequency of the signal. As shown in Eq. 2.5, \( s(t) \) depends on the FT of the distribution of magnetization, \( M(\vec{r}_o) \), along the direction of the gradient. If \( M(\vec{r}_o) \) is symmetric along this direction, then its FT is purely real and does not affect \( \phi(t) \). If \( M(\vec{r}_o) \) is asymmetric, then its FT is complex, which confounds the motion measurement.

The analysis of this effect is similar to that for signal contamination. As shown in Fig. 2.3, any profile can be decomposed into symmetric and anti-symmetric components. The resulting RMS frequency error, \( \sigma_{fp} \), is given by:

\[
\sigma_{fp} \approx \frac{f_A}{2} \cdot \frac{S_A}{S_S} \quad \text{for } S_S \gg S_A, \tag{2.13}
\]
where \( S_s \) and \( S_A \) represent the signal magnitudes from the symmetric and anti-symmetric profiles, respectively, and \( f_A \) is the frequency of \( S_A \). This approximation requires that \( S_s \) is large relative to \( S_A \).

### 2.3 Materials and Methods

A pulse sequence to measure displacement according to the method outlined above was implemented and tested on a commercial 1.5 Tesla (T) whole-body MRI system (GE Signa Advantage, General Electric Medical Systems, Milwaukee, WI) with fast gradient hardware (maximum amplitude 22mT/m, rise time 184\( \mu \)s). Two volume-selective methods were implemented: stimulated-echo acquisition mode (STEAM)\[15\], and two-dimensional (2D) selective excitation\[16\] (see Fig. 2.4). A slice-selective 180° pulse was used in conjunction with the 2D-selective excitation to obtain three-dimensional localization. Both excitation
CHAPTER 2. MOTION MEASUREMENTS FROM INDIVIDUAL MR SIGNALS 35

schemes required 15ms to execute.

These two volume-selective methods were evaluated by comparing their associated SNR and signal contamination in the brain of a human subject. For this purpose, an imaging sequence was added to the end of each excitation to depict the excited VOI. These images also verified the location of the excited VOI for subsequent motion measurements. All data were collected using a three-inch diameter surface coil placed posterior to the head. Sequence parameters for imaging were: TR/TE = 800ms/20ms, FOV = 24cm, and matrix size 256x256. The size of the VOI varied, but was approximately 5mm along the direction of motion and 10-20mm in the orthogonal dimensions, depending on the size of the anatomy.

Gradient spoiling was used in the STEAM sequence to reduce unwanted stimulated echoes. Increased spoiling reduces signal contamination but lengthens TE and reduces SNR. The SNR and contamination were measured in vivo to find the optimal amount of spoiling. Spatial presaturation was used to suppress signal from tissue between the VOI and the surface coil. The 2D-excitation pulse was designed such that the first aliasing ring occurred outside the body or far from the surface coil.

The SNR for each sequence was calculated using the mean signal amplitude in a region within the VOI and in a region containing only background noise. Contamination was calculated by thresholding each magnitude image to remove background noise (which would have appeared as a large contaminant) and then computing the fraction of signal outside the VOI. Based on its superior suppression of signal from surrounding structures, STEAM was chosen for subsequent motion measurements.

The impact of several sequence parameters on the signal strength was investigated
Figure 2.4: Diagram of (a) STEAM and (b) 2D-selective sequences for performing motion measurements. The STEAM sequence consists of three slice-selective excitations along orthogonal axes to produce a signal from a block of tissue. The 2D-selective sequence excites a column of tissue and, when followed by a slice-selective 180° pulse, produces signal from a disk of tissue. Readout occurs shortly after excitation during the application of trapezoidal gradients which encode motion and periodically rephase the signal. In both sequence diagrams, only eight readout trapezoids are shown, although as many as 64 were used in practice.
experimentally. These factors included echo-train length (ETL), volume size, and gradient amplitude.

Motion measurements were performed on a phantom to validate the method and assess its accuracy. The phantom consisted of a plastic sphere (inner diameter approximately 9cm) filled with CuSO$_4$-doped water ($T_1$ and $T_2$ both approximately 80ms). The phantom was translated along the bore of the magnet by moving the patient table at a constant velocity. Sequence parameters for these measurements were: TR/TE = 2000ms/20ms, matrix size 2048x64, and receive bandwidth of ±16kHz. The size of the VOI along the readout direction and the size of the readout gradient were limited by the bandwidth of the signal they produced. The orthogonal dimensions of the volume were between 10 and 15mm.

An oscillating trapezoidal gradient was used as the readout gradient for the motion measurement. The strength and width of these trapezoids varied, depending on the expected range of motion. Typical values for the maximum gradient strength were 1-2mT/m, with 32 bipolar trapezoids over approximately 65ms. Since the data collected during gradient ramping were discarded, the number of trapezoids used during readout was capped at 64 to limit the amount of dead-time. When using positive and negative trapezoids of equal amplitude (2mT/m), the dead-time was 6%.

Despite efforts to reduce systematic errors, sub-millimeter displacements continued to be affected by errors attributed to an asymmetric profile. To remove this error from the measurement of small displacements, a baseline signal was calculated and its phase was subtracted from each motion measurement. The baseline was generated by computing the mean of signals collected without gating. The effects of motion on the baseline were
assumed to average to zero, leaving only systematic effects to dominate any changes in phase. Frequency calculations were then performed by differentiating the baseline-corrected phase of each MR signal. From these calculations, \( r(t) \) was found using Eq. 2.3. It was unnecessary to apply a baseline correction to data collected while the phantom was moving quickly, since motion effects dominated \( \phi(t) \) in that case.

Displacement calculations were temporally averaged (i.e., smoothed) to improve SNR and obtain a suitable displacement resolution (see Eq. 2.10 and the description at the bottom of page 30), which also reduced the effective time resolution of the measurement. All data used in these averages were weighted equally. Before smoothing the data, it was necessary to remove the effect of the oscillating gradient from the phase of the signal. This was accomplished by inverting the phase measurements acquired during the odd trapezoids, and then piecing them back together with the remaining phase measurements. Smoothing the data without first removing the effects of the gradient leads to biased frequency calculations, because both motion and the readout gradient alter the frequency of the signal. Examples of pre- and post-processed phase measurements are provided in the Results section.

Displacement measurements were performed while moving the phantom at various constant velocities. The phantom velocity was then calculated from the slope of each displacement-time curve and compared to the known velocity imparted by the patient table.

The relatively plug-like motion of blood in the descending aorta[17] of a human subject was investigated as an in-vivo demonstration of this new method. Data acquisition was ungated with a TR of 250ms, and used a five-inch diameter surface coil. The high velocity of blood in the aorta was monitored with a gradient strength of 0.5mT/m, which
allowed a relatively thick VOI of approximately 10mm along the direction of the gradient. Baseline corrections were not necessary, because systematic phase changes were negligible compared to the phase changes caused by blood flow.

Blood velocity was calculated from the slope of a linear fit to the collection of displacement measurements. A linear fit was chosen based on observations that the blood velocity was often constant over the acquisition period. This velocity was then compared with velocity measurements made with a commercial retrospectively-gated PC technique. Displacement-time curves which did not appear to have constant velocity were not used for these calculations.

2.4 Results

The accuracy of displacement measurements made with this method was found to depend on the quality of the volume-selective excitation. An in vivo comparison of the STEAM and 2D-selective excitations is presented in Table 2.1. As expected, the SNR from the STEAM sequence was approximately one-half that of the 2D excitation[18] when normalized by the volume thicknesses of 6mm and 5mm, respectively. Signal emanating from fat in the scalp

<table>
<thead>
<tr>
<th></th>
<th>STEAM</th>
<th>2D Selective</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNR</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>% Contamination</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Volume Thickness (mm)</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>
was a problem with the 2D excitation, even when spatial presaturation was used. STEAM resulted in considerably less contamination when adequate gradient spoiling was used. Based on these contamination measurements, the relative RMS error in the IF calculation would be 1% and 3% for the STEAM and 2D-selective excitations, respectively (see Eq. 2.12).

The dependence of the signal amplitude on ETL, volume size, and gradient amplitude is shown in Fig. 2.5. A large ETL was essential to maintain high SNR during the entire readout. By refocusing the signal often, the time over which accurate displacement measurements could be made was increased (see Fig. 2.5b). The duration of each trapezoid was less than the time needed to dephase the signal with the gradient.

Figure 2.5: Phantom data illustrating the effect of several parameters on the signal amplitude: (a) reference, with typical values used for the measurements, (b) echo-train length (ETL), (c) volume thickness along the direction of the readout gradient, and (d) readout-gradient amplitude.
CHAPTER 2. MOTION MEASUREMENTS FROM INDIVIDUAL MR SIGNALS 41

A second step for preserving the signal strength was to limit dephasing by reducing the bandwidth of the signal. This was accomplished by varying the volume thickness and readout-gradient amplitude. The effect of these parameters on the signal amplitude is shown in Figs. 2.5c and d. Increasing the volume thickness resulted in a larger maximum amplitude, but also a sharper drop in amplitude between echoes. This was similar to the effect from increasing the gradient strength, which improves motion sensitivity without altering the maximum signal amplitude.

The results from applying the motion measurement method to a moving phantom are shown in Fig. 2.6. These measurements were performed over a wide range of velocities, although the results for only one case are plotted. The velocity calculated from the slope of these displacement data is indicated in Fig. 2.6, which agrees with the velocity calculated from projections of the moving phantom collected every 50ms.

The amplitude and frequency of the oscillating readout gradient were chosen such that the SNR of the signal was continuously greater than 30 during the entire readout. The resulting displacement calculation was then smoothed to increase SNR and achieve a theoretical displacement accuracy of approximately ±3μm, as determined from Eq. 2.10. This smoothing reduced the temporal resolution of the displacement measurement to approximately 2.6ms.

Differences between these displacement measurements and the linear fit to the data were greater than expected from only random noise (reduced-χ² of 25). This discrepancy was likely a result of actual variations in the phantom motion, and errors introduced at the boundaries of each readout trapezoid by the procedure for removing the effects of the
Figure 2.6: Experimental validation of motion measurement using a phantom moving at a constant velocity. (a) Signal refocused 64 times with an oscillating trapezoidal gradient of 2mT/m to maintain a large signal amplitude. (b) Raw phase of the signal. (c) Frequency and displacement calculated from (b). The uncertainty of each position measurement was determined from the SNR of the signal at each time and the amount of smoothing. After averaging adjacent data from one signal, the effective time resolution was approximately 2.6ms. The uncertainty is not shown because it was smaller than the plotting symbol. The systematic error in the displacement is attributed to the unsteady motion of the patient table. The line in (c) represents a linear fit to the data which was used to calculate the velocity of the phantom.
readout gradient. These additional errors translate to relatively small errors in absolute displacement.

The displacement of blood down the descending aorta was measured with this method at different points in the cardiac cycle. The phase of several signals exhibiting signs of motion (i.e., non-linear phase) are shown in Fig. 2.7a, and the displacement calculated from one of these curves is shown in Fig. 2.7b. After smoothing the data, the effective time resolution of the displacement measurement was approximately 2ms. The resulting

![Figure 2.7](image_url)

Figure 2.7: In vivo measurement of blood flow in descending aorta. The processed phases of several signals which exhibit obvious motion effects are shown in (a). The black arrow in (a) indicates the data used to calculate the displacement in (b). After smoothing the data, the effective time resolution of the displacement calculation was 2ms. The error of the displacement measurements was smaller than the plotting symbol and is not shown. A linear fit was performed to estimate the velocity of the blood (solid line in (b)).

displacement measurement was least-squares fitted with a line to estimate the velocity of the blood. The calculated velocity from this fit, 83±2 cm/s, was similar to the maximum
velocity measured using retrospectively-gated PC imaging (90 cm/s).

2.5 Discussion

The goal of this chapter was to develop a fast method for measuring motion. This goal was accomplished using volume-selective excitations, which enabled a greater fraction of the acquisition to be devoted to measuring motion as opposed to encoding position. This approach allows time-resolved displacement measurements to be made using only one MR signal, provided that the SNR is sufficiently large. Furthermore, the method provides a high temporal resolution, potentially as high as the sampling rate of the MR scanner. The method can be extended to monitor motion in multiple directions by applying gradients along different directions, either during one acquisition or across multiple acquisitions.

Acquiring motion information from just one MR signal is appealing for several reasons. First, measurements acquired in a single heartbeat make no assumptions about the periodicity of the flow. Second, the likelihood of gross patient movement increases with longer scan times, which can obfuscate the motion measurement. Third, displacement calculations made with this method are available immediately after each signal is acquired, making this measurement suitable for real-time applications.

In the phantom and aorta experiments, continuous displacement calculations were possible for approximately 65ms after one excitation. Displacement measurements over a longer period could be concatenated from consecutive data acquisitions. Data from different cardiac cycles can also be averaged to increase the SNR of the displacement measurements.
If the motion is not exactly periodic, for example as a result of arrhythmia, the separate displacement measurements will shift and/or stretch in time with respect to the acquisition window. With this method it is possible to reduce these errors by realigning the separate displacement measurements prior to averaging. This is possible because displacements are measured from each signal independently.

High temporal resolution is important for measuring the pulsatile motion of blood and other rapidly changing motions in the body[19]. Peaks in velocity or acceleration can be missed if the temporal resolution is too low. As shown by Eq. 2.10, the temporal resolution of the method depends on several factors. In the experiments, a reliable displacement measurements could be made with a temporal resolution of 2-3ms. This resolution can be increased by allowing a greater error in the calculated displacement. In this way, the spatial and temporal resolutions can be adjusted during post-processing, and do not need to be determined during data acquisition.

The method developed is fundamentally different from PC MRI in that the motion is measured relative to the moving structure (particle frame of reference). In contrast, PC MRI techniques measure velocity at a designated location in space. This property may circumvent errors associated with acceleration in traditional MR methods that measure velocity at a particular spatial location. For example, PC measurements assume that the velocity of the blood is constant during the velocity-encoding period, which is questionable for certain patterns of motion. Pulsatile flow or convective acceleration in the presence of stenoses leads to errors in such velocity measurements[20, 21, 22]. Acceleration and higher-order motions do not introduce errors to the displacement measurement presented in this
chapter. However, this method is restricted in scope to structures that move as a plug, or with a small dispersion of velocities across the VOI, such as the flow of blood in the aorta.

One potential application of this method is to measure the acceleration of blood in large vessels, which is related to vessel distensibility and blood pressure. Velocity and acceleration can be calculated by differentiating the displacement measurements from this method with respect to time. Differentiation amplifies noise, so greater averaging may be necessary to reduce the uncertainty.

The pulse sequence for measuring displacement is similar to that for performing volume-localized FVE[10]. The difference is that, whereas the approach presented in this chapter produces a time-resolved measurement of displacement, FVE produces a velocity spectrum from the entire data-acquisition period. An advantage of creating a velocity spectrum is that signal contamination from stationary tissue appears at the origin of the spectrum, separated from the larger velocities in the VOI. In contrast, the calculation of displacement from the IF of the signal requires contamination to be negligible.

The simple method chosen to derive the IF calculates the mean frequency of the excited VOI. This calculation assumes that the signal has a frequency spectrum that is symmetric about a mean frequency, at each point in time. If this criterion is not met, either because of contamination or volume asymmetry, then the resulting IF estimation will be erroneous. It seems likely that greater accuracy can be achieved with more sophisticated methods for calculating the IF, which perhaps include a priori knowledge about the shape of the VOI or the nature of the motion.

In conclusion, a novel method for measuring the displacement of an excited volume of
blood was developed and validated. An analysis of the sources of error associated with this method was developed to determine the theoretical accuracy of the displacement measurements, and the relative impact of the different errors. This method is suitable for measuring the flow in large vessels, but only reports the motion of a single bolus of blood. The following chapter proposes an extension to this work that is able to measure blood flow at multiple sites along a vessel.
References


REFERENCES


REFERENCES


Chapter 3

Fast Measurements of the Motion and Velocity Spectrum of Blood Using MR Tagging

3.1 Introduction

Quantitative measurements of blood motion are used to assess a range of cardiovascular conditions, including the severity of stenoses, the volumetric blood-flow to tissues, and the mechanical properties of vessel walls. While many of these measurements are currently performed with Doppler ultrasound, there are advantages to using magnetic resonance (MR) instead, such as the ability to view entire vessels, regardless of vessel angle, depth, and acoustic window.

Unfortunately, traditional MR measurements of blood motion are slow, and must often combine data from multiple cardiac cycles to improve their temporal resolution. Cardiac gating filters such measurements, and aperiodic motion introduces complex

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1This chapter has been accepted for publication in Magnetic Resonance in Medicine.
CHAPTER 3. TAGGING MEASUREMENT OF BLOOD FLOW

distortions[6]. The risk of gross patient motion also increases during longer scans. These problems would be avoided if the data from each cardiac cycle were acquired and processed independently.

This chapter demonstrates the use of volume-selective excitations to provide accurate measurements of blood motion within a single heartbeat. The measurement is an adaptation of cardiac tagging, a method first developed to measure the motion and mechanical properties of the heart[7]. Cardiac tagging often involves the simultaneous excitation of a series of parallel planes through the heart. As the heart deforms, the excited regions (or “tags”) deform as well. Rapid images of this deforming pattern provide information about the motion of the heart. Others have since exploited the high temporal resolution of tagging to visualize fluid flow[8, 9, 10]. Assuming that blood moves primarily along one dimension through large vessels, it is sufficient to apply tags to a cylinder of blood within the vessel and monitor tag motion along that dimension only. By acquiring a series of one-dimensional (1D) projections across the vessel, it is hypothesized that blood motion can be measured with high temporal resolution, similar to M-mode ultrasound[11].

Previous uses of tagging to measure fluid motion implicitly assume that tag displacement represents the mean displacement of the fluid. It is shown in this chapter that this is not strictly true. The effect of the velocity and cylindrical-excitation profiles on the evolution of these projections is studied under constant flow conditions. It is also shown that the velocity spectrum of the blood within the excited cylinder can be calculated from the interference between tags moving at different velocities. These spectra can be used to assess or remove the signal produced by static tissue, which would affect the accuracy of
the blood-displacement measurements.

3.2 Theory

One-dimensional projections of tagged blood can be used to measure blood motion. Suitable tags can be created by combining a SPAMM excitation[8] with a 2D-selective excitation[12] positioned within the vessel lumen. One-dimensional projections encode a single spatial dimension, in this case along the length of a vessel, and collapse the MR signals from the entire volume onto that axis. One complication of this approach is that the initial tagging pattern will disperse and its projection will blur when more than one velocity is present across the vessel. Figure 3.1 illustrates this theoretical effect for sinusoidal tags in a parabolic velocity profile. The motion and shape of the projections depend on $\tilde{A}(v)$, the velocity spectrum of the excited blood. The form of $\tilde{A}(v)$ depends on both the velocity profile and the excitation profile. This section derives the relationship between $\tilde{A}(v)$ and quantitative tagging measurements of motion, and examines in detail the special case of a parabolic flow profile. The section concludes with a derivation of $\tilde{A}(v)$ from projection measurements. The theory assumes that convective and pulsatile acceleration are small (i.e., $\tilde{A}(v)$ is independent of position along the vessel, $z$, and time, $t$), but extensions to pulsatile flow are presented in the Methods and Discussion sections.
3.2.1 General Description of 1D Tagging Measurements

Measurements of tagged blood with 1D projections provide information about blood flow. The magnitude of the 1D projections as a function of space and time, $g(z, t)$, is affected by several factors, including $\tilde{A}(v)$ and the initial pattern of transverse magnetization following tagging, $M(x, y, z; t = 0)$. These factors can be combined to represent the tagging pattern as $\tilde{A}(v) \cdot M(z - vt)$. This assumes that additional factors such as signal decay, coil sensitivity, and magnetic-field inhomogeneity, are uniform across the vessel cross section. These additional factors are represented collectively by the modulation function $h(v, z, t)$. The
projections can thus be considered a summation of tags moving at different velocities, each of which has the shape of the initial tagging pattern and an amplitude determined by the amount of blood moving at that velocity. The summation is given by the following integral:

$$g(z, t) = \int_{-\infty}^{\infty} \tilde{A}(v) \cdot M(z - vt) \cdot h(z, v, t) dv.$$  \hspace{1cm} (3.1)

A measurement of $g(z, t)$ is referred to as the position-time matrix in this thesis. Each column of this matrix represents a single 1D projection. Stacking 1D projections from a succession of gradient echoes as columns of a 2D matrix conveniently displays the evolution of the projections, as shown in Fig. 3.2. This figure also shows qualitatively how

Figure 3.2: Simulated effect of velocity profile and excitation profile on tag evolution. (a) Two velocity profiles, plug-like and parabolic, across a hypothetical vessel, with a maximum velocity of 0.057 m/s (chosen to match the experimental measurements in Fig. 3.7). The shaded region beneath each profile indicates the extent of a cylindrical excitation. (b) Corresponding position-time matrices, in which each column represents the intensity of a 1D projection. Signal decay was not included in the simulation.

$\tilde{A}(v)$ affects the motion of the projections. In the left frame of Fig. 3.2b, the peaks of the projections are well defined over the entire acquisition since the bulk of the flow is moving
at the same velocity. In the middle frame, tag interference results from the wide range of excited velocities. In the right frame, only the central 25% of the vessel diameter is excited. The more narrow range of excited velocities reduces tag interference, increases the velocity of the 1D projections (slope of the bright peaks in the position-time matrix), and lowers the signal amplitude.

Equation 3.1 describes 1D projections for a general tagging pattern. Assuming that phase errors due to magnetic-field inhomogeneities do not greatly affect the projected magnitude, $h(z, v, t)$ is independent of velocity and can be extracted from the integral. If a two-pulse SPAMM excitation[8] is used to tag the blood, Eq. 3.1 becomes:

$$g(z, t) = \left| \int_{-\infty}^{\infty} \tilde{A}(v) \cdot \left( 1 - \frac{\sin(\alpha)}{2} \cdot (1 - \sin[2\pi k_z (z - vt)]) \right) dv \right| \cdot h(z, t), \quad (3.2)$$

where $\alpha$ is the total SPAMM flip angle and $k_z$ is the spatial frequency of the tags. If $\alpha$ is $\pi/2$, the magnitude of the tags follows a sinusoidal pattern, and Eq. 3.2 simplifies to the following expression:

$$g(z, t) \propto (\tilde{a}(0) + \text{Im}\{e^{i2\pi k_z z} \cdot \tilde{a}(k_z t)\}) \cdot h(z, t), \quad (3.3)$$

where $\text{Im}\{\cdot\}$ denotes the imaginary component of its argument and $\tilde{a}(k_z t)$ is the Fourier transform of $\tilde{A}(v)$. The shape and motion of the 1D projections can be calculated for specific velocity and excitation profiles using Eq. 3.3. A parabolic flow profile and a cylindrical or Gaussian excitation profile are considered below.
3.2.2 Cylindrical or Gaussian Excitation Profiles & Parabolic Flow

The velocity profile of fully-developed laminar blood flow in a straight and rigid vessel is parabolic, provided that the flow is steady[13]. These conditions are not strictly met in vivo, but an analysis of parabolic flow elucidates the relationship between $g(z, t)$ and $\tilde{A}(v)$.

The velocity profile for laminar flow in a vessel of radius $R$ as a function of radial coordinate, $r$, is modeled by the general expression:

$$v(r) = v_{\text{max}} \left[ 1 - \left( \frac{r}{R} \right)^\beta \right] \quad \beta > 1,$$  

(3.4)

where $v_{\text{max}}$ is the maximum velocity, and $\beta$ is a real number. A larger value of $\beta$ models a more plug-like profile, and a value of $\beta = 2$ corresponds to parabolic flow.

The velocity spectrum for flow modeled by Eq. 3.4 is given by the following expression:

$$A(v) = \frac{2}{\beta \cdot v_{\text{max}}} \left( 1 - \frac{v}{v_{\text{max}}} \right)^{\frac{3}{\beta} - 1} \quad v \in [0, v_{\text{max}}].$$  

(3.5)

While Eq. 3.5 describes the velocity spectrum for the entire vessel, the excitation profile determines the region of the velocity profile that contributes to the MR signal. The form of $\tilde{A}(v)$ approaches that of the full spectrum, $A(v)$, as the flow becomes more plug-like or the excited cylinder encompasses more of the vessel. An ideal cylindrical excitation of radius $r_{\text{max}}$ centered in a vessel reduces the maximum signal strength by $(r_{\text{max}}/R)^2$, and does not excite the slower flow near the vessel wall. For the case of parabolic flow and a cylindrical
excitation, the position-time matrix from Eq. 3.3 equates to the following expression:

\[ g(z, t) \propto \left( \frac{r_{\text{max}}}{R} \right)^2 \cdot \left( 1 + \text{sinc}[k_z t \Delta v] \cdot \sin[2\pi k_z (z - \langle v \rangle t)] \right), \tag{3.6} \]

where \( \Delta v \) and \( \langle v \rangle \) are the velocity range and mean velocity of \( \tilde{A}(v) \), respectively. Equation 3.6 represents a sinusoidal projection moving at velocity \( \langle v \rangle \) and temporally modulated by a sinc envelope. The signal envelope, calculated from the expression \( \left( \frac{r_{\text{max}}}{R} \right)^2 \cdot \text{sinc}[k_z t \Delta v] \), is plotted in Fig. 3.3. Each row of Fig. 3.3 depicts this envelope for a given cylinder width, as a function of time after the SPAMM tags are applied. The periodic dark bands in the matrix correspond to the zeros of the sinc envelope. These zeros result from complete destructive interference of the tagging pattern across the vessel, which occurs when
the displacement between the fastest and slowest moving blood is an even multiple of the tagging period. For example, if \( k_x \cdot v_{\text{max}} = 0.05\text{ms}^{-1} \) and the entire vessel is excited, the tags periodically disappear every 20ms (see Fig. 3.2b and top row of Fig. 3.3). The frequency of the zeros can be decreased by exciting a more narrow cylinder, but this also reduces the maximum strength of the signal.

In practice, the excitation profile is not a perfectly sharp cylinder, but has rounded edges. If the profile is Gaussian with a width determined by \( \sigma \) and if signal from static tissue outside the vessel is ignored, the velocity spectrum of the excited volume becomes:

\[
\tilde{A}(v) = A(v) \cdot \exp \left[ \frac{-R^2}{2\sigma^2} \left( 1 - \frac{v}{v_{\text{max}}} \right)^{\frac{3}{2}} \right].
\] (3.7)

The Gaussian profile does not excite all velocities equally, as shown in Fig. 3.4. The width of each excitation in Fig. 3.4 is determined by the ratio \( R/\sigma \), which equals \( \sqrt{0.2}, \sqrt{2} \), and \( \sqrt{20} \) for RF1, RF2, and RF3, respectively. Assuming parabolic flow, the mean velocity of Eq. 3.7 is given by the equation:

\[
\langle v \rangle = v_{\text{max}} \cdot [(1 - e^{-R^2/2\sigma^2})^{-1} - 2\sigma^2/R^2],
\] (3.8)

which converges to \( v_{\text{max}} \) as \( R/\sigma \) becomes large.

### 3.2.3 General Analysis of Tag Motion

The motion of the 1D projections can be understood through an analysis of the velocity spectrum, \( \tilde{A}(v) \), similar to that developed by Hamilton et al.[14] to explain phase-contrast
velocity measurements. First, $\tilde{A}(v)$ is shifted such that it is centered about $\langle v \rangle$, and decomposed into the sum of an even function, $\tilde{A}_E (v - \langle v \rangle)$, and an odd function, $\tilde{A}_O (v - \langle v \rangle)$.

Substitution of this sum into Eq. 3.3 results in the following expression:

$$g(z,t) \propto \tilde{a}(0) + \tilde{a}_E (k_z t) \cdot \sin[2\pi k_z (z - \langle v \rangle t)] + i \cdot \tilde{a}_O (k_z t) \cdot \cos[2\pi k_z (z - \langle v \rangle t)],$$

(3.9)

where $\tilde{a}_E (k_z t)$ and $\tilde{a}_O (k_z t)$ are the Fourier transform of $\tilde{A}_E (v - \langle v \rangle)$ and $\tilde{A}_O (v - \langle v \rangle)$, respectively.

Equation 3.9 reveals an important relationship between the displacement of a 1D projection and the mean velocity of the fluid. If $\tilde{A}(v)$ is symmetric about the mean velocity
(i.e., $\tilde{A}(v - \langle v \rangle) = \tilde{A}_E (v - \langle v \rangle)$), the third term in Eq. 3.9 vanishes and the projection moves at a velocity of $\langle v \rangle$, and its amplitude is modulated temporally by $\tilde{a}_E (k_z t)$. Otherwise, the projection is a superposition of two phase-shifted sinusoids propagating at the same velocity but having different time-varying amplitudes. As their relative amplitudes change, the positions of the peaks in the projection shift relative to the true displacement of the fluid. The size of this erroneous shift, $\Delta z$, relative to the spatial period of the tags, $z_T$, is given by the following expression:

$$|\Delta z/z_T| = (1/2\pi) \cdot \tan^{-1}( | \tilde{a}_E (k_z t) / \tilde{a}_O (k_z t) | ) - 1/4,$$

which is calculated from the derivative with respect to position of Eq. 3.9. Initially, the error is zero because $\tilde{a}_E(0) > 0$ and $\tilde{a}_O(0) = 0$. As the ratio $|\tilde{a}_E/\tilde{a}_O|$ decreases, the error increases. The rate of increase is proportional to $\Delta v$, because making the velocity spectrum narrower corresponds to slowing the evolution of $\tilde{a}(k_z t)$. Hence, a narrower excitation profile will reduce the erroneous shift for a given acquisition period.

### 3.2.4 Calculation of Velocity Spectrum

The preceding analysis considered the effect of the velocity profile and excitation profile on projection measurements of tagged blood. It is also possible to compute $\tilde{A}(v)$ by analyzing sections of the position-time matrix. This analysis is similar to Doppler ultrasound calculations of velocity[15].

Velocity spectra are important clinically for the assessment of stenoses[1]. In the
context of tag motion, the spectra indicate how much signal contamination from static tissue is present. Contamination decreases the accuracy of the blood-displacement measurements, but can be removed by nulling the zero-velocity component of the spectra. The following analysis extracts $\tilde{a}(k_zt)$ from Eq. 3.3, from which $\tilde{A}(v)$ can be derived.

The first step in isolating $\tilde{a}(k_zt)$ is to eliminate the term $\tilde{a}(0) \cdot h(z,t)$ from Eq. 3.3. This is done by subtracting the spatial mean of each projection, $\langle g(z,t) \rangle_z$, from the corresponding column of the position-time matrix, $g(z,t)$. Assuming that the coil sensitivity is uniform across the field-of-view (FOV) and that the spatial period of the tags is small relative to the FOV, $\langle g(z,t) \rangle_z \approx \tilde{a}(0) \cdot h(z,t)$.

The second step is to construct the analytic signal from this processed matrix, which allows the imaginary operator to be dropped from Eq. 3.3. This is accomplished by applying the Hilbert transform[16] to the spatial dimension of the matrix. Alternatively, the Hilbert transform could be applied to the temporal dimension, but signal decay and tag interference would lead to greater truncation artifacts.

The analytic-signal matrix is then processed using synchronous homodyne detection[17], which is a method for removing undesired phase variations. First, the phase variation introduced by the initial sinusoidal tags is removed by demodulating each column of the matrix. This removes the exponential term from Eq. 3.3. Rather than assuming a specific demodulation frequency, the frequency is measured from the analytic signal of the first projection (i.e., the Fourier transform of the first MR echo), because it is affected the least by signal decay. The Fourier transform with respect to the product of spatial frequency and time, $\mathcal{F}_{k_zt}\{\cdot\}$, is then calculated. The real component of the transform, $\tilde{A}(z,v)$, is related to $\tilde{A}(v)$...
by the following expression:

\[ \tilde{A}(z, v) = C(z) \cdot \tilde{A}(v) \ast \mathcal{F}_{k_t}\{D(t)\}, \]  

(3.11)

where \( \ast \) denotes the convolution with respect to velocity, \( C(z) \) is the coil sensitivity along the vessel, and \( D(t) \) is the signal-decay envelope. The transform of \( D(t) \) is a Lorentzian, assuming mono-exponential decay, making the measured velocity spectrum a smoothed version of \( \tilde{A}(v) \). An example calculation of \( \tilde{A}(v) \) using Eq. 3.11 is shown in Fig. 3.5, for parabolic flow and two excitation profiles. The Gaussian excitation matches that labeled RF2 in Fig. 3.4.

![Figure 3.5: Calculation of velocity spectra from simulated tagging data. (a) Tag interference at one location produced by parabolic flow and two RF excitation profiles: a cylindrical profile (dashed line) and a Gaussian profile (solid line). Each line represents a row of data from a position-time matrix. The simulation includes signal decay, with T2=250ms. (b) Calculated velocity spectra from projection measurements, as described in the text.](image)

The signal decay rate in this simulation (T2=250ms) was chosen to approximate that of fully oxygenated blood[18]. Signal decay causes the edges of the spectra to be rounded, as predicted by Eq. 3.11.

The maximum velocity that can be measured with this approach (i.e., the aliasing
velocity) is equal to \((2k_z \Delta t_{1D})^{-1}\) and the velocity resolution is equal to \((2Nk_z \Delta t_{1D})^{-1}\), where \(\Delta t_{1D}\) is the time between successive projections and \(N\) is the total number of projections. These expressions show that velocity resolution can be increased in two ways: by collecting more projections, which is limited by signal decay, and by increasing the spatial frequency of the tags, which is limited by velocity aliasing and the spatial resolution of each projection.

This section has derived a general expression for the effect of flow on tags, and applied that expression to representative velocity and excitation profiles. This expression is useful because it provides information about blood displacement each time a projection is acquired, and it provides velocity spectra through a collective analysis of multiple projections. Experimental validation of this theory is the focus of the next two sections.

### 3.3 Materials and Methods

A 3D-selective excitation (1D SPAMM with 2D cylinder) was implemented on a GE (GE Medical Systems, Milwaukee, WI) Signa LX 1.5 Tesla MR system (see Fig. 3.6a). The 2D pulse consisted of a 16-loop spiral lasting 12 ms. This long pulse duration was chosen to allow the excitation of narrow cylinders. The orientation of the cylinder was prescribed graphically using a series of spin-echo scout images. The spatial period of the tags varied, but was typically 5-20 mm. The period was chosen to avoid aliasing, which occurs when the 1D projections move more than one-half their spatial period between consecutive projections. A train of 32-256 gradient echoes was collected after excitation using a five-inch diameter surface coil and a sampling bandwidth of ±32 kHz. The spatial resolution of a projection
was chosen to satisfy the Nyquist sampling rate of the tagging pattern. A 1D projection was collected every 2-8ms, depending on the number of samples per echo, which varied between 64 and 256. A representative measured projection, with a tagging period of 10mm, is shown in Fig. 3.6b. The decrease in tag amplitude at the edges of the FOV is a result of coil sensitivity.

The pulse sequence was tested with a flow phantom in experiments designed to validate Eq. 3.3 under controlled conditions. The key experimental variables were the velocity profile and the width of the 2D-excitation profiles, which are the most significant determinants of $A(v)$. The phantom consisted of a rigid cylindrical pipe of inner diameter 22mm,
through which water flowed at a constant rate (Reynolds number approximately 620). A parabolic flow profile was expected under these conditions provided that the flow was laminar and well developed[19]. Laminar flow was expected because of the low value of the Reynolds number (less than 1000). Well-developed flow was expected because the entrance length of the flow in the pipe was 55cm[13], while flow measurements were performed a minimum of 60cm beyond this distance. Therefore, a total pipe-to-measurement distance of 115cm was used. Phase-contrast measurements confirmed that the flow profile was parabolic (see Results).

Tagging measurements were conducted using different cylinder widths and steady parabolic flow. The motion of the 1D projections was tracked by fitting a five-point cosine template to each peak. The locations of the peaks in the first projection were estimated by an observer and used as initial values for the fit. Subsequent projections were fit automatically, based on peak locations from previous projections.

Equation 3.6 predicts that the projections move at a velocity of \( \langle v \rangle \) for parabolic flow. To test this, the mean velocity of the excited volume was calculated from cross-sectional images of the velocity and excitation profiles. The velocity image was created with a conventional phase-contrast sequence. The excitation-profile image was created in the absence of flow using a spin-echo sequence with the first slice-selective excitation replaced with the 2D-selective excitation. The velocity of the projections was calculated from a linear fit to their measured trajectories and compared with the conventional calculation of \( \langle v \rangle \). Velocity spectra were also calculated from the tagging data, according to Eq. 3.11.

The motion of blood in the descending thoracic aorta of human volunteers was mea-
sured to test the tagging measurement in vivo. Various cylinder widths were used to explore the influence of the aortic flow profile on the measurement. Chemical saturation was used to suppress contamination from fat. Collection of these data began 5ms after the gating signal, which corresponded to the peak blood oxygenation detected with a pulse-oximeter attached to the index finger, and continued for approximately 150ms with a 1D projection every 2.3ms. This captured diastolic flow in the thoracic aorta. From these measurements, a time-dependent velocity spectrum (velocity spectrogram) was calculated.

The velocity spectrogram was calculated by temporally windowing\(^2\) the position-time matrix in a manner similar to that performed in Doppler ultrasound[15]. Over each window, the velocity spectrum was considered constant, which allowed the previously developed theory to be applied to the plug-like flow (see Eq. 3.11). A single-sided, 32-point Hanning function (i.e., the positive half of a 64-point Hanning function) was used to window the data. An asymmetric window was used because the homodyne detection expects data starting from \(t=0\). The Hanning window also reduced truncation artifacts in the calculated spectra. The window provided a velocity resolution of approximately 0.2m/s, based on its full width at half maximum (FWHM), and produced an independent velocity spectrum every 36.8ms. The window was translated across the position-time matrix in steps of 8 samples (18.4ms), and a velocity spectrum was calculated at each step. As a result, the effective temporal resolution of the spectrogram was increased, but approximately 50% of the data was shared between successive spectra. Finally, each column of the velocity spectrogram was normalized to have the same maximum intensity, to compensate for signal decay.

---

\(^2\)"Temporal windowing" refers to the isolation of a segment of data by multiplying the data by a function that approaches zero at short and long times.
### 3.4 Results

Application of the pulse sequence to water flowing at a constant velocity through a rigid pipe yielded data as shown in Fig. 3.7. Each position-time matrix was filled with data collected from 32 projections, following a single excitation. The phase-contrast measurements found the velocity profile to be approximately parabolic, with a maximum velocity of $0.057 \pm 0.002 \text{m/s}$ (see Fig. 3.8). This velocity measurement was used to simulate the position-time matrices shown in Fig. 3.2, which show good agreement with the experimental measurements in Fig. 3.7a and b. The velocity of the projections in Fig. 3.7a was approximately 59% that of Fig. 3.7b, reflecting the mean velocity in each excited cylinder. Equation 3.6 predicts that the first zero of the sinc envelope should occur approximately 175 ms after the SPAMM excitation if the entire velocity profile is excited. This agrees with Fig. 3.7a, in which tag contrast was lost momentarily at $180 \pm 10 \text{ ms}$.

Velocity spectra were calculated from the experimental tagging data (see Fig. 3.7c and d). Regions over which the coil sensitivity was relatively constant were chosen for the calculations, corresponding to the central 60 mm of the position-time matrices. The temporal resolution of the data in Fig. 3.7 was 8 ms, leading to an aliasing velocity of $\pm 0.625 \text{m/s}$ for tags with a period of 10 mm. The velocity resolution of the spectra was approximately $0.02 \text{m/s}$.

The shape of each calculated spectrum follows directly from Eq. 3.7. Figure 3.7d exhibits a spike at the maximum velocity (measured with phase-contrast imaging) since the excitation was narrow and centered in the vessel, while Fig. 3.7c ranges from zero to
Figure 3.7: Experimental tagging measurements of constant flow in a straight tube. 
(a),(c) Position-time data and calculated velocity spectrum for cylindrical excitation wider than tube. (b),(d) Data for narrow cylindrical excitation (FWHM = 16% of tube diameter). Time t=0 corresponds to the end of the SPAMM excitation. The velocity spectra were calculated by averaging six separate spectra, with the error bars representing the standard deviation. The dashed lines mark the velocity bounds measured with phase-contrast imaging. Only the relevant range of velocities is presented.
the maximum velocity since the entire pipe was excited. Both spectra appear to extend
below zero velocity and above the maximum velocity. This is attributed to the low velocity
resolution and truncation artifacts.

Measurements of mean velocity calculated from images of the 2D-excitation and
velocity profiles are listed in Table 3.1, along with measurements of tag velocity. The

Table 3.1: Comparison between tag velocity and mean velocity in excited volume (measured
with phase contrast).

<table>
<thead>
<tr>
<th>FWHM (mm)</th>
<th>tag velocity (mm/s)</th>
<th>(v) (mm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5</td>
<td>57.9 ± 0.3</td>
<td>56.7</td>
</tr>
<tr>
<td>6.5</td>
<td>56.4 ± 0.5</td>
<td>55.6</td>
</tr>
<tr>
<td>14.0</td>
<td>40.0 ± 0.4</td>
<td>39.8</td>
</tr>
<tr>
<td>≥22.0</td>
<td>34.2 ± 0.3</td>
<td>32.4</td>
</tr>
</tbody>
</table>

a FWHM: full width at half maximum of cylindrical excitation

quoted cylinder diameters represent the FWHM of each profile, since the profiles were
roughly Gaussian (see Fig. 3.8). Tag interference in Fig. 3.7a introduced errors into the
tracking algorithm (see Eq. 3.10). For this reason, tag velocity was calculated from the
first 12 projections only, before interference became significant. The SNR in the phase-
contrast image was approximately 20, which produced a negligible error in the volumetric-
flow calculations.

The close agreement between the tagging and phase-contrast measurements in Ta-
ble 3.1 was surprising at first, given that the excitation profile was Gaussian. As shown in
Eq. 3.7, such a profile makes \( \tilde{A}(v) \) asymmetric, which introduces an artifact in the velocity
of 1D projections. The close agreement is a result of the tag velocity being estimated using
Figure 3.8: Contour plots of experimental (a) velocity profile (values in mm/s) and (b) 2D-excitation profile, used to calculated \( v \). Each contour represents a 10% intensity increment. (c) Line plots corresponding to the solid and dashed horizontal lines in (a) and (b). The velocity scale on the vertical axis corresponds to the velocity profile only. The developed flow profile is approximately parabolic, while the RF profile is approximately Gaussian. The overlap of these two profiles determines \( \tilde{A}(v) \).
only the first 12 projections. These projections were not significantly affected by the asymmetry of $\tilde{A}(v)$ because they were acquired while $|\tilde{a}_E(k,t)/\tilde{a}_O(k,t)|$ was large, as predicted by Eq. 3.10. This observation emphasizes the need to make $\Delta v$ as small as possible.

Representative data from the application of the pulse sequence to flow in the upper thoracic aorta of a human subject are presented in Fig. 3.9. These particular measurements were collected late in the cardiac cycle using an excitation cylinder with a FWHM of 14mm and a tagging period of 15mm. A cardiac-gated image was collected to show the extent of the initial tagging pattern (see Fig. 3.9a). The projection measurements from a single heart cycle are shown in Fig. 3.9b. A velocity spectrogram was calculated (see Fig. 3.9c) using the bottom half of the position-time matrix in Fig. 3.9b. Successive tagging measurements could be concatenated to build a velocity spectrogram over a longer period of time. The aliasing velocity of the acquisition was approximately $\pm3.3\text{m/s}$, with a velocity resolution of
approximately 0.2m/s. The spectrogram shows that the mean velocity of the tags gradually decreased from a maximum of 0.5±0.2 m/s down to 0.2±0.2 m/s. The SNR of the velocity peak in the first column of Fig. 3.9c is approximately 26, based on the standard deviation of the background noise. The amplitude of the signal at zero velocity is approximately 10% that of the velocity peak (SNR ≈ 3).

Several observations can be made about the in-vivo measurements in Fig. 3.9b. First, the tags did not interfere greatly over the acquisition. This suggests a plug-like flow profile at this location in the aorta. This is consistent with observations from other data (not shown) in which the motion of the 1D projections did not depend strongly on the cylinder width. It is also corroborated by published measurements of aortic flow profiles[20]. Second, the deceleration of blood is apparent later in the acquisition. It was assumed in the Theory section that acceleration was small. Third, tag intensity remained strong for at least 150ms. The ratio of initial to final projection intensity was approximately 4.5. This is a result of the lack of tag interference and the long T2 of fully oxygenated blood. Finally, as fresh, unexcited blood flowed into the FOV, the superior section of the aorta became dark (upper right quadrant of Fig. 3.9b).

3.5 Discussion

This research derived the relationship between fluid motion and the displacement of 1D tags, and explored the influence of specific excitation and velocity profiles on the tagging measurement. A simple model revealed that the 1D projections move at the mean velocity
of the fluid, provided that the velocity spectrum is symmetric about that mean. In that case, the projections can be considered a macroscopic representation of the particle motion of the fluid along one dimension. This was confirmed experimentally with constant-velocity flow through a rigid pipe. Also, an expression for the velocity spectrum of the signal was derived by analyzing the interference between tags moving at different velocities. To my knowledge, this is the first use of magnitude tagging to obtain velocity spectra. This approach holds promise as a means of collecting the particle motion of a fluid or its velocity spectrum from data collected in a single heartbeat.

Measurements of particle motion are interesting because they provide complete information about the displacement of a fluid. From such measurements, higher orders of motion can be calculated directly. For example, particle acceleration can be obtained, from which spatial pressure gradients can be estimated[21]. The experiments with steady flow provided gross measurements of particle motion. However, if the velocity range of each tag remains small, either because the flow is plug-like or the excitation profile is narrow, the tags will move according to the particle motion of the fluid even if the flow is unsteady. The aorta measurements in Fig. 3.9 support this, showing little tag dispersion over the 150ms acquisition, despite the deceleration of the blood.

Particle motion can be constructed from phase-contrast data, but it requires the velocity data to be integrated through time. Eddy-current effects and low spatial and temporal resolution cause position errors to accumulate during integration[22]. This error can be reduced if the moving object returns periodically to the same position[23], but this condition does not apply generally to blood flow. Tagging measurements are immune to
CHAPTER 3. TAGGING MEASUREMENT OF BLOOD FLOW

this problem because they track the particle displacement of blood directly.

The motivation in this chapter for calculating velocity spectra is to assess the signal contamination produced by static tissue. Such contamination reduces the accuracy of the blood-displacement measurements, so its elimination from the position-time matrix is essential. The in vivo measurements showed that it is possible to obtain tagging measurements of blood motion with little (i.e. approximately 10%) contamination from static tissue.

The expression for the velocity spectrum of the signal was derived by analyzing the interference between tags moving at different velocities. This is akin to Fourier velocity encoding (FVE)[24], which analyzes the phase interference produced by magnetization moving at different velocities through a magnetic-field gradient. While current FVE methods[25] encode velocity during data acquisition, tagging performs its encoding at the time of excitation, and subsequent displacement produces tag interference.

The spectrum calculation assumes that data are collected starting immediately after the tags are applied. In reality, there is a delay between the end of the SPAMM excitation and the start of the acquisition, which introduces an error into the homodyne detection. This truncation accentuates the edges of the calculated spectrum. Plug-like flow is less affected by this artifact because its velocity spectrum is a narrow spike. For this reason, it was possible to calculate the velocity spectrogram in Fig. 3.9 by temporally windowing the tagging measurements retrospectively.

Rather than windowing the measurements retrospectively, it is possible to collect fewer projections following each excitation, allowing a shorter repetition time between excitations. The velocity spectrum would be considered constant during these short acquisitions,
which is the strategy used successfully in real-time FVE[25]. A practical limitation of this approach is the deadtime during excitation, but this is relatively short if a wide cylinder is used. A short repetition time provides velocity spectra under more complicated flow conditions than plug flow, but prevents the tracking of individual tags over long periods.

Under simple flow conditions, the experimental results agreed well with theory. These experiments suggest measurement strategies for more complicated flow conditions. A narrow cylindrical excitation is desirable for tag tracking, because it samples a smaller range of velocities, reducing interference and preserving tag intensity. For spectral calculations, the width of the cylinder is less important, because tag interference is inevitable for a complex spectrum.

One expected complication with in-vivo flow profiles is that they will be asymmetric. Fortunately, positioning the cylinder slightly off-center from the velocity profile does not greatly affect the measured motion if the cylinder is narrow, because the velocity profile changes slowly near its peak under laminar conditions.

In the experiments presented in this chapter, a two-pulse SPAMM excitation that creates a sinusoidal tagging pattern was used because it is fast. Longer sequences designed to create sharper tags are probably unnecessary, because flow quickly blurs the pattern. The effect of flow during excitation is expected to be minimal since the SPAMM gradient typically lasts only 350μs and the total length of the SPAMM excitation is less than 2ms. The 2D pulse is relatively long (12ms), but the associated magnetic-field gradients are perpendicular to the primary direction of flow. The 2D pulse can be shorter if the width of the excited cylinder exceeds 3.5mm, which seems likely for large vessels.
The spatial frequency of the tags used in the experiments was chosen to avoid aliasing, but it also affects the motion sensitivity. The motion sensitivity of tagging measurements is governed by the ratio of the spatial resolution to the spatial frequency of the tagging pattern, and the contrast-to-noise ratio between the tag and background signals[26]. Further analysis of these parameters will allow the measurement to be optimized for different flow conditions.

The algorithm used to track motion analyzed each 1D projection separately, and was chosen for its simplicity. Tracking could be improved by constraining the displacement between successive projections, perhaps by fitting a curve to the peaks of the position-time matrix directly. Although a cosine function was fit to both the peaks and the troughs, it is not strictly appropriate to fit the troughs in this way, because the troughs have a Rayleigh noise distribution that slightly blunts their shape[27]. This distortion did not appear to affect the fits significantly, but the template could be modified to account for this SNR effect.

Alternatively, the phase of the signal could have been tagged instead of the magnitude. Even in the absence of flow, however, magnetic-field inhomogeneities would produce phase variations that mimic flow. A second acquisition would be required to correct for this. Unfortunately, respiration and other motion create inconsistencies between these two acquisitions. Magnitude tagging was chosen because it provides independent measurements from each cardiac cycle.

The theoretical analysis presented in this chapter assumed that the velocity spectrum is identical at all positions along the vessel. A more complicated model that considers differences in flow along the vessel would enable the study of a wider range of \textit{in-vivo}
conditions. One anticipated application is the measurement of pulse-wave velocity (PWV), which could be calculated from the lag-time between the displacement of peaks in the 1D projections. FVE has been used to measure the PWV in the aorta by tracking the foot of the time-resolved velocity spectrum[28]. Tagging, once developed further, may provide similar information in a single heart cycle, enabling us to study rapid changes in PWV (e.g., from drug therapy) and avoid errors resulting from cardiac arrhythmia and trigger inaccuracy. The development of a PWV measurement using 1D tagging is presented in the following chapter.
References


REFERENCES


REFERENCES


REFERENCES


Chapter 4

Pulse-Wave Velocity Measured in One Heartbeat Using MR Tagging

4.1 Introduction

This chapter introduces a method suitable for measuring the elastic properties of large arteries like the aorta. As described in Chapter 1, the elastic nature of the aortic wall enables the aorta to smooth the pulsatile flow of blood ejected from the heart, and is affected by a number of factors including age[1], fitness[2], and certain diseases[2, 3, 4, 5].

The mechanical properties of a vessel wall can be quantified using a parameter named distensibility, which is the relative change in vessel cross-sectional area for a given change in blood pressure. Pressure changes are currently measured using an intravascular pressure transducer. However, this invasive procedure can be avoided by using a measurement of distensibility based instead on the pulse-wave velocity (PWV)[6].

The PWV can be calculated from time-resolved measurements of the velocity of
blood at different positions along a vessel[6]. Existing magnetic resonance (MR) measurements of PWV are relatively slow, however, and require data to be collected over multiple heartbeats[7, 8]. These data are later combined using an electrocardiogram (ECG) as a temporal reference. Respiration and cardiac arrhythmia alter the relationship between the ECG and blood flow, which produces a temporal misalignment of the combined data[9, 10, 11]. Because the PWV usually exceeds 3m/s[6], even small temporal errors translate to significant displacements of the pressure wave.

This chapter presents a method for measuring the PWV using the MR tagging approach described in the previous chapter. A brief summary of this tagging approach is included. A processing algorithm is then presented that determines the PWV from the motion of the tagged blood. It is hypothesized that this method can provide an independent measurement of the PWV each heartbeat, making it insensitive to the triggering errors that affect existing MR methods. The beat-to-beat variation in tag motion, relative to the ECG trigger, is used to quantify these trigger errors. An initial in vivo validation of this approach is conducted by measuring the aortic PWV in six volunteers.

4.2 Methods

A pulse sequence that generates a column of disc-shaped tags was implemented on a General Electric (GE Medical Systems, Milwaukee, WI) Signa LX 1.5T MR system (see Fig. 4.1). The magnetic-field gradients on this system were able to reach a maximum amplitude of 40mT/m in 268μs (150mT/m/ms). This sequence, which combined a SPAtial Modulation of
Figure 4.1: Pulse sequence used to measure tag motion in the aorta. Two parallel spatial-saturation bands are applied on either side of the aorta to reduce signal contamination. Next, a two-pulse SPAMM excitation sinusoidally modulates the signal amplitude along the vessel. A 2D-cylindrical pulse then excites a column of blood approximately centred in the vessel lumen. A train of 128 gradient echoes is collected after each excitation.

Magnetization (SPAMM) pulse[12] with a two-dimensional (2D) selective excitation[13, 14], was introduced and evaluated in Chapter 3. The sequence was used to tag a column of blood within a vessel, and acquire a series of 1D projections of the tagged blood. These projections provided a measurement of blood displacement with high temporal resolution. From these measurements, it is possible to calculate the PWV. A description of how to do so is provided later in this section.

Aortic blood motion was measured in 6 volunteers using this sequence. The age and sex of each volunteer are listed in Table 4.1. The volunteers consisted of 4 normal controls
and 2 patients. None of the volunteers smoked or had a history of hypertension. The patients had the Marfan syndrome, a genetic condition affecting vessel-wall elasticity[15], and were expected to have elevated PWV values[5].

All volunteers were scanned in the supine position using the following protocol. A series of scout images were acquired to determine the orientation of the descending aorta. From these images, the tagging pulse sequence was prescribed graphically at the level of the diaphragm. The acquisition of tagging data began 50-90ms after the R-wave was detected by the ECG, and continued for approximately 256ms. This captured the acceleration of the blood during cardiac systole. The trigger delay was determined from a scout tagging measurement in each subject. A 1D projection was acquired every 2ms (128 gradient echoes) using a five-inch surface coil or the body coil (the body coil was later adopted because it provided greater spatial coverage). Even and odd echoes were processed separately, which led to an effective temporal resolution of 4ms. For each echo, 64 samples were collected using a bandwidth of ±31.25kHz and a field of view (FOV) of 240mm. The spatial period of the tags was 20mm and the full width at half maximum (FWHM) of the cylindrical excitation was approximately 11mm.

The spatial frequency of the SPAMM tags used in these experiments conformed to two constraints. A spatial frequency that is too high would lead to a long acquisition time for each projection, which would lower both the temporal resolution of the measurement and the aliasing velocity of the tags[16]. These effects placed an upper bound on the spatial frequency of the tags. On the other hand, a spatial frequency that is too low would violate the assumption that a tag moves as a plug. The pressure wave should traverse a tag in less
time than it takes to acquire successive projections. This constraint placed a lower bound on the spatial frequency of the tags. In practice, a spatial frequency of 0.05mm\(^{-1}\) was found to be a reasonable compromise between these two extremes.

The motion of the tags down the aorta of each volunteer was measured and used to calculate the PWV. These measurements were conducted to show that the tagging method was sensitive to the passage of the pressure wave, and to verify that the calculated PWV values were within the range expected from the literature. Measurements in two Marfan patients were conducted also, to test the method under realistic clinical conditions. The details of the PWV calculation are described with the presentation of the tagging data in the Results section. Eight to 32 separate PWV measurements were made in each individual, using data collected over 16 to 64 heartbeats (i.e., one PWV measurement from each heartbeat; TR=2\(\times\)R-R interval). Breath holding was not used because the tagging measurements of PWV were expected to be independent of respiratory state. From these measurements, the mean PWV and its standard error were calculated.

### 4.3 Results

#### 4.3.1 Description of Position-Time Matrix

Representative tagging measurements of blood flow in the descending aorta of a volunteer are shown in Fig. 4.2a. The data matrix in Fig. 4.2a displays the measured tag intensity as a function of position and time, and is referred to as the “position-time matrix” in this chapter. Each column of this matrix represents one of the 1D projections collected using
Figure 4.2: Sample calculation of the PWV in a human aorta from representative tagging data. (a) Position-time matrix collected using the pulse sequence in Fig. 4.1. The level of the diaphragm is indicated by the white arrow. (b) Manually-tracked trajectories (solid lines) of the tags in (a). Each circle indicates the time \( t_0 \) at which the downward motion of the corresponding tag was detected, using the fitting algorithm described in the text. The dashed line represents a linear fit to these time points, and corresponds to the propagation of the pressure wave down the aorta. (c) Expanded region of (b), to display the data and fit more clearly. (d) Data as in (c), except using the fitting parameter \( t_f \) to detect tag motion. A \( \chi^2 \) value of 7 was expected for both linear fits.

The position-time matrix provides information about the motion of blood at different positions along a vessel. For example, the acceleration of blood is depicted clearly in Fig. 4.2a. Initially, there is little blood flow, and the tags remain stationary (i.e., horizontal bands at the left side of the position-time matrix). As the left ventricle contracts, blood accelerates down the aorta. This is reflected by the rapidly increasing slope of the tags in the position-time matrix, starting at approximately 50ms. There is also a time delay between the motion of the tags which increases with distance down the aorta, and results from the propagation velocity of the pressure wave. By measuring the time delay from the
position-time matrix, the PWV can be calculated.

The calculation of the PWV first required the trajectory of each tag to be measured. These measurements were performed manually using the 1D projections of the tags. Examples of tracked trajectories are displayed as solid lines in Fig. 4.2b.

The time over which each tag could be tracked varied, depending on signal loss. Although the initial tag intensities were approximately equal (SNR≈50), their rates of decay varied. In Fig. 4.2a, for example, the tag initially located at approximately 55mm faded more quickly than the adjacent tag initially located at approximately 75mm, with respective intensity decay-constants of approximately 18ms and 49ms. This difference is attributed to signal dephasing across the aorta caused by magnetic-field inhomogeneities, although this was not tested specifically. The inhomogeneity affecting the tag at 50mm may have resulted from the air-water interface at the diaphragm. Loss of tag intensity at the diaphragm was observed in all volunteers. Data were also collected during breath-holding to confirm that this decay was not an artifact of respiratory motion. Similar signal loss at the diaphragm has been observed in other studies of the PWV using volume-selective excitations[7], and attributed to the respiratory motion of the diaphragm.

Dephasing increases if a tag remains in a region of inhomogeneity for a longer period of time. Tags therefore can pass through a region of inhomogeneity and not dephase completely. This is shown in Fig. 4.2a by the tag initially at 10mm, which passes through the level of the diaphragm but remains visible throughout the acquisition.
4.3.2 Model of Tag Motion

The time delay between the displacement of the tags was calculated by least-squares fitting a model of the flow to each manually-tracked trajectory. The flow was modeled as the sum of two functions: a straight line to account for constant-velocity diastolic flow, and a single-sided parabola to account for systolic acceleration. The parabola was chosen to be a fixed length of 10 points (36ms), because this was a reasonable duration to assume constant blood acceleration during systole[17]. The expectation of constant acceleration was explained in Chapter 1 (see p. 7) using a simple model of pressure-wave propagation. The fitting function is shown in Fig. 4.3, and is described by the following equation:

\[
z(t) = \begin{cases} 
z_f + v_f \cdot t & t \in [0, t_f] \\
z_f + v_f \cdot t + \frac{a_f}{2}(t - t_f)^2 & t \in [t_f, t_f + 36ms]. \end{cases}
\]  

(4.1)

The non-linear fit had four parameters: the starting position of the tag, \(z_f\), the initial (diastolic) velocity of the tag, \(v_f\), the systolic acceleration of the tag, \(a_f\), and the time at which the tag began to accelerate, \(t_f\). The value of \(a_f\) was constrained to be greater than 5m/s² to prevent the minimization from fitting only the initial straight segment of the tag trajectory (i.e., by setting \(a_f\) and \(t_f\) approximately to zero). The mean value (±standard deviation) of \(a_f\) obtained from fits to the trajectories in Fig. 4.2b was \((20±2)\text{m/s}^2\), which agreed with measurements of the systolic acceleration of aortic blood in the literature[18], and was much greater than the lower-bound constraint of 5m/s².

The error in the measured tag positions was estimated from each fit[19]. The variance
Figure 4.3: (a) Schematic of the fitting function used to detect the motion of the tagged blood. This example was generated using Eq. 4.1 with the following values: \( z_f = 2 \text{mm}, \quad v_f = 1 \text{cm/s}, \quad a_f = 10 \text{m/s}^2, \quad \text{and} \quad t_f = 60 \text{ms}. \) The dashed extrapolation of the linear section of the function represents the trajectory the tag would have followed in the absence of acceleration. Tag motion is detected when the tag has moved beyond a threshold distance, \( d_0, \) relative to the extrapolated trajectory. The circles at times \( t_f \) and \( t_0 \) represent two methods for detecting systolic acceleration, as described in the text. (b) Representative fit of Bow model (solid line) to experimental tag trajectory (circles). The asterisk represents the position and time of the tag when the onset of flow was detected.

The position measurements, \( \sigma_z^2, \) was obtained from the following equation:

\[
\sigma_z^2 = \frac{\sum_{i=1}^{N} (z_i - f_i)^2}{(N - 4)}
\]  

(4.2)

where \( N \) is the number of points in the fit, and \( z_i \) and \( f_i \) are the measured and fitted tag positions, respectively. The factor \( N - 4 \) indicates the number of degrees of freedom of the fit \((N \) independent position measurements \(- 4 \) fitting parameters). Equation 4.2 assumes that the noise is equal for all points in the trajectory. The covariance matrix[19] corresponding to each fit was also calculated. This provided a measurement of the variance in each fitting
parameter, and the covariance between any two parameters. From these error estimates, the error in the PWV measurements could be calculated, as detailed below.

4.3.3 Detection of Pressure-Wave Position

In order to detect the passage of the pressure wave, the time at which each tag began to accelerate was calculated. It was first thought that the fitting parameter \( t_f \) would be suitable for this purpose. However, an analysis of the covariance matrix showed that the quality of the fits (i.e. \( \chi^2 \)) did not depend strongly on this parameter. For example, the uncertainty in \( t_f \) was calculated to be as large as \( \pm 3.6 \text{ms} \) in some cases. Assuming a PWV of 5m/s, this temporal error translated to an error in the position of the pressure wave of approximately \( \pm 18 \text{mm} \). In addition, \( t_f \) was correlated with the other fitting parameters (e.g., the correlation between \( a_f \) and \( t_f \) was 0.66 or greater). These properties made \( t_f \) less suitable for pressure-wave detection because they increased the uncertainty in the PWV measurement.

In an attempt to reduce this uncertainty, a threshold tag displacement, \( d_0 \), was used to detect tag acceleration instead (see Fig. 4.3). This displacement was relative to the diastolic motion of the tag, and so resulted from the systolic acceleration of the tag only. The start of acceleration, \( t_0 \), was calculated for each tag from the following equation:

\[
t_0 = t_f + \sqrt{\frac{2d_0}{a_f}}. \tag{4.3}
\]

A value of \( d_0=5\text{mm} \) (i.e., 25% of the tag period) was used for the PWV measurements
in each volunteer. This threshold appeared to be a reliable detector of tag acceleration, although it may not be the optimal value. The relationship between \( d_0 \) and the error in \( t_0 \) is derived below.

The variance of \( t_0 \), \( (\sigma_{t0})^2 \), was calculated from Eq. 4.3 and resulted in the following expression:

\[
(\sigma_{t0})^2 = (\sigma_{tf})^2 + \frac{d_0}{2 a_f^3} (\sigma_{af})^2 - \sqrt{\frac{2 d_0}{a_f^3}} (\sigma_{af,tf})^2 ,
\]

where \( (\sigma_{tf})^2 \) and \( (\sigma_{af})^2 \) are the variances of \( t_f \) and \( a_f \), respectively, and \( (\sigma_{af,tf})^2 \) is the covariance of the two parameters. Values obtained from the covariance matrix were as large as: \( (\sigma_{tf})^2 \approx 13\text{ms}^2 \), \( (\sigma_{af})^2 \approx 5\text{m}/\text{s}^4 \), and \( (\sigma_{af,tf})^2 \approx 0.005\text{m}^2/\text{s}^2 \). The positive covariance caused the last term in Eq. 4.4 to be negative, which offset the error contributions of the first two terms. The value of \( d_0 \) that minimized \( (\sigma_{t0})^2 \) was calculated by differentiating Eq. 4.4 with respect to \( d_0 \) and setting the result equal to zero. Solving this expression for \( d_0 \) resulted in values between 5mm and 30mm, depending on the covariance matrix of the corresponding fit.

An example of the \textit{in vivo} detection of tag motion based on representative measurements of \( t_0 \) is shown in Fig. 4.2b. The circles correspond to the points at which the tags had accelerated beyond the prescribed threshold, as a result of the passage of the pressure wave. A straight line was fit to these points (dashed line), with the resulting slope equal to the PWV (i.e., the change in position of the pressure wave as a function of time). An enlargement of this fit is shown in Fig. 4.2c, along with the calculated PWV and \( \chi^2 \) of the
straight-line fit. The uncertainty in the PWV measurement was obtained from the error in the slope of the linear fit. The error bars in Fig. 4.2c represent the quadrature sum of the uncertainty in \( t_0 \) mapped onto the vertical axis (i.e., by multiplication with the slope of the fit), and the uncertainty in \( z(t_0) \) determined from Eq. 4.1. An equivalent calculation based on measurements of \( t_f \) is presented in Fig. 4.2d. As expected, the uncertainty in the calculated PWV is greater when using \( t_f \) to detect tag motion.

Tags at the edges of the FOV were often not used to measure the PWV. The most distal tag quickly moved outside the FOV, so could not be used. In some cases, the proximal tags were already accelerating at the start of acquisition, and could not be used. Better estimates of \( v_f \) were obtained when the acquisition began earlier in the cardiac cycle because more data were collected prior to tag acceleration. However, this also produced greater signal loss for tags near the diaphragm because they remained within a magnetic-field inhomogeneity for a longer period.

4.3.4 Reproducibility of PWV Measurement

The reproducibility of the PWV measurement was assessed by acquiring 32 independent measurements from one volunteer. These measurements are plotted in Fig. 4.4 as a function of the acquisition number. The data used to generate this plot were acquired in approximately 70s, over which time the physiological state of the volunteer was assumed to be constant. A straight-line fit \( (\chi^2=20) \) to the data in Fig. 4.4 was unable to detect any systematic change in the PWV measurement with time, based on its slope of \((0.002 \pm 0.008)\text{m/s/acquisition.}\)
Figure 4.4: Consecutive measurements of the aortic PWV in one individual, collected over approximately 70s. The horizontal line indicates the mean of 32 measurements, and the shaded region indicates their standard deviation. The mean PWV and standard error of the mean are shown. The uncertainty in each PWV measurement was calculated from the linear fit to the tag trajectory data, as in Fig. 4.2c.

4.3.5 Effect of ECG Error on PWV Measurement

The reproducibility of the measurements in Fig. 4.4 supports the hypothesis that tagging measurements of PWV made in one heartbeat are not significantly affected by respiration or cardiac arrhythmia. From the tagging data, beat-to-beat fluctuations were observed in the time of the onset of flow, relative to the start of the acquisition. The size of these fluctuations was quantified by first choosing one of the position-time matrices as a reference. The temporal shifts that maximized the correlation between the reference matrix and the remaining position-time matrices were then calculated. The matrices were linearly interpo-
lated to a higher resolution (256x256) in order to quantify temporal shifts smaller than the spacing between projections.

When the calculated shifts were plotted as a function of the acquisition number, a periodicity was observed. Two series of tagging measurements were made to determine if the periodic fluctuations coincided with respiration: one during free breathing and the other during breath-holding (maximum exhale). Respiratory motion was recorded simultaneously using a bellow.

The respiratory and flow-delay measurements are shown in Fig. 4.5. The flow delay

![Figure 4.5: Variability of the onset of flow in the aorta relative to the ECG trigger. The top frames of (a) and (b) indicate the respiratory position measured with a bellow during free breathing and breath holding (maximum exhale), respectively. The bottom frames present the temporal fluctuations in the onset of flow, relative to the smallest delay after the ECG trigger, measured with tagging. Note that the scales of the horizontal axes in (a) and (b) differ, while the scales of the vertical axes are equal.](image-url)
in the bottom frame of Fig. 4.5a was found to vary in synchrony with respiration. The correlation between these two waveforms was 0.78. As expected, this periodicity disappeared during breath-holding (Fig. 4.5b), but was replaced by a steady decrease in the delay. Surprisingly, the range of flow delays measured during breath-holding was over double that measured during free breathing. This effect was reproduced in further studies. This large variation in the flow delay was not predicted from the respiratory data, which confirmed that the effect of respiratory motion was small (top frame of Fig. 4.5b). This finding suggests that breath-holding studies may actually be more susceptible to errors when combining data collected across multiple heartbeats.

There are several mechanisms that could be responsible for the observed fluctuations in the onset of flow. One possible mechanism is the effect of breathing on the ECG signal. Breathing produces significant displacements of the heart[20], which alters the received ECG signal and can affect the detection of the R-wave[9, 10].

This mechanism could also explain the breath-hold measurements in Fig. 4.5b. Immediately prior to scanning, the volunteer initiated a breath-hold. This caused a sudden change in the strength of the received ECG. The scanner used in this study adjusts the amplification of the ECG based on the ECG amplitude averaged over several previous heartbeats. As a result, the amplification may not immediately reach a steady value following a sudden change in the ECG amplitude, which could affect the detection of the R-wave.

A physiological mechanism may also contribute to the effects observed in Fig. 4.5. For example, the respiratory state influences the physiology of the heart, including the heart rate and contractility[17, 21]. By externally processing the ECG signal and triggering the
acquisition, these potential factors could be investigated.

4.3.6 \textit{In Vivo} Measurements of PWV

Pulse-wave velocity measurements were performed in a series of volunteers using the method depicted in Fig. 4.2 in order to test the method under realistic conditions. These measurements (mean ± standard error of mean) are tabulated in Table 4.1. The PWV values in the

Table 4.1: Calculated PWV for each volunteer (mean ± standard error of mean). Volunteers are labeled as (N)ormal or (M)arfan.

<table>
<thead>
<tr>
<th>Volunteer</th>
<th>sex</th>
<th>age</th>
<th>PWV (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>M</td>
<td>29</td>
<td>4.75 ± 0.06</td>
</tr>
<tr>
<td>N2</td>
<td>F</td>
<td>27</td>
<td>3.6 ± 0.1</td>
</tr>
<tr>
<td>N3</td>
<td>M</td>
<td>29</td>
<td>3.9 ± 0.1</td>
</tr>
<tr>
<td>N4</td>
<td>M</td>
<td>28</td>
<td>5.4 ± 0.2</td>
</tr>
<tr>
<td>M1</td>
<td>M</td>
<td>27</td>
<td>4.2 ± 0.1</td>
</tr>
<tr>
<td>M2</td>
<td>M</td>
<td>29</td>
<td>4.1 ± 0.2</td>
</tr>
</tbody>
</table>

(a) PWV: Pulse Wave Velocity

non-Marfan volunteers fell within the range expected from the literature, and had an uncertainty much less than the biological variability in humans[6]. Although a higher PWV was expected in the two Marfan patients[5], this was not observed. Given the large biological variation of PWV values[22], tagging measurements in a greater number of Marfan patients and controls are required to confirm this result.
4.4 Discussion

This chapter introduced a non-invasive method for measuring the aortic PWV using data collected in a single heartbeat. The method sinusoidally tags a column of blood within a vessel, and then rapidly acquires a series of 1D projections of the tags. From these projections, the relative motion of blood at different positions along the vessel is measured and used to infer the passage of the pressure wave. The method was applied to a group of six volunteers, and produced PWV values in agreement with published values[6]. Consecutive PWV measurements in one volunteer confirmed that the PWV measurement was reproducible despite the inaccuracies of the ECG trigger. By acquiring an independent PWV measurement each heartbeat, errors introduced by arrhythmia and trigger variability appear to be avoided. Arrhythmia and poor ECG signals are common problems among cardiovascular patients, making this approach attractive for such studies.

Fluctuations in the onset of systolic flow relative to the ECG trigger were observed in the aorta. This error was found to be correlated with the respiratory cycle. However, a significant change in the delay between the trigger and the onset of systolic flow was also measured during a breath-held acquisition. This observation raises a concern that errors in the triggering may not be corrected by breath-holding, but in fact may be worse. Triggering errors of 30ms or less are probably not significant in studies which acquire data during diastole. However, cardiac images or flow measurements collected during systole should consider this source of error[23] if they combine data collected from multiple heartbeats.

The primary benefit of this approach, relative to other MR methods, is its abil-
ity to collect a separate PWV measurement each heartbeat. As a result, the method is inherently insensitive to beat-to-beat variations of the cardiac cycle and ECG trigger. Because the PWV is measured multiple times, the method also provides an uncertainty for the PWV value in each individual. Slower measurements based on MR imaging require breath-holding[8], which is often difficult or impossible for cardiac patients. As a result, these slower PWV measurements are generally conducted only once in each individual, and the measurement error must be estimated by other means.

Previous PWV measurements made with MR have used velocity encoding rather than tagging to detect the pressure wave. Non-imaging approaches have been implemented, also based on 2D selective excitations, as a means of improving the temporal resolution of the velocity encoding[7]. Even with these adaptations, data from multiple heartbeats must be combined to measure the PWV. As described previously, combining flow data collected during different heartbeats can introduce errors if the flow is not periodic. The benefit of phase-based measurements is their sensitivity to small displacements, allowing them to measure PWV over relatively short distances[24].

It is difficult to validate in vivo PWV measurements non-invasively. Catheter measurement of the PWV are considered a "gold standard" for this purpose, but their invasiveness limits their application. Measurements can be validated in phantom apparatus, but such equipment is unlikely to exhibit the complications that may arise in vivo (e.g., signal contamination and vessel curvature). For this reason, an in vivo implementation was first performed. Now that the method has been demonstrated in vivo, a validation of its accuracy in a phantom study of the PWV may be justified. This is a component of the
In conclusion, a method was developed for measuring the PWV in a single heartbeat. This method appears insensitive to variations in the cardiac cycle and ECG trigger. The initial application of this method to a group of volunteers indicates that it is able to detect the passage of the pressure wave down the aorta, and to produce PWV values within the expected range. There are several future goals for this work, which are discussed in more detail in the next chapter.
References


REFERENCES


REFERENCES


Chapter 5

Summary and Conclusions

5.1 Thesis Summary

The hypothesis of this thesis was that volume-selective excitations could be used to acquire independent MR measurements of blood flow with high temporal resolution each cardiac cycle. In support of this hypothesis, Chapters 2 to 4 developed and validated novel methods for measuring blood flow quickly, using volume-selective excitations. A goal of this work was to obtain non-invasive measurements of the aortic PWV in a single heartbeat, which was also achieved. A summary of the work is presented below.

- Chapter 1 began by describing the relationship between aortic function and aortic distensibility. This was followed by a brief description of processes that can change the distensibility. A method was then described for measuring the distensibility from non-invasive measurements of blood flow. The importance of measuring flow quickly and with high temporal resolution was explained, and a general MR strategy was
presented for obtaining fast measurements using volume-selective excitations. The novel use of volume-selective excitations in MR measurements of blood flow, the focus of this thesis, was investigated in Chapters 2 to 4.

- Chapter 2 presented a method for measuring the motion of a bolus of blood in the aorta. The method used a volume-selective excitation (STEAM) with 1D spatial encoding to measure blood displacement with a temporal resolution of several milliseconds. The trajectory of the excited block of blood was derived from the time-dependent frequency of the MR signal, which changed as the volume moved through a magnetic-field gradient. Phantom and in-vivo experiments confirmed that the method could monitor the trajectory of plug-like structures accurately, with signal decay (T2*) limiting the measurement period. The displacement of flowing blood in a human aorta was measured for 65ms from one MR signal, with an accuracy of 0.25mm and an effective time resolution of 2ms.

- Chapter 3 built on the work in Chapter 2 by extending the blood-flow measurement to multiple locations within the aorta, simultaneously. This enhancement required the development of a volume-selective excitation that combined a 1D SPAMM excitation with a 2D cylindrical excitation. A series of 1D projections of the tagging pattern was acquired from a train of gradient echoes. The influence of specific excitation profiles and velocity profiles on the motion of the tags was explored for steady flow. It was shown mathematically, and confirmed with phantom experiments, that the velocity of a tag equals the mean velocity of the excited fluid when the velocity spectrum is
symmetric about its mean velocity. The velocity spectrum was derived by analyzing the interference between tags moving at different velocities. To our knowledge, this is the first use of magnitude tagging to obtain velocity spectra. Measurements of tag displacement in a human aorta were presented to assess feasibility in vivo.

- Chapter 4 applied the tagging method developed in Chapter 3 to the measurement of pulsatile flow in the aorta. An algorithm was developed to detect the relative motion of the tags, from which the PWV could be calculated. This algorithm fit a model of the flow to the measured tag trajectories, in order to determine the time at which each tag had moved a threshold distance. A straight line was fit to these points to calculate the PWV.

Measurements of the PWV in several volunteers were presented in Chapter 4. These measurements confirmed that the aortic pressure wave could be detected using data collected from one heartbeat, despite potential problems that might arise in vivo (e.g., signal contamination, low SNR, vessel curvature, diaphragmatic dephasing). Measurements in two Marfan patients showed that the method could also detect the pressure wave under realistic clinical conditions. Because the PWV could be measured multiple times in each individual, it was possible to calculate the mean PWV and its standard error. Each PWV measurement fell within the published physiological range for the aorta.

A periodic variation in the onset of flow in the aorta relative to the ECG trigger was detected, and found to be positively correlated with the respiratory position. During
a breath-held acquisition, this periodicity vanished, but was replaced with a trigger delay that decreased over the acquisition. Surprisingly, the range of the trigger delay was much greater during the breath-held scan than during the free-breathing scan, which suggested that breath-held scans may be more susceptible to trigger errors. Potential reasons for this variation were suggested, including changes in the strength of the measured ECG as respiration moves the heart, and changes in cardiovascular physiology during breathing.

While Chapter 3 presented an expression for the error in tag displacement, it is difficult to quantify this error in practice since the flow profile and excitation profile may not be known exactly. In specific cases, such as blood flow in the aorta, the flow profile is known to be plug-like[1, 2] in the absence of factors that greatly affect the vessel geometry (e.g., stenoses). For this reason, the application of the tagging method is well suited to measurements of blood flow and the PWV in the aorta.

5.2 Opinions and Future Explorations

An aim of this thesis was to develop blood-flow measurements that are suitable for studying aortic distensibility. There are several other applications, however, which should benefit from this work. The following discussion explores some potential extensions to the distensibility measurement, and proposes some new directions for the work.
5.2.1 Real-Time Flow Measurement

The fast methods developed in this thesis are suitable for integration into a real-time interface to the MR scanner. Real-time interfaces have been developed for a number of applications, including interactive scan prescriptions for imaging[3], and automated detection of contrast-agent arrival[4]. Major manufacturers of MR scanners have started to integrate real-time applications into their products. As these systems become more common, the use of real-time measurements will increase rapidly. For cardiovascular measurements, the real-time interface permits the heart or vessel orientation to be defined interactively, which removes the need for slower scout images. Furthermore, flow measurements could be displayed immediately after they are collected. This technological advancement promises to transform an MR scanner from a passive data-collection device into an interactive tool for studying flow and other physiological processes.

Integrating the blood-flow measurements into a real-time interface requires two steps. First, the MR pulse sequences developed in this thesis must be modified to communicate with the real-time interface. In our laboratory, the interface runs on a Sun Ultra 60 workstation (Sun Microsystems, Palo Alto, CA) connected to the scanner via a BiT3 network card (SBS Technologies, Albuquerque, NM). The sequences must accept control parameters (e.g., the position and orientation of the volume-selective excitation) from the workstation, and it must supply MR data back to the workstation for processing. Second, the algorithms used to process the MR data must be written as computer programs that can interact with the real-time software, in order to display the flow measurements.

The data-processing algorithms that are used to produce real-time flow measurements
must be fully automated, and they must be able to finish processing the data from one acquisition before the next acquisition completes. The instantaneous-frequency calculation described in Chapter 2 satisfies both of these criteria: the forward difference of the phase of the acquired signal is a simple and fast computation. The velocity-spectrum calculation presented in Chapter 3 is also relatively fast. Based on processing benchmarks on the real-time workstation\(^1\), creating a velocity spectrum from a position-time matrix of size 32×32 should require less than 5ms. Simply displaying the acquired position-time matrices in real-time would enable the researcher to judge if the volume-selective excitation is properly positioned within the vessel, and to adjust the position if it is not.

Alternatively, quantitative measurements could be extracted from the tagging data and displayed in real-time. An algorithm was presented in Chapters 3 for semi-automatically tracking tag displacement, but it was found that the fit would mistakenly centre on adjacent peaks as a tag distorted or faded. A manual tracking procedure was adopted in Chapter 4 to avoid this problem. Fully automating the tracking procedure would allow a greater volume of data to be processed without increasing the workload of the researcher. It would also remove a potential operator bias from the measurement. The prospects of automating the tag-tracking procedure are discussed in the next section.

\(^1\)The 1D Fast-Fourier Transformation (FFT) of a 128-element vector required approximately 200μs to complete on the real-time workstation. The processing period of an FFT scales as \(n \cdot \log n\), where \(n\) is the length of the data vector. The algorithm used to calculate the velocity spectrum would perform two FFTs and two inverse FFTs to each row of the 32×32 position-time matrix, leading to an estimated processing time of approximately 5ms.
5.2.2 Automated Tracking of Tag Motion

A fully-automated procedure for tracking the tags in a position-time matrix would simplify the PWV calculations presented in Chapter 4. The first attempt to track tag motion in Chapter 3 ignored a priori information about the flow when fitting the peaks of each projection. This information could have been used to constrain the tracking algorithm, for example by limiting the displacement of a tag between consecutive projections. A different approach is to model the effect of blood flow on the tags in order to create a simulated position-time matrix, and then fit that model to the measured data. By fitting the lines in the position-time matrix directly, the problem becomes similar to that of tracing lines in a tagged image of the heart[5].

The development of a model-based algorithm for tag tracking has already been explored. This algorithm was applied to the data collected in Chapter 4 in an attempt to automate the PWV measurement. The model of systolic tag motion presented in Chapter 4 (see Fig. 4.3) was used to construct a 2D fitting matrix. The size of this matrix was equal to that of the acquired position-time matrix (e.g., 64×64). The tags were modeled as a three-point cosine with a period equal to the tagging period prescribed in the experiments. As with the 1D fits used in Chapter 4, the unknown parameters in this fitting matrix included the initial position ($z_f$) and velocity ($v_f$) of each tag, the systolic acceleration of each tag ($a_f$), and the time at which each tag began to accelerate ($t_f$). Additional parameters were required in the 2D fit to account for the initial amplitude ($A_f$) and the signal-decay rate ($D_f$) of each tag. Hence, there were six parameters for each tag.

A number of constraints were applied to the fit in order to reduce the processing
time, and to increase the likelihood of the least-squares fit converging to the correct solution. These constraints were as follows: $v_f$ was restricted to the range $-0.05\text{m/s}$ to $0.05\text{m/s}$, $a_f$ was restricted to the range $5\text{m/s}^2$ to $50\text{m/s}^2$, $t_f$ was forced to be monotonically increasing as a function of tag number (to account for the passage of the pressure wave), $A_f$ was restricted to the range $0.1$ to $1$ (the position-time matrix was normalized to have a maximum intensity of one), and $D_f$ was restricted to the range $15\text{ms}^{-1}$ to $100\text{ms}^{-1}$.

An example of the application of this algorithm to in vivo tagging data is shown in Fig. 5.1. Qualitatively, the intensities and shapes of the fitted tags closely resemble those of the measured data. A future quantitative evaluation of this algorithm will involve its application to simulated data, which can be created using known model parameters and different SNR values. The values of $t_f$ and $a_f$ obtained from the fit will be compared with the values used to simulate the data, for different levels of SNR.

The algorithm could be further validated using phantom data. The phantom would consist of an elastic tube connected to a pulsatile pump. A pair of pressure transducers placed at different positions within the tube could provide a comparative measurement of the PWV. These experiments would provide more realistic data than the simulations, and the effect of different levels of SNR could be determined and compared with the results from the simulation.

The application of this algorithm to the position-time matrix relies on a valid model of aortic blood flow. The model described above is suited only for data collected during systole. More general models will be necessary for this approach to work with data collected from arbitrary phases of the cardiac cycle. Methods used for tracing lines in a tagged myocardial
Figure 5.1: Preliminary results from an automated tag-fitting method. (a) Representative tagging data of blood flow in the aorta. (b) Results from fitting a model of tag motion to the data in (a).

image may be appropriate for this more general case, because they are designed to track the arbitrary distortion of the heart.

5.2.3 Clinical Studies of Distensibility

As discussed in Chapter 1, many processes can affect aortic distensibility, including aging and fitness training, as well as disease processes like the Marfan syndrome and diabetes. Given the non-specific nature of global distensibility, the clinical potential of its measurement may rest in the assessment of previously diagnosed disease. In cases where the disease mechanism is known, distensibility may provide information about the response of the disease to therapy[6]. It has also been proposed as a potential measurement of risk of aneurysm rupture[7]. By the same argument, low distensibility may be a risk factor for aortic dis-
section in Marfan patients. Further research is required to substantiate these propositions, and the new tool presented in this thesis is suited to such research.

The prospect of non-invasively obtaining mechanical information about the aortic wall of Marfan patients is an exciting potential direction for this research. The risk of aortic dissection in Marfan patients is often assessed from family history and from imaging measurements of the aortic-root diameter[8, 9, 10]. It is recommended that the aorta of a Marfan patient is assessed at least once a year[9], so it is important that the assessment is non-invasive, both from a patient-comfort perspective and from a cost perspective. Because of the high fatality rate in Marfan patients developing aortic dissection[11], an enlarged aortic root is often repaired as a prophylactic guard against dissection or rupture. Given the seriousness of this operation, additional risk factors are sought to help assess when this surgery is warranted[10]. It is now possible to diagnose the Marfan syndrome through genetic analysis[12, 13], and grossly stratify risk based on specific mutations[14]. Distensibility is a reasonable candidate for improving the evaluation of these patients, and should be studied further in this context.

The study of distensibility in clinical research is bound to grow, given the availability of fast imaging sequences on newer clinical scanners. Without standards for acquiring and processing these data, however, conflicting results from different research groups (i.e., due to confounding factors such as wave reflections) may obscure the utility of such measurements. While the validity of distensibility measurements has been tested recently in healthy individuals or animal models[15, 16, 17, 18], further studies are required to validate such measurements in human disease. For example, the effect of pressure-wave reflections ap-
pears to be small in the aorta of healthy individuals [15], but this will likely not be true in diseases that severely alter vessel morphology (e.g., advanced atherosclerosis). The Marfan syndrome was chosen as a focus of this research because it affects the mechanical properties of the aorta systemically before morphological changes are apparent. When pressure-wave reflections are significant, a more robust measurement of the PWV is required, as presented in the next section.

Few technical advances in MR measurements of the PWV have appeared since the start of my own research. General Electric (GE Corporate Research, Schenectady, NY) and Johns Hopkins University have collaborated to further their 1D measurement of the PWV[19, 20]. They have shown their phase-based measurement to be highly sensitive to the onset of blood flow, enabling the PWV to be measured over short vessel segments (e.g., several centimeters long). However, the method collects data over several minutes to obtain a PWV measurement. To shorten the acquisition time, the Hopkins group has recently presented work towards an invasive PWV measurement using an intravascular loopless antenna[21]. The purpose of this work was to measure the PWV in small vessels in real-time. The goal of integrating such measurements with interventional MR procedures is an interesting possibility. However, the merit of this approach is offset by its invasiveness, especially since the method must now compete with other catheter-based measurements.

5.2.4 Improved Calculation of the PWV

The accuracy of the PWV calculation used in this thesis depends on the accuracy of the associated blood-flow measurements, and also on the intensity of reflections from distal
vessel segments. Reflections are problematic near changes in vessel geometry and in disease states in which a low distensibility causes a faster rebound of pressure waves[22]. These potential errors motivated Urchuk and Plewes to develop a method for measuring the PWV that is inherently tolerant of reflections[23]. Their method could potentially be improved by combining it with the blood-flow measurement developed in this thesis, as described next.

Consideration of the Navier-Stokes equation, continuity, and the concept that pressure can be approximated by a linear traveling wave leads to the following equation:

\[ \frac{\partial^2 v}{\partial t^2} = (\text{PWV})^2 \cdot \frac{\partial^2 v}{\partial z^2}, \quad (5.1) \]

where \( z \) is the position along the vessel, \( v \) is the velocity of the blood in the \( z \) direction, averaged over the vessel cross-section, and \( t \) is time. Correlation of the second spatial and temporal derivatives of \( v \) yields the PWV. Unlike the PWV calculation developed in Chapter 4, which examines the "foot" of the systolic pressure wave only, this correlation method can use data from the entire cardiac cycle.

In order to compute the derivatives in Eq. 5.1, velocity must be measured at three or more positions along the vessel, and over an extended portion of the cardiac cycle. The relative accuracy of this PWV calculation can be improved by increasing the temporal resolution of the velocity measurements, or by increasing the distance over which velocity measurements are made[23]. Using conventional MR velocity measurements, increasing the temporal resolution or obtaining velocity measurements from additional positions can lead to prohibitively long scans. In the original paper, for example, it required 12.8 minutes to
image one flow cycle at three positions with a temporal resolution of 20ms.

One way to increase the temporal resolution and spatial coverage of the velocity measurements would be to use the tagging approach developed in Chapter 4. To do so would require the acquisition of position-time matrices from multiple phases of the cardiac cycle. Tag velocities could be calculated from these matrices, and then amalgamated to produce velocity measurements along the length of the vessel that span the cardiac cycle. Equation 5.1 could then be applied to the amalgamated data in order to calculate the PWV.

By combining these two methods, one could potentially gain the improved tolerance to pressure-wave reflections afforded by the correlation approach, yet acquire the necessary velocity data with higher temporal resolution, higher spatial resolution, larger spatial coverage, and reduced acquisition time. A shorter scan time would be an important step towards making this measurement clinically viable.

5.2.5 Extension to Pulse Pressure

The research proposed in this section offers the potential of obtaining non-invasive measurements of pulse pressure much faster than previously possible. Combined with measurements of vessel area, this would enable the calculation of "pressure-area curves", a common method for displaying physiological information about the cardiovascular system, and its response to therapy[24].

Two methods for calculating distensibility were presented in Chapter 1. The first relied on changes in the cross-sectional area of a vessel for a given change in pressure (Eq. 1.1), while the second relied on the PWV (Eq. 1.2). By equating distensibility in these
two equations and applying properties of continuity, the following expression for pressure can be derived[25]:

\[ p(z, t) - p(z, t_0) = -\frac{\rho \cdot \text{PWV}^2}{A} \int \frac{\partial v}{\partial z} dt', \]  

(5.2)

where \( p(z, t) - p(z, t_0) \) is the measured pulse-pressure waveform. The term \( p(z, t_0) \) represents an unknown offset pressure at time \( t_0 \) that reflects the fact that absolute pressure, \( p(z, t) \), cannot be measured in this fashion.

Equation 5.2 requires measurements of the PWV and blood-flow velocity. These can both be obtained by using the tagging approaches described in Chapters 3 and 4, and Section 5.2.4. Again, the tagging method appears well suited to this problem because it measures blood flow with high temporal resolution, and with high spatial resolution in \( z \). The equation also requires measurements of vessel area. A fast method for measuring vessel area has recently been published[26] that could be applied to this problem. Although measurements of the PWV and the vessel diameter may not be possible within the same heartbeat, the combination of these two methods could yield MR measurements of pulse pressure much faster than previously possible. Plotting the pressure as a function of vessel area over a full cardiac cycle produces the desired pressure-area curve.

The potential of fast and non-invasive measurements of pressure-area curves in the aorta is an interesting direction for this work. Although Stefanadis et al. have developed a catheter-based device to measure vessel diameter and absolute pressure simultaneously[27], the invasiveness of the device precludes its general use. Fast, non-invasive MR measure-
ments of these curves could enable longitudinal studies on larger groups of subjects than possible with methods that require catheterization. A drawback of the MR measurement is its inability to determine absolute pressure, making it insensitive to vertical shifts of the pressure-area curve. However, this method can detect changes in the shape of the curve, which may provide insight into the response of the vessel wall to surgical or pharmaceutical interventions[27].

5.3 Conclusions

The work in this thesis explored the ability of volume-selective excitations to provide fast MR measurements of aortic blood flow. The results have demonstrated that, as hypothesized, independent blood-flow measurements can be made each cardiac cycle using volume-selective excitations. This is significant because it enables measurement of blood motion despite potential beat-to-beat fluctuations in the flow. The novel use of volume-selective excitations and the development of new data-processing methods were essential components of this work. The research culminated in a non-invasive measurement of the pulse-wave velocity that could facilitate the study of vascular mechanics. Use of this tool could lead to a greater understanding of cardiovascular physiology, particularly the mechanism through which disease processes and therapeutic interventions affect the mechanical properties of the aortic wall.
References


REFERENCES


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