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Understanding and measuring flow in aortic stenosis with MRI

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Associate Professor Brett Cowan and Dr Matthew Robson

This thesis, submitted in partial fulfilment of the requirements for a
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in Bioengineering,
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The University of Auckland,
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is entirely my own work and, except where otherwise indicated,
describes my own research.
This thesis is dedicated to my family

Strongest hand uppermost
Abstract

In patients with aortic stenosis, accurate assessment of severity with echocardiography is central to surgical decision making. But, when image quality is poor or equivocal results obtained, another robust non-invasive technique would be invaluable. Cardiac magnetic resonance (CMR) may be a useful alternative.

Phase contrast CMR can measure flow and velocity, therefore it is theoretically possible to estimate the main determinant of severity aortic valve area, using the continuity approach. However, it was found that the phase contrast estimate of stroke volume, sampled in the stenotic jet, systematically underestimated left ventricular stroke volume. This underestimation was greater with increasing aortic stenosis severity.

Critical clinical treatment decisions depend on the ability to reliably differentiate between patients with moderate and severe aortic stenosis. To achieve accurate estimation of aortic valve areas the velocity and flow data obtained in these turbulent, high velocity jets must be accurate.

In this thesis, non-stenotic and stenotic phantoms were designed and constructed to experimentally interrogate the error. It was determined that signal loss, due to intravoxel dephasing, decreased the reliability of the measured forward flow jet velocities. Extreme signal loss in the jet eventuated in salt and pepper noise, which, with a mean velocity of zero, resulted in the underestimation.

Intravoxel dephasing signal loss due to higher order motions, turbulence and spin mixing could all be mitigated by reducing the duration of the velocity sensitivity gradients and shortening the overall echo time (TE). However, improvements in an optimised PC sequence (TE 1.5ms) were not satisfactory. Flow estimates remained variable and were underestimated beyond the aortic valve.

To reduce the TE further, a new phase contrast pulse sequence based on an ultra short TE readout trajectory and velocity dependent slice excitation with gradient inversion was designed and implemented. The new sequence’s TE is approximately 25% (0.65ms) of what is currently clinically available (TE 2.8ms). Good agreement in the phantom was maintained up to very high flow rates with improved signal characteristics shown \textit{in-vivo}. This new phase contrast pulse sequence is worthy of further investigation as an accurate evaluation of patients with aortic stenosis.
Acknowledgements

This PhD thesis is the culmination of several year’s work and would not have been possible without the help and support of many people.

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A PhD is never possible without considerable input, advice and assistance from colleagues. I will begin with extending an all encompassing thanks to my colleagues at the Auckland Bioengineering Institute and the Centre for Advanced MRI. But, I would particularly like to single out the contributions from

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Aortic stenosis a narrowing of the aortic valve that causes the formation of a jet during systole.
Diastole relaxation or dilation phase of the heart.
Rheumatic fever inflammatory disease due to a group A streptococcal infection that can affect the heart, joints, skin and brain.
Systole the ejection/contraction phase of the heart.

Magnetic Resonance Imaging is the creation of soft tissue images by manipulating the precessional frequency of hydrogen nuclei.
$T_1$ relaxation is the time taken for the longitudinal magnetisation ($M_z$) to return to 63% of its original value $M_0$.
$T_2$ relaxation time taken for the NMV’s transverse magnetisation ($M_{xy}$) to decay to 37% of its original value.
$T_2^*$ relaxation is the combined loss of phase coherence due to true $T_2$ and inhomogeneities, it defines the FID envelope.
Echo time (TE) time between the excitation RF pulse and readout centres.
Intra voxel Dephasing the phase dispersal of spins within a voxel.
Higher order motion encoding refers to the additional phase accrual due to acceleration, jerk and other higher order motions.
Isodelay time is the effective dephasing time that results in the phase dispersion.
Partial excitation occurs when a spin does not remain in the desired slice for the duration of the RF pulse.
Partial voluming is where the signal from a voxel has a mixture of different tissues, or experiences bi-directional flow.
Spin mixing is the mixing of fast and slow moving spins within a voxel due to the delay between excitation and readout.
K-space is the spatial frequency representation of a magnetic resonance image.
Phase contrast is a Magnetic resonance imaging technique that allows for the quantification of velocity and flow.
Pulse sequence an instruction set of gradient and RF pulses and ADC events that describes how the MR scanner manipulates spins.
Repetition time (TR) time between two successive excitation RF pulses centres.
Ultrashort TE (UTE) a family of pulse sequences that can achieve very short TEs for imaging of tissues with a majority of short $T_2$ components.
Venc is the maximal encoding velocity or aliasing velocity of a PC sequence.

Turbulence the random velocity fluctuations superimposed on the flow.
Boundary layer is a region with steep velocity gradients, typically near surfaces or in bidirectional flow. It is characterised by large shear stresses and turbulence.
Reynolds number ($Re$) the ratio of inertial and viscous forces acting on a fluid.
List of Acronyms

ADC analogue to digital converter.
AR aortic root.
ascAo ascending aorta.
AV aortic valve.
AV0cm image plane located on the aortic valve.
AV1cm image plane located 1cm distal to the aortic valve.
AV2.5cm image plane located 2.5cm distal to the aortic valve.
AVA aortic valve area.
CIM Cardiac Image Modeller.
cineCT cine computed tomography.
CMR cardiac magnetic resonance.
CO cardiac output.
DoF degrees of freedom.
Doppler continuous wave Doppler.
FID free induction decay.
fMRI Functional magnetic resonance imaging.
FOV field of view.
LV left ventricle.
LVOT left ventricular outflow tract.
LVSV left ventricular stroke volume.
MPA main pulmonary artery.
MR magnetic resonance.
NMR nuclear magnetic resonance.
NMV net magnetisation vector.
PC phase contrast.
PCSV PC estimate of stroke volume.
PET positron emission tomography.
RF radio-frequency.
ROI region of interest.
RSI relative signal intensity.
SI signal intensity.
SNR signal to noise ratio.
STJ sino-tubular junction.
SV stroke volume.
VTI velocity time integral.
ZEST New Zealand Eplerenone in Aortic Stenosis Trial.

For ease of reading, the acronyms are redefined each chapter.
Introduction

1.1 Motivation

Aortic stenosis is a narrowing of the aortic valve from either congenital or acquired defects. The obstruction causes the blood to form a high velocity turbulent stenotic jet as it is ejected from the heart. In the United States approximately six million people suffer from aortic stenosis [3]. Congenital valve defects, e.g. a person born with two valve leaflets instead of three leaflets (Section 1.3), occur in approximately 1 – 2% of the populace [4]. Acquired aortic stenosis is caused from the accumulation of calcium deposits on the valve leaflets which reduces their ability to open fully. Recent trends reveal that the incidence of acquired aortic stenosis in the United States is increasing [3].

1.1.1 Aortic stenosis: its special significance in New Zealand

In Rheumatic fever, the anti-bodies produced to combat the bacteria Streptococcus also react with heart valve tissue and make the valve more susceptible to calcium deposits [4]. Rheumatic fever induced aortic stenosis in other OECD countries has been mainly eliminated with the containment of strep throat or scarlet fever, the precursor to rheumatic fever. In New Zealand, additional to the rising ageing population, rheumatic fever remains prevalent. Consequently, there is a greater significance of aortic stenosis in our cardiovascular fatality rate, especially in our Maori and Pacific Island populations [4].

Aortic stenosis can only be treated through surgery (Section 1.3.3). Unfortunately for the patient, the expense of surgery, the disease severity and their...
CHAPTER 1. INTRODUCTION

likelihood of recovery, often forces the surgeon into a difficult decision regarding the timing and the benefit of them undergoing treatment.

1.1.2 An alternative modality is needed

Accurate assessment of disease severity relies on the correct measurement of the velocities in the jet. Current assessment is based on transthoracic and Doppler echocardiography (Section 1.5.2). However, when image quality is poor or equivocal results obtained (Section 1.5.3) then an alternative non-invasive robust technique would be invaluable. At present, only invasive investigations such as cardiac catheterisation (Section 1.5.1) or trans-oesophageal echocardiography are used to verify disease severity.

Cardiac magnetic resonance (CMR) (Section 1.6) may be a potential alternative. CMR can also be used to measure jet velocities using a technique known as phase contrast (PC) velocity mapping. The overriding motivation of this thesis was to investigate the application of PC velocity mapping to supply an alternative indicator of aortic stenosis severity.

1.1.3 Discrepancies in the ZEST data

In the literature many recent investigations comparing velocity mapping to Doppler echocardiography have reported good correlations (Section 1.6.3). In contrast, data from the New Zealand Eplerenone in Aortic Stenosis trial\(^1\) (ZEST) containing moderate-severe aortic stenosis patients [5], did not find a similar good agreement with Doppler (Section 1.6.2). In the other studies the known errors associated with velocity mapping were not addressed, or perhaps not apparent, because these studies were limited in size and restricted to mild-moderate disease severity.

The motivation for the work in this thesis was to: i) interrogate the cause of this discrepancy and to build up an understanding of the errors associated with measuring stenotic jets with CMR’s PC velocity mapping; and ii) to provide

\(^1\)The ZEST trial investigated the use of Eplerenone’s, a selective aldosterone-receptor antagonist, ability to reduce left ventricle (LV) hypertrophy to delay the requirement for interventional surgery [5].
1.1. MOTIVATION

an alternative more robust technique for accurately quantifying the velocity and flow information required to assess aortic stenosis severity.

1.1.4 Chapter overview

This thesis embarks on a journey that revisits early experimental work (Chapters 3 and 4), optimises the standard PC sequence (outlined in Chapter 2) and implements it in a patient study (Chapters 5 and 6). It ends with the development of a new PC sequence (Chapter 7) designed to tackle the problems specific to quantifying high velocity stenotic jets.

Firstly though this chapter provides a background into: a) basic heart anatomy and function; b) aortic stenosis causes, pathology and treatment; c) the basic characteristics of blood flow; d) the current clinical diagnostic methods of catheterisation and echocardiography; and e) the potential of cardiac magnetic resonance as an alternative measure of aortic stenosis severity, including recent studies from the literature and the results of the clinical ZEST study that motivates this work.
1.2 Basic heart anatomy and function

The heart’s role is to pump blood around the body. The heart consists of four chambers, two atria and two ventricles. The direction of blood flow through the heart is controlled through a series of one-way valves, Figure 1.1. The right side of the heart pumps deoxygenated blood to the low pressure pulmonary circuit where carbon dioxide is exchanged for oxygen in the lungs; the left side of the heart pumps oxygenated blood through the high pressure systemic circuit and provides oxygen for the body’s metabolic processes [7], Figure 1.2.
1.2.1 The cardiac cycle

The heart’s rhythmic beat is controlled electrically. **Systole**, the heart’s contraction phase, is electrically activated; **diastole**, the relaxation or dilation phase, occurs when the myocytes\(^2\) are in their resting electrical state. The following description of the cardiac cycle, Figure 1.3, concentrates on the left hand side of the heart, its changing pressures, the open and closed states of the valves and the ejection of blood from the LV whilst describing the electrical events that can be seen in an electrocardiogram\(^3\) (ECG) and important ventricular volumes [7].

**Passive filling** The cardiac cycle begins with all chambers in a relaxed low pressure state. The aortic semi-lunar valve is closed preventing blood returning to the LV and the mitral atrioventricular valve is open. The returning blood from the pulmonary circuit gives the left atria a slightly elevated pressure. The pressure gradient causes the LV to passively fill with blood, as it equilibrates the passive filling of the ventricle diminishes.

**Late or active filling** The Sino-atrial node is the heart’s intrinsic pacemaker. When the Sino-atrial node’s cells become electrically activated, an electrical activation wave propagates through the atria signalling the myocytes to contract. Atrial systole causes an active pressure gradient to be established between the left atrium and the LV. Blood is forced into the LV in what is known as late or active filling. Atrial activation is measurable on the surface, it forms the P-wave in the ECG. The volume in the LV at the end of filling is known as the left ventricular end-diastolic volume (LVEDV).

**Isovolumetric contraction** When the activation wave reaches the atrioventricular node, the electrical signal is passed into the fast conducting Purkinje fibres. These fibres ensure that the electrical activation of the ventricles results in a co-ordinated contraction. Because of their large mass, the ventricles give rise to the large QRS-wave in the ECG. At the beginning of ventricular systole, the pressure inside the LV rapidly increases. The active filling pressure gradient reverses and blood attempts to flow back into the left atrium. Regurgitant flow

---

\(^2\)Cardiac muscle cells.

\(^3\)The electrocardiogram is a surface representation of the heart’s electrical activity.
is prevented by the closing of the mitral valve. The blood is trapped in the ventricle.

**Ventricular systole** When the LV pressure exceeds the systemic circuit pressure the aortic valve abruptly opens, ejecting blood from the heart—*Rapid Ejection*. The continued ejection of blood and the initiation of ventricular relaxation reduces the ability of the LV to maintain a forward pressure gradient—*Reducing*
1.2. BASIC HEART ANATOMY AND FUNCTION

Ejection. The flow rate begins to reduce until it eventually reverses causing the aortic valve to close. The T-wave, the last measurable wave in the ECG signal, indicates the return of the ventricular myocytes to their resting electrical state. The volume of blood in the LV at the end of ejection is known as the end-systolic volume (LVESV).

Isovolumetric relaxation. The mitral valve remains closed until the pressure in the LV drops below the left atrium. The mitral valve then opens, and blood rushes into the LV down the pressure gradient, this is known as Early filling4.

1.2.2 Cardiac indexes

There are a number of cardiac indexes used to assess cardiac function. The indexes mainly focus on the left side of the heart. Systolic indexes try to quantify how well the LV pumps blood and diastolic indexes quantify how well the LV is filled, for example [9]:

- Stroke volume (SV) is a measure of how much blood (in mL) is ejected each heart beat.

\[ SV = LVEDV - LVESV \]  

(1.1)

- Ejection fraction (EF) is a measure of how well the heart ejects blood from the ventricle (%).

\[ EF = \frac{LVEDV - LVESV}{LVEDV} \times 100\% = \frac{SV}{LVEDV} \times 100\% \]  

(1.2)

- The cardiac output (CO) is a measure of how much blood (in L/min) the LV ejects in a minute.

\[ CO = SV \times HR \]  

(1.3)

where HR is the number of heart beats per minute.

- E/A ratio is used to describe the left ventricular filling pattern. The E-wave is a measure of early or passive filling and the A-wave a measure of active or late filling of the LV. Commonly the peak velocity of the E and A-waves are used.

4It is hypothesised that stored myocardial elastic forces may actively suck the blood into the LV.
1.2.3 The aorta and its valve

The aorta is an elastic artery that is very distensible. During systole the aorta expands temporarily storing the blood’s kinetic energy [7], Figure 1.4. In diastole the aorta recoils, converting the potential energy back into kinetic energy. The aorta’s distensibility smooths out the pulsatile nature of the heart and maintains forward pressure and blood flow throughout early diastole (dicrotic wave in Figure 1.3). In late diastole, retrograde flow is observed, which supports the filling of the coronary arteries.

The aorta can be divided into several parts: the ascending aorta (ascAo) begins at the aortic valve or aortic root (AR), which leads into the aortic arch where the aorta curves downwards into the thoracic and abdominal descending aorta [7].

![Figure 1.4: The aorta’s anatomy and role in managing blood flow (adapted from [7]).](image)

The aortic valve is made up of three equal sized semi-lunar valve leaflets or cusps. When fully open, the leaflets allow blood to pass through unimpeded. Behind each leaflet is a Valsalva sinus, a small out-pocket in the AR used to pool blood for the coronary arteries [7]. The leaflets are separated by a commissure and are supported by a fibrous annulus. The free edge of the leaflet curves upwards from the commissure and is slightly thicker at the midpoint or the Arantius nodule. When the three leaflets come together, the Arantius nodule ensures a tight fit. The leaflets partially overlap creating the characteristic “Y” (Mercedes) shape of a closed valve, an effective prevention to regurgitant flow [10], Figure 1.5.
1.3 Aortic stenosis

A valve’s primary role is to prevent regurgitant blood flow and to open fully allowing blood to flow forward unimpeded. Valve diseases are related to these two functions [3].

*Incompetence* or a leaky valve is where the valve does not close properly causing a regurgitant jet to form.

*Stenosis* is where the forward flow becomes obstructed, usually due to valve narrowing, and results in the formation of a stenotic jet.

1.3.1 Causes of aortic stenosis

*Aortic stenosis* is most commonly caused by a narrowing of the aortic valve [3; 4; 10]. Obstructions of the aortic valve are either acquired or congenital.

Acquired aortic stenosis is predominately due to senile degenerative calcification and rheumatic heart disease. Senile degenerative calcification occurs when calcium deposits begin accumulating on the valve leaflets as a consequence of haemodynamic stress. The calcium deposits cause the leaflets to stiffen, reducing their mobility and increasing their resistance to opening [3; 10]. Rheumatic fever is associated with the bacteria Streptococcus (strep throat). The antibodies produced to combat Streptococcus react with the valve tissue causing abnormal thickening. The valve thickening affects the valve’s mobility and predisposes the valve to additional calcium build-up [4].

Figure 1.5: Examples of a normal, bicuspid and calcified aortic valve (obtained from [11]).
CHAPTER 1. INTRODUCTION

**Congenital heart defects** are where a person is born with either a unicuspid, bicuspid, or even quadricuspid valve. Unicuspid valves are the most common cause of aortic stenosis in neonates and infants (< 1 year old) and in symptomatic aortic stenosis patients < 15 years old. Bicuspid valves are not stenotic at birth and do not cause significant narrowing in childhood. The inherent narrowing worsens as a consequence of growth. The induced turbulent flow causes valve trauma. The leaflets undergo fibrosis increasing the rigidity and calcification [3].

### 1.3.2 Pathophysiology of aortic stenosis

In aortic stenosis the obstruction usually worsens over a long period of time. Gradually the resistance or afterload the heart faces to eject blood increases. In parallel, the LV undergoes concentric hypertrophy at the expense of cavity size. This compensatory mechanism preserves left ventricular wall stress and systolic function. Normal resting cardiac output is maintained despite an increasing pressure gradient. But, the heart increasingly fails to rise in response to exercise [3].

![Figure 1.6: The ramification due to the presence of aortic stenosis on the left ventricle (adapted from [12]).](image)

Further to the LV remodelling, a pseudo-normal diastolic filling pattern can be observed [10]. The thickening of the heart wall and the increased afterload

---

5 Concentric LV hypertrophy is an increase in relative wall thickness and LV mass.
1.3. AORTIC STENOSIS

reduces left ventricular compliance and early filling of the ventricle. As a result a larger proportion of filling occurs during atrial systole (low E/A ratio). Active filling of the ventricle helps to prevent elevated left atrial pressure, consequent rises in pulmonary pressure\(^6\) and helps ensure effective ventricular contraction [3]. When the ventricle can no longer match the afterload, CO, SV and the aortic valve’s forward pressure gradient begin to decline [10].

1.3.3 Treatment

The primary treatment for aortic stenosis is interventional surgery. Medical treatments are available, but they are not as effective. These treatments are reserved for patients where surgical intervention is not possible due to heart failure, infective endocarditis\(^7\) or arrhythmia [3].

![Figure 1.7: Valvuloplasty repair method and examples of replacement valves (obtained from [13; 14]).](image)

Valve repair with percutaneous aortic balloon valvuloplasty can be used to partially treat the patient. A balloon catheter is placed inside the aortic valve and inflated in an attempt to increase the ability of the aortic valve to open. Valve repair is often used to reduce the symptoms in critical patients before they undergo surgery or in patients where surgery is not possible [3; 4].

Valve replacement surgery is the treatment of choice for most patients. If systolic left ventricular dysfunction is due solely to aortic stenosis the patient is likely to

\(^6\)Maintenance of normal pulmonary pressure is vital to facilitate normal oxygen carbon dioxide exchange in the lungs or pulmonary congestion.

\(^7\)Endocarditis is the inflammation of the inner surface wall of the heart, the endocardium.
CHAPTER 1. INTRODUCTION

completely recover after surgery; however, if the underlying systolic left ventricular dysfunction is due to other causes (e.g. myocardial infarction) the patient will often fail to recover. It is still recommended that the patient undergo surgery, survival rate is better with interventional surgery rather than medical treatment. But, the surgeon often faces a balancing act between i) the cost; ii) disease severity; iii) the resultant pathology; and iv) the likelihood of recovery. The issue of determining the dysfunction and its underlying cause is a considerable problem with current diagnosis techniques and is an active area of research [3].
1.4. CHARACTERISTICS OF BLOOD FLOW

1.4 Characteristics of Blood Flow

1.4.1 Flow regimes

Flow is characterised based on the concept of dynamic similarity. To have an identical flow field in blood vessels of different diameters, the ratio of inertial and viscous forces acting on a volume element of fluid must be the same [15]. This ratio is a dimensionless number, known as the Reynolds number, \( Re \).

\[
Re = \frac{\text{Inertial forces}}{\text{Viscous forces}} = \frac{\rho \bar{U} d}{\mu}
\]

where \( \rho \) is the fluid density, \( \bar{U} \) is the average velocity, \( d \) is the diameter of the vessel, and \( \mu \) is the fluid viscosity. Flow fields are categorised into laminar, transitional or turbulent flow regimes according to their Reynolds number.

In laminar flow the viscous effects dominate, the Reynolds number is low, \( \leq 1200 \). Laminar flow in a straight pipe is characterised by a parabolic flow profile with a magnitude of zero at the walls. Radial and tangential velocities are small so fluid particles remain at the same radial position through the flow. The fluid particles can be thought to move in concentric cylindrical shells of a given velocity.

Transitional flow begins to show oscillations in the streamlines\(^8\). Radial and possibly tangential velocities experience measurable changes in magnitude, thereby the flow cannot be considered purely laminar or turbulent.

The critical Reynolds number (2300\(^9\)) describes the transition to purely turbulent flow. Turbulent flow is dominated by inertial forces and is characterised by random fluctuating velocities. Injecting a stream of ink into turbulent flow would cause it dissipate quickly to the walls [16].

1.4.2 Turbulence

Turbulence describes the random fluctuating velocities that characterise turbulent flow. Transport of fluid is considered not as a particle but as a packet of par-

\(^8\)Streamlines are a family of curves that show the tangential velocity of the fluid flow.

\(^9\)Laminar flow can be maintained at higher Reynolds numbers if disturbances are minimised. Inversely, transition to turbulent flow can occur at lower Reynolds numbers if additional obstructions or disturbances are experienced by the flow.
CHAPTER 1. INTRODUCTION

ticles called *eddies* [17]. **Instantaneous Velocity** is given by the time-averaged velocity ($\bar{U}$) plus the random fluctuating component ($u$)

$$ U = \bar{U} + u $$

where $\bar{U} = \frac{1}{T_m} \int_{-T_m}^{T_m} U(x, t) \, dt$.

$T_m$ is the measuring time required to smooth out the velocity fluctuations [18].

The degree of turbulence is directly related to the root mean square of the fluctuating velocity ($u_{rms} = \sqrt{u^2}$). Turbulence intensity ($I$) is:

$$ I = \frac{u_{rms}}{\bar{U}} \times 100\% $$

Though two spatial locations may be experiencing the same mean velocity, $\bar{U}$, they may experience quite different degree of turbulence, $I$. For example, the velocity profile of turbulent flow in a straight pipe, termed plug flow, is centrally very flat. The flat central region results in a steep drop off in velocity at the wall developing higher shear stresses and greater turbulence.

<table>
<thead>
<tr>
<th>Laminar</th>
<th>$Re &lt; 1200$</th>
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<tr>
<td>transitional</td>
<td>$1200 \geq Re &lt; 2300$</td>
</tr>
<tr>
<td>Turbulent</td>
<td>$2300 \geq Re$</td>
</tr>
</tbody>
</table>

Table 1.1: Reynolds number thresholds for flow regimes in a straight pipe (from [17]).

Figure 1.8: Effect of pulsatile flow on velocity stability (adapted from [16]).

1.4.3 Unsteady flow

Flow in the heart is pulsatile. Though the concepts discussed are useful in certain cases, e.g. peak flow in the cardiac cycle, they neglect the effect pulsatility can have on the flow field.

Acceleration has a a stabilising effect and deceleration a destabilising effect on turbulence [19]. In the cardiac cycle, though we may be above the critical Reynolds threshold for turbulence, the velocity profile under acceleration can
be relatively smooth, see the upstroke of Figure 1.8. In the deceleration phase turbulence begins to occur. In subsequent cardiac cycles the acceleration phase dampens the remaining turbulence causing re-laminarisation of the flow.

The development of turbulence is related to the time between successive pulses. High frequency unsteady flow may not have enough time between pulses for turbulence to develop. The acceleration’s stabilising and deceleration’s destabilising effects cancel each other out, causing the Reynolds number required for laminar to turbulent transition to increase [16]. The critical Reynolds number depends on the frequency of the pulsatile flow and is expressed through the (dimensionless) Womersley number.

\[
N_w = \frac{d}{2} \sqrt{\frac{\rho \omega}{\mu}}
\]

where \( \omega \) represents the circular frequency of the heart’s cardiac cycle \( (2\pi \times \frac{\text{beats}}{s}) \). The Womersley number is an unsteady Reynolds number. In an \textit{in vivo} dog study conducted by Nerem and Seed [19], it was found that as the Womersley number increased, the critical Reynolds number also increased. They estimated that for humans the critical Reynolds number at peak systole would have to be approximately 8000 to cause turbulence [19]. Turbulence intensity may vary throughout a pulsatile flow field; implying that different locations in a flow field may experience turbulent flow while the core flow can remain laminar.

1.4.4 Blood flow in the heart

Characterising flow in the human heart is very complex. Turbulence can occur at a certain place and at a certain time in the cardiac cycle while absent in another [16]. Turbulence is critically dependant on heart rate. Under healthy conditions when the valves are able to open fully, the blood flow is relatively unobstructed and free from disturbances. Thus blood flow is assumed to be laminar [16]. In valve disease, discussed in Section 1.3, a severe obstruction to flow may lead to enough of an increase in Reynolds and Womersley numbers so that the flow transitions into turbulent flow. Consequently, turbulence may occur [19; 16].
CHAPTER 1. INTRODUCTION

1.5 Clinical diagnosis of aortic stenosis

Aortic stenosis is routinely assessed by transthoracic 2D and Doppler echocardiography. It is cheap and non-invasive. Previously, cardiac catheterisation was used. It is invasive and comparatively expensive. In current practice cardiac catheterisation is only performed if Doppler ultrasound measurements can not adequately distinguish disease severity [3; 10].

1.5.1 Catheterisation

Catheterisation was the first diagnostic tool available to investigate cardiovascular diseases. Stephen Hales, in 1711, placed a catheter in the left and right ventricles of a horse’s heart. Claude Bernard, the father of physiology, performed the first formal animal study of cardiac function in the 1840s. The first human examination was undertaken by Werner Forssmann, on himself, in 1929 [20].

Catheterisation provided a means to measure pressure, cardiac output and other haemodynamics of the heart. The establishment of the diagnostic angiogram, in 1958 by Charles Dotter, made catheterisation an integral tool in the diagnosis and treatment of cardiovascular diseases [20].

Left heart catheterisation in patients with aortic stenosis is commonly performed using a cannula inserted into the right femoral artery [20]. A J-tipped guide-wire, or in severely stenotic valves a straight guide-wire, attached to a pigtail catheter is advanced across the aortic valve. Pressure traces can be recorded inside the ascending aorta (prior to crossing the valve), in the LV and as the catheter is withdrawn (the pull-back method) [20], Figure 1.9.

Figure 1.9: Pressure recording across the aortic valve from a J-tipped pigtail catheter using the pull-back method (adapted from [20]).

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1.5. CLINICAL DIAGNOSIS OF AORTIC STENOSIS

Cardiac output can be estimated by thermodilution using a Swan-Ganz catheter. A small amount of cold saline at a known temperature is injected at the tip of the catheter while temperature measurements are recorded downstream using the same catheter. Cardiac output can be estimated using the Steard-Hamilton equation [21]

\[ CO = \frac{V_i(T_b - T_i)K_\rho K}{\int T_b(t) \, dt} \]  

(1.8)

where \( V_i \) and \( T_i \) are the volume and temperature of the injected saline, \( T_b \) and \( T_b(t) \) are the initial and the time-varying blood temperature recording, \( K_\rho \) is a density constant and \( K \) is a computation constant.

1.5.2 Echocardiography

The first time-varying echoes of the human heart were recorded by Drs. Edler and Hertz, in 1953 [22]. In the 1980s echocardiography became common place [23]. Initially ultrasound was used to provide a preliminary investigation prior to cardiac catheterisation. Echocardiography has since undergone many advances.

- **Doppler** ultrasound was first used to measure vascular blood flow in 1967 [24];
- Harvery Feigenbaum in 1968 established *M-mode* echocardiography as a means to investigate pericardial effusion [25];
- the first 2D *echocardiography* scanners were presented in 1971 [26] and Dekker et al are credited with performing the first 3D echocardiogram in 1974 [26];
- **Tissue Doppler** was developed to quantify myocardial velocity [27]; and
- **Speckle tracking** uses the interference pattern of the reflected sound waves to track and quantify tissue deformation [27].

Echocardiography is now often the first line imaging technique for most cardiovascular diseases [10].
CHAPTER 1. INTRODUCTION

Basic principles

Echocardiography is based on the reflection of sound waves by objects in the body (e.g. the valves and red blood cells) [10; 27; 28]. Sound is the transmission of energy at a fixed velocity ($c$) through a medium using longitudinal compression and decompression waves.

Ultrasound is generated by passing an alternating current across a piezoelectric crystal causing it to vibrate. Audible sound ($15 - 20KHz$) is refractory and can be heard from around a corner. High frequency sounds, generated by the piezoelectric transducers ($1 - 12MHz$), travel in straight lines and tend to be reflected [27].

The same transducer can be used to record the reflected ultrasound wave. The position of an object can be determined using the known velocity of sound in soft tissue, Table 1.2, and by measuring the time it takes for the reflected signal to return to the transducer. The amount of time spent in the transmit mode is controlled by the duty factor [10],

$$Duty\ factor = \frac{Pulse\ length}{Pulse\ Duration} \quad (1.9)$$

and relates to the depth of field since a greater listening time equals a deeper field of view.

<table>
<thead>
<tr>
<th>Material</th>
<th>Velocity (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>330</td>
</tr>
<tr>
<td>Water</td>
<td>1497</td>
</tr>
<tr>
<td>Fat</td>
<td>1440</td>
</tr>
<tr>
<td>Blood</td>
<td>1570</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>1540</td>
</tr>
</tbody>
</table>

Table 1.2: The velocity of sound in various mediums (from [27]).

Resolution

Different factors affect the ability to distinguish between objects oriented axially or laterally to the ultrasound beam.

Axial resolution refers to the ability to distinguish between two objects along the path of the beam. Axial resolution depends on the size of an object that can
1.5. CLINICAL DIAGNOSIS OF AORTIC STENOSIS

Figure 1.10: An ultrasound beam is created from applying a short electrical pulse over a piezoelectric transducer. The transmitted beam gets reflected by an object or scatter. The reflected beam is picked up by the same or a different piezoelectric transducer (adapted from [27]).

reflect a sound wave and the beam’s wavelength ($\lambda$), which is inversely related to the frequency ($f$) (Eq. 1.10) of the ultrasound beam.

$$c = \lambda f$$  \hfill (1.10)

In general, higher frequencies are desirable because smaller objects reflect the beam and shorter pulse lengths increase the likelihood that two closely positioned objects can be separated.

The lateral resolution is affected by the beam width [10; 27]. Objects that reflect an ultrasound beam are displayed as if the ultrasound beam was infinitely narrow. All objects appear at the centre of the beam [10]. Figure 1.11. The width of the beam varies as a function of depth. An ideal beam, initially focussed using a concave transducer surface, converges (near field) before it begins to diverge (far field) as it propagates through the medium. The transition distance ($T$) reflects the length of the focussed near field and is a function of the transducer frequency and diameter ($a$) [10; 29].

$$T = \frac{4a^2 - \lambda^2}{4\lambda}$$  \hfill (1.11)
The size of a transducer is limited by its transmission frequency. High frequencies require small transducers [29]. Consequently, transducers are normally designed to keep a constant ratio of $\frac{\lambda}{2a} = 0.08$ between the wavelength and the transducer’s diameter [29]. From Figure 1.11, this results in a similar far field beam width for each transmission frequency. Though the lower frequencies have a larger transition distance, the width of the transducer causes a wider near field. High frequencies achieve better lateral resolution at the expense of beam divergence and shorter focused near fields.

Furthermore, the gain also affects lateral resolution. At low gains, only strong reflecting objects at the edge of the beam will produce a strong signal: if the gain is increased, the signal from weaker reflecting objects will be included at the expense of lateral resolution [10].

The ability to distinguish between different tissues, contrast resolution, is highly dependent on the pre and post processing algorithms used to create the image. These algorithms rely on the strength of the signal therefore the size of the object and the signal gain. Lateral and contrast resolution are extremely operator dependent. The image can easily be distorted through incorrectly locating objects whilst trying to increase contrast resolution [10] Figure 1.11.

Creating a 2D-echocardiography image

There are three ways of displaying an ultrasound signal [27], Figure 1.12
1.5. CLINICAL DIAGNOSIS OF AORTIC STENOSIS

1. A-mode displays the amplitude of the received signal as a function of depth;
2. B-mode converts the amplitude into a brightness value; and
3. M-mode extends B-mode by plotting it as a function of time.

Figure 1.12: The three 1-D Echo display modes (adapted from [10]).

Figure 1.13: The formation of a 2D ultrasound image results from combining many B-Mode lines (adapted from [27]).

To develop a 2D image, the ultrasound beam, displayed in B-mode, is repeatedly scanned across a specified sweep angle (Φ), Figure 1.13. The image is formed, in polar co-ordinates, with the known reflection distance and the angle of projection φ [27; 28].

The temporal resolution or sweep rate of the image is dependent on the sweep angle, the number of lines desired per degree and the pulse repetition duration. The different ultrasound lines are updated and combined with previously collected lines, improving the resultant frame rate seen by the operator. The frame rate is typically half the sweep rate [10].

The Doppler effect

Apart from being able to produce qualitative anatomical images of heart function, echocardiography can quantify function through the Doppler effect [10; 27; 28]. Christian Doppler, an Austrian physicist, noticed changes in the wavelength of light whilst investigating double stars. He used the analogy of a ship to explain how the frequency of waves depends on the relative motion of the observer and the wave source [28], Figure 1.14. Doppler ultrasound uses changes in transmitter
frequency \( f_o \) to infer the velocity of the object \( v_{obj} \).

\[
\Delta f (hz) = \frac{2f_ov_{obj}}{c} \cos \theta
\]  

(1.12)

The velocity resolution is constrained by the carrier frequency. For low velocities, high carrier frequencies (> 5Mhz) are desirable; the high velocities associated with aortic stenosis are best resolved using low carrier frequencies (1–3Mhz) [27; 28]. This is opposite to 2D echocardiography where high carrier frequencies obtain better spatial resolution.

Assessment of aortic stenosis is performed using continuous wave Doppler. The transducer simultaneously transmits and receives, sacrificing the ability to distinguish position, to obtain better temporal resolution. Continuous wave Doppler (Doppler) displays the direction and spectra of the velocity as a function of time [28].

1.5.3 Assessment of aortic stenosis

The presence of aortic stenosis is determined by imaging the aortic valve with 2D echocardiography. A cross-sectional image of the closed aortic valve can be used to determine the number of valve leaflets [10]. Although 2D echocardiography provides a good qualitative diagnosis, clinical decisions are normally based on
1.5. CLINICAL DIAGNOSIS OF AORTIC STENOSIS

Figure 1.15: Doppler ultrasound creates a velocity spectra by comparing the change in frequency between the transmitted and reflected ultrasound beams (adapted from [28]). The result is displayed as a velocity spectra in time.

quantitative measurements using Doppler and, if required, catheterisation [3]. Measurements of the pressure gradient across the valve and the effective aortic valve area (AVA), a measure of the valve’s ability to open, are used classify the severity of the stenosis, Table 1.3.

The correct timing of surgery critically depends on the accurate differentiation between moderate to severe patients, but unfortunately, due to limitations this is not always possible and many patients are currently misdiagnosed.

The methods and their limitations

Catheterisation provides a direct measure of the mean pressure gradient. The AVA is estimated with the Gorlin equation

\[ \text{AVA} = \frac{CO}{HR.SEP.K.\sqrt{\Delta P}} \]  

(1.13)

Where \( CO \) is estimated with thermodilution, \( HR \) is the average heart rate (beats/minute), \( SEP \) is the systolic ejection period, \( K \) is the empirically derived Gorlin constant and \( \Delta P \) is the pressure gradient measured using the pull back method [20].

The main limitation of catheterisation is that it is invasive. Correct measurement of the pressure gradient can be position dependent and the Gorlin equation has
limited accuracy at low CO due to the empirically derived constant \( K \) \[20\].

**Doppler** can only measure velocity. Both the pressure gradient and the AVA are inferred.

\[
\Delta P = 4V_{pk}^2 \tag*{(1.14)}
\]

\[
AVA = \frac{VTI_{LVOT}d_{LVOT}\pi^2}{4VTI_{Jet}} \tag*{(1.15)}
\]

The modified Bernoulli equation (Eq. 1.14\(^{10}\)) calculates the maximum pressure gradient by using the peak instantaneous velocity or provides a mean gradient by planimetry of the multiple velocity spectra, Figure 1.15. The peak velocities are typically averaged over several heartbeats \[28\]. Alternatively the mean pressure gradient is estimated from the peak pressure gradient with the formula

\[
\Delta P_{\text{mean}}(\text{mmHg}) = \frac{\Delta P_{\text{max}}}{1.45} + 2\text{mmHg} \tag*{10}.
\]

The continuity equation (Eq. 1.15) estimates AVA using the conservation of mass principle \[10; 27; 28\], the volume of ejected blood before and after the valve must be equal. The diameter \( d_{LVOT} \) of the left ventricular outflow tract (LVOT) is determined from 2D echocardiography. The velocity time integral (VTI) in the LVOT \( VTI_{LVOT} \) and the Jet \( VTI_{Jet} \) are estimated by integrating the planimetry envelope from the Doppler spectra, Figure 1.15.

The main reported limitation is that the Doppler beam must be aligned parallel to the jet \[10; 27; 28; 3\] \( \cos\theta \) in Eq. 1.12). In many cases the available acoustical windows, due to the lung, chest wall, size and positioning of the patient, restrict the ability to align the jet, introducing an operator dependency \[28\].

The location of the aortic valve requires the Doppler assessment to use the far field of view. The large beam width may encompass multiple jets \[29\]. This is

\footnote{The modified Bernoulli equation is dimensionally inconsistent: to be consistent “4” must have units of \( \text{mmHg.s}^2 \). The source of these units can be determined from investigating the derivation of the modified Bernoulli equation. The Bernoulli equation states that along a stream line the total pressure (hydrostatic + dynamic) is constant, \( P_{\text{tot}} = P + \frac{1}{2}\rho V^2 \). By considering two points along a stream line, where the cross sectional area of the first region is much larger compared to the second region, i.e. the LV versus the AS-jet, so that \( V_2 >> V_1 \) then the pressure difference can be considered to be \( P_1 - P_2 = \Delta P = \frac{1}{2}\rho V_2^2 \). Given that the density of blood is 1050 \( \frac{kg}{m^3} \) and that \( 1\text{mmHg} = 133.3\text{Pa} \) then the density of blood \( \rho \) in \( \text{mmHg.s}^2 \) is \( \approx 8 \), thus the “4” in the modified Bernoulli equation.}
1.5. CLINICAL DIAGNOSIS OF AORTIC STENOSIS

<table>
<thead>
<tr>
<th>Severity</th>
<th>Mean Gradient (mmHg)</th>
<th>Aortic valve area (cm$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>$&lt;25$</td>
<td>$&gt;1.5$</td>
</tr>
<tr>
<td>Moderate</td>
<td>25-50</td>
<td>1.0-1.5</td>
</tr>
<tr>
<td>Severe</td>
<td>$&gt;50$</td>
<td>$&lt;1.0$</td>
</tr>
<tr>
<td>Critical</td>
<td>$&gt;80$</td>
<td>$&lt;0.7$</td>
</tr>
</tbody>
</table>

Table 1.3: Classification of aortic stenosis severity (from [3]).

useful when there are multiple jets associated with the same stenotic valve; however, mitral regurgitation jets share a similar velocity spectra and alignment [28]. Without positional differentiation it is possible to misinterpret the identity of the recorded signal.

Poor transthoracic 2D-echocardiographic images of the LVOT make the measurement of the diameter difficult. Furthermore, it is assumed that the LVOT is circular and that the LVOT diameter and VTI are measured at the same location. These assumptions create doubt that the estimate of the ejected volume prior to the valve and thereby the calculated AVA [3] is accurate and reliable.
CHAPTER 1. INTRODUCTION

1.6 Cardiac magnetic resonance, a potential alternative?

The phenomenon of nuclear magnetic resonance (NMR) was first considered an artefact. An American physicist Dr Isidor Rabi, observing atomic spectra in the late 1930’s, thought the NMR echo was a fault in his experimental apparatus [30]. It was not until 1946 that the NMR experiment was successfully repeated. Felix Bloch and Edward Purcell independently demonstrated that nuclei in a magnetic field absorbed and re-emitted energy from the radio frequency range of the electromagnetic spectrum [31; 1],

NMR spectroscopy quickly followed and led to an analytical method for analysing the atomic composition of chemical compounds. Dr Raymond Damadian in 1971, working on physiologist Gilbert Ling’s theory that “the structure of water in healthy and cancerous tissue is different,” demonstrated different relaxation times in human tissue [31]. He stated that these properties could lead to the creation of a new diagnostic device [30].

In 1973, after facing initial rejection [30], Paul Lauterbur published in Nature the idea of using magnetic gradients to spatially localise the NMR signal [1], Figure 1.16 [32]. Sir Peter Mansfield, whom had a similar proposal, further utilised the gradients by proposing the first rapid sampling scheme, echo-planar imaging, that enabled magnetic resonance (MR) to become a useful imaging technique [33]. These are considered the two key developments that signalled the birth of MR imaging [30].
1.6. CARDIAC MAGNETIC RESONANCE, A POTENTIAL ALTERNATIVE?

1.6.1 Development into a clinical tool

The first full body (MR) image, showing the chest cavity, was demonstrated by Damadian’s ‘Indomitable’ in 1977 [30]. MR gave clinicians a new diagnostic imaging device that was capable of producing high resolution images of soft tissue with superior contrast over ultrasound and X-ray [1]. MR was quickly popular in musculoskeletal, abdominal and neurological imaging (Figure 1.17). The wide variety of different contrasts available and the continued developments of new techniques has made MR a significant modern clinical and research imaging modality [34].

In 1992, after once again experiencing initial rejection, two independent groups published papers that measured and linked different blood oxygenation levels to human brain activity. Functional magnetic resonance imaging (fMRI) gave researchers, in particular psychologists, a simple yet effective tool to directly investigate brain activity. FMRI has lead to many new insights into how the brain works [30]. Consequently at present, spine (26%) and brain (25%) imaging dominate the market [35]. But, with the continued development of MR hardware, imaging and processing techniques MR, is expanding into new areas of application [34].

Advantages over its competitors

The first real-time movie or cine of the heart was acquired in 1987, but unlike fMRI, CMR was not as revolutionary. CMR faced advanced competition [36]. In the late 1980’s two other modalities entered the field ultra fast cine computed tomography (cineCT) and positron emission tomography (PET). These modalities offered the collection of 3D tomographic data at a high quantitative accuracy and reproducibility. PET provided a means to measure regional myocardial metabolism, blood flow and function [36]. CineCT and CMR both offered comprehensive assessment of cardiac anatomy and function with superior contrast and spatial resolution [13; 36; 37].

The different modalities available have caused the wide spread use of CMR to lag behind the uptake of fMRI. The recent technical and procedural improvements have caused a marked increase in clinical interest [34]. Modern scanners are now able to acquire images in 4 – 20 seconds. Respiratory motion can be reduced by asking the patient to hold their breath and timing the image acquisition to
the correct phase in the cardiac cycle by monitoring the (ECG) [1]. An array of procedures (Figure 1.18) have been developed to provide CMR with a series of images with different contrasts [38]:

- **Spin-echo** or black-blood procedures are commonly used for multi-slice anatomical images [31; 1; 33];
- **Gradient echo** or bright-blood and **Steady State Free Precession** procedures are commonly used to investigate function through cine acquisitions [31; 1; 33];
- **Pre-saturation pulses** manipulate image contrast in infarct/viability imaging to null healthy myocardium\(^\text{11}\);
- **MR angiography** injects MR contrast agents into the blood to visualise the cardiovascular system for stenoses [39];
- **Myocardial perfusion** or delayed enhancement uses MR contrast agents and ultra fast imaging to visualise myocardial infarcts [31; 1];
- High resolution images of the the coronary arteries can be built up over long periods by timing the acquisition with patient breathing [31];
- **MR tagging** creates lines of magnetisation saturation over the tissue to investigate regional motion [40]; and
- **PC velocity mapping** is a procedure where the MR signal is made sensitive to velocity enabling the quantification of flow [41].

CMR’s wealth of different contrast mechanisms, high reproducibility and lack of ionising radiation makes it an attractive choice to clinicians [34]. With improving image hardware it is now possible to obtain more diagnostic information from a single examination than with any other test. The qualitative and quantitative morphological and functional information makes it the gold standard modality for many cardiac indexes [37; 13].

**CMR’s role in aortic stenosis**

CMR has been proposed as an alternative for the clinical assessment of the valvular disease aortic stenosis [42; 43; 44; 45; 46; 47; 48; 49]. Haghi et al [50] avoided

\(^{11}\)Heart tissue.
1.6. CARDIAC MAGNETIC RESONANCE, A POTENTIAL ALTERNATIVE?

![Spin Echo and Gradient Echo](http://atlas.scmr.org)

**Long Axis** | **Short axis** | **Long Axis** | **Short axis**

**Tagging** | **Velocity Mapping of the aorta**

**Long Axis** | **Short axis** | **Magnitude** | **Phase difference**

Figure 1.18: Examples of cardiac magnetic resonance imaging (http://atlas.scmr.org).

Errors associated with echocardiographic estimation of the LVOT diameter and VTI measurements by replacing them with the left ventricular stroke volume estimated by volumetric MR, widely regarded as the best method for stroke volume estimation. Velocity mapping using PC magnetic resonance has recently been proposed as an alternative to locating and quantifying velocity across the aortic valve. In particular, due to the ability to freely position the image plane, there is greater flexibility to ensure the velocity measurement is parallel to the stenotic jet.

One of the impediments to widespread application of phase contrast in clinical studies has been the relatively long acquisition times [39]. Now, with advances in parallel imaging and hardware it is possible to acquire PC cine in a single breath-hold. Several groups have since investigated using PC to determine the peak velocity [42; 43; 44], pressure gradients [45], a Doppler-derived AVA [46; 47; 48] and more recently a PC specific AVA [49]. All report good agreement between PC and echocardiography.
1.6.2 The ZEST trial

In a substudy from the New Zealand Eplerenone in Aortic Stenosis Trial (ZEST) trial, PC data was acquired in 31 moderate to severe aortic stenosis patients. PC estimate of stroke volume (PCSV) was compared to Doppler echocardiography and left ventricular stroke volume (LVSV).

The patients underwent a clinical echocardiographic assessment including evaluation of mitral regurgitation and peak velocity and velocity time integrals in the LVOT. Patients were excluded if the LV obstruction was not due to aortic stenosis, mitral regurgitation was significant (> 10 ml), there was evidence of other significant valvular heart disease (moderate or worse severity), or contraindications to MR.

LV cines were obtained with a standard retrospectively gated steady state free precession breath-hold (8-15s) sequence, using a phased array surface coil and ECG triggering. The LV was imaged from apex to base with six equally spaced short axis slices and three orthogonal long axis slices orientated at 60° increments around the LV, Figure 1.19. PC cines (25-40 images) were acquired 1 cm above the valve in the AR and 1 cm below the valve in the LVOT with a free-breathing (2-3 minutes) retrospectively-gated through-plane velocity encoded sequence with velocity compensation in the readout direction\(^{12}\). Typical image parameters can be found in Table 1.4.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value 1</th>
<th>Value 2</th>
<th>Value 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE</td>
<td>1.6 ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TR</td>
<td>30 ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flip angle (α)</td>
<td>60 deg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slice thickness Δz</td>
<td>6 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Field of View (FOV)</td>
<td>300 mm</td>
<td>300 - 380 mm</td>
<td></td>
</tr>
<tr>
<td>Acquisition matrix (%)</td>
<td>256</td>
<td>256 × 128</td>
<td></td>
</tr>
<tr>
<td>VENC LVOT (cm/s)</td>
<td>-</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td>Aortic root (cm/s)</td>
<td>-</td>
<td>500</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.4: Image parameters used in the ZEST substudy.

LVSV was determined by interactively fitting a 3D LV finite element model to the images, using the software package Cardiac Image Modeller (CIM) v4.6 (Auckland MRI Research Group, University of Auckland, New Zealand) [51].

\(^{12}\)This sequence will be referred to as the standard PC sequence, specific details are covered in chapter 2. In the latter stages of the thesis it will be adapted it will be referred to as the modified or optimised PC sequence.
1.6. CARDIAC MAGNETIC RESONANCE, A POTENTIAL ALTERNATIVE?

Figure 1.19: Planning of various slice orientations in the heart.

![Short axis](image1)

![Long axis](image2)

![Aortic valve](image3)

![Main Pulmonary artery](image4)

Table 1.5: Patient characteristics of the ZEST substudy.

<table>
<thead>
<tr>
<th>Description</th>
<th>mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66 ± 10</td>
</tr>
<tr>
<td>Male (number, %)</td>
<td>22(71%)</td>
</tr>
<tr>
<td>Body mass index (kg/m$^2$)</td>
<td>27.7 ± 3.9</td>
</tr>
<tr>
<td>Heart rate (beats/minute)</td>
<td>66 ± 19</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>143 ± 17</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>82 ± 11</td>
</tr>
<tr>
<td>Doppler echocardiography</td>
<td></td>
</tr>
<tr>
<td>Aortic peak velocity (cm/s)</td>
<td>383 ± 65</td>
</tr>
<tr>
<td>Aortic valve area (cm$^2$)</td>
<td>0.96 ± 0.30</td>
</tr>
<tr>
<td>Aortic valve area, max/min (cm$^2$)</td>
<td>1.86/0.46</td>
</tr>
<tr>
<td>Magnetic resonance imaging</td>
<td></td>
</tr>
<tr>
<td>LV mass index (g/m$^2$)</td>
<td>101 ± 24</td>
</tr>
<tr>
<td>Volumetric SV (mL)</td>
<td>96 ± 22</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>67 ± 8</td>
</tr>
</tbody>
</table>
The PC data were analysed by manually tracing around the LVOT and AR in each frame using ARGUS Syngo MR 2004V (Siemens Medical Systems, Erlangen, Germany). Flow at each frame was calculated by multiplying the average velocity within each contour by its area. PCSV was determined by summation of flow through the cardiac cycle.

A summary of patient characteristics is provided in Table 1.5. Doppler echocardiography found an average peak velocity of 383 cm/s with 11/31 patients having jet velocities greater than 400 cm/s and 2 patients greater than 500 cm/s. Bland-Altman comparisons between the gold standard LVSV with the PC SV estimate
1.6. CARDIAC MAGNETIC RESONANCE, A POTENTIAL ALTERNATIVE?

in the LVOT and AR are shown in Figure 1.20(a,b). The average underestimation of flow was worse in the AR (mean±standard deviation $-41 \pm 21\%$) than in the LVOT ($-24 \pm 21\%$).

Background phase correction did not improve these errors. SV errors are plotted against Doppler peak velocity in Figure 1.20(c) showing that the errors larger with increasing Doppler peak velocity, and that they were more marked in the aorta than the LVOT. PC peak velocities, obtained using no neighbourhood averaging, at the level of the AR are plotted against Doppler peak velocity in Figure 1.20(d) showing poor correlation and demonstrating that 10 patients had peak velocities close to the maximal encoding velocity (Venc) of 500cm/s.

1.6.3 Previous phase contrast results in the literature

The results of the ZEST substudy contradicts the “good agreement” between Doppler and MR found in several studies in the literature. The ZEST substudy showed significant underestimation of the stroke volume and severe discrepancies in the estimation of the peak velocity. This study raised uncertainties in the reliability of PC methods to accurately distinguish between moderate to severe patients. These discrepancies may have been missed or overlooked in previous studies due to a) their limited size or b) the restriction to patients with mild or moderate aortic stenosis, Figure 1.21.

Caruthers et al. [46] compared PC with Doppler in 24 patients with aortic stenosis. They reported that PC began to underestimate aortic stenosis severity when the Doppler velocity time integral exceeded 0.8m. Considering only those patients with severe aortic stenosis (defined as an aortic valve area of less than 1.0cm²), more than half were underestimated by PC. In another study by the same group [48], 23 patients were examined to investigate cross-correlation techniques for measuring jet eccentricity by acquiring two axial images were acquired in the AR. The authors reported good agreement of flow and velocity profiles between the two slices. However, 22/23 patients had peak velocities below 400cm/s and the one patient above 400cm/s had an obvious discrepancy between the two image planes.

Sondergaard et al. [47] investigated 12 patients with aortic stenosis, reporting good agreement between PC and Doppler, but 11/12 patients had peak PC velocities that underestimated the peak Doppler velocities. Similarly, a case study
CHAPTER 1. INTRODUCTION

(a) Caruthers et al. [46]
(b) Sondergaard et al. [47]
(c) Kilner et al. [42]
(d) Yap et al. [49]

Figure 1.21: Contradictory aortic stenosis results from the literature.

of 4 patients presented by Nayak et al. [43], using a spiral readout pulse sequence, reported good agreement of patients up to 420 cm/s, but PC still underestimated Doppler in all subjects. Kilner et al. [42] evaluated 29 patients with mitral or aortic stenosis (7 with Doppler velocities greater than 400 cm/s), with 3 showing clear discrepancies between PC and Doppler peak velocities. Finally, Yap et al. [49] applied a MR specific AVA calculation on 20 patients with congenital aortic stenosis; however, they had AVA disagreements of more than 0.4 cm$^2$!
1.7 Ultra short TE imaging

Most clinical imaging has been restricted by the echo time (TE) to tissues with a majority of long $T_2$ components (see Section 2.2.4) such as grey-matter, white-matter and muscle. The minimum available TE ranges from $1 - 2\, ms$ for gradient echo to $8 - 10\, ms$ for spin echo sequences [1; 52]. The signal from tissues with very short $T_2$, such as cortical bone, tendons, ligaments and menisci, rapidly decays away and usually appear dark in a $T_2$ weighted image.

Recently, with the advent of new techniques, coined ultra short TE (UTE), the imaging of short $T_2$ tissues has become possible. UTE methods can achieve TEs in the range of $0.05 - 0.20\, ms$ using half-pulse excitation and centric radial readouts [52]. For example, a fracture in the tibial plateau (cortical bone$^{13}$ $T_2 = 0.42 - 0.50\, ms$, periosteum$^{14}$ $T_2 = 5 - 11\, ms$) can be imaged using UTE with fat suppression, Figure 1.22. The UTE image in Figure 1.22(a) has signal from tissues with both long and short $T_2$ components. By acquiring a second image at a longer TE, an image dominated by long $T_2$ components can be simultaneously acquired. The difference of these two images reveals the short $T_2$ components (b). The periosteum is just visible in (b) but after enhancement with intravenous gadodiamide it is better visualised (d) (arrows).

UTE methods enable the investigation of tissues where the signal was previously rapidly lost. They have opened up an array of new possible applications in musculoskeletal MR and more recently in MR angiography [53]. Continued development and comparisons with current techniques are ongoing in order to establish the clinical role of UTE methods [52]. The ability of UTE methods to minimise TE makes them attractive for providing a faster “snapshot” of the velocity and flow that may be more robust to the underestimation of flow with standard PC sequences.

---

$^{13}$Cortical bone or compact bone is the external layer of long bones that provides the protection, support and resists the stresses produced from weight and movement [7].

$^{14}$Periosteum is the layer of connective tissue that surrounds the bone and contains the undifferentiated cells from which the bone substances are produced [7].
(a) TR/TE = 500/0.08ms before enhancement
(b) TR/TE = 500/0.08ms minus TE 5.95ms before enhancement
(c) TR/TE = 500/0.08ms after enhancement
(d) TR/TE = 500/0.08ms minus TE 5.95ms after enhancement

Figure 1.22: Coronal image of the cortical bone in the knee using UTE imaging with fat suppression (a) and a difference image (b) before enhancement and the same images with enhancement (c,d). (obtained from [52]).
1.8 Thesis Outline

The aim of this thesis is to determine the cause and develop a solution to the discrepancy seen in the PC velocity mapping of the turbulent jets characteristic of valvular diseases such as aortic stenosis.

**Chapter 2** gives a detailed description of the underlying MR principles behind the standard PC sequence and includes brief overviews on the practical considerations that are required to realise a PC cine.

**Chapter 3** details the design and construction of the high velocity phantoms. It develops and verifies the experimental protocol and the analysis procedure. The nature of the discrepancies and the possible effect of the TE on the accuracy of PC estimates of flow is investigated.

**Chapter 4** discusses the cause of the discrepancy (intravoxel dephasing). The structure of a stenotic jet is described and related to intravoxel dephasing. The experiments are extended to investigate various proposed mechanisms that affect intravoxel dephasing in a stenotic jet. The chapter attempts to identify areas of the pulse sequence that would benefit from further optimisation.

**Chapter 5** applies the current standard PC sequence and two modified variants in a small clinical trial of 15 patients. New issues concerning background phase became apparent.

**Chapter 6** examines algorithms for the correction of background phase errors, and applies these to the results of the clinical study. The results showed that modifications to the standard PC sequence are insufficient to achieve substantial improvement in SV, peak velocity and VTIs.

**Chapter 7** develops a phase contrast implementation of an ultra short TE sequence to further reduce the effects of intravoxel dephasing. Validation experiments in phantoms, normal volunteers and case study patients are presented.

**Chapter 8** summarises the main findings of the thesis and indicates areas of future work to be undertaken to further improve and validate phase contrast mapping of stenotic jets.
You know what these people do is really clever. They put little spies into molecules and send radio signals to them, and then they have to radio back what they are seeing.

Niels Bohr

The phase contrast pulse sequence

2.1 Introduction

A magnetic resonance (MR) image is created by manipulating the precession of spins through the application of radio-frequency (RF) and magnetic gradient pulses. Most images are based on the hydrogen nucleus or proton. The proton is the most abundant nucleus in the human body and therefore gives the strongest MR signal. The scanner’s instruction set, a pulse sequence, creates the different contrasts by differing the strength, duration, position and frequency of the pulses.

The purpose of this chapter is to step through the clinical phase contrast (PC) pulse sequence used in the ZEST trial, Figure 2.2, to introduce relevant MR concepts that are important for understanding the work in this thesis. The concepts behind the various parts of the PC sequence: selective slice excitation (i); through-plane velocity compensation (ii) and encoding (v); flow compensated Cartesian readouts (iii); and gradient spoiling on the slice select axis (iv) will be discussed. MR parameters with specific significance to PC will be defined, along with various imaging strategies required for clinical implementation.
Figure 2.2: The clinical PC pulse sequence consists of a velocity compensated (ii) acquisition followed by a velocity encoded acquisition (v). Excitation (i) is performed using a central lobe rectangular RF-pulse with flow compensated readouts (iii) and gradient spoiling (iv) on the slice select axis.
2.2 MR basic principles

2.2.1 A brief review of the quantum physics

Spin angular momentum, nuclear moments and Zeeman splitting

Nuclei with an odd number of protons and neutrons [54] exhibit the quantum property spin angular momentum, the rotation of nuclei about its own axis, Figure 2.1. A small magnetic field or nuclear magnetic moment is created, proportional to the charge, mass and rate of spin of the nuclei.

Nuclei can occupy different spin states \( M_I \) defined by its spin quantum number \( I \). The number of spin states follows the relation \( 2I + 1 \), each spin state is separated by the next with an integer value of \(-1\) [2]. The proton may occupy two spin states \( (M_I = \pm 1/2) \). Zeeman splitting describes, in the presence of an external static magnetic field \( (B_0) \), the different energy levels \( (E_I) \) experienced by a proton according to its current spin state [54]

\[
E_I = -\frac{h}{2\pi} \gamma B_0 M_I \tag{2.1}
\]

where \( h \) is Planck’s constant and \( \gamma \) is the gyromagnetic ratio [33], Figure 2.3. The difference in energy between these two states is given by:

\[
\Delta E = \frac{h}{2\pi} \gamma B_0 \tag{2.2}
\]

Figure 2.3: Zeeman splitting of a proton’s two spin states (adapted from [2]).
CHAPTER 2. THE PHASE CONTRAST PULSE SEQUENCE

The Larmor equation

The proton’s two energy states are referred to as spin up for the low energy state, parallel to the magnetic field and spin down for the high energy state, opposing the magnetic field. Transition between these two states can be achieved through the absorption/emission of a photon of electromagnetic radiation ($\Delta E$) at a particular frequency $\nu_0$ [33]:

$$\Delta E = h\nu_0$$

Equation 2.3

Equating equations 2.2 and 2.3 shows that the frequency ($\omega_0$) required to cause a transition from the spin up to spin down energy states is

$$\Delta E = \frac{h}{2\pi} \gamma B_0 = h\nu_0$$

$$\omega_0 = 2\pi\nu_0 = \gamma B_0$$

Equation 2.4

The Larmor frequency, $\omega_0$, underpins MR [2; 31; 1; 33; 39; 54]. Nuclear magnetic resonance (NMR) spectroscopy uses knowledge about different nuclei’s gyromagnetic ratio and $B_0$ to determine a sample’s nuclear composition by identifying the radio frequencies that are absorbed and emitted [33; 39; 54].

A spin ensemble

Samples do not consist of only one proton; they comprise of many [2]. Throughout the thesis the term spins$^1$ will be chosen to describe a group of protons all precessing at the same Larmor frequency.

In an external magnetic field the protons experience a torque that causes them to precess, Figure 2.4. They are either aligned (spin up) or opposed (spin down) to the magnetic field depending on their current energy state. The ratio of protons in the spin up ($N_{up}$) and spin down ($N_{down}$) states follows a Boltzmann distribution,

$$\frac{N_{up}}{N_{down}} = \exp\left(\frac{\Delta E}{k_B T}\right)$$

Equation 2.5

where $k_B$ is the Boltzmann’s constant and $T$ is the temperature [54].

$^1$In the literature a group of nuclei may be referred to as a spin isochromat, a spin ensemble, or spins.
At equilibrium the low energy spin up state is favoured, Figure 2.5. Summation of the individual magnetic moments results in the spins acquiring a net weak longitudinal\(^2\) magnetization (on the order of \(\mu T\)) \[1\]

\[ M_o = \frac{\rho_o \gamma^2 h^2}{4\kappa B T} B_0 \]  

where \(\rho_o\) is the density of spins per unit volume; the transverse\(^3\) components destructively combine. The summation of magnetic moments can be represented by a net magnetisation vector (NMV) that precesses about the external magnetic field at the same frequency as the spins within it.

The application of a RF-pulse \((B_1)\) rotating (in the transverse plane) at the Larmor frequency changes the distribution between the proton’s spin states and results in the protons simultaneously precessing about \(B_0\) and \(B_1\). Equilibration of the proton distribution reduces the longitudinal magnetisation, but the new precession about \(B_1\) results in the weak net magnetisation lying in the transverse plane. The result is that the NMV appears to rotate into the transverse plane. The quantum physics can be simplified to a classical mechanics description that describes how pulse sequences manipulate the NMV to create an MR image \[54\].

2.2.2 Classical magnetic resonance

The Bloch equations

Felix Bloch derived a set of phenomenological differential equations that describe the changes that occur to the spins’ NMV \[1\]. If the NMV \((M)\) is placed in a magnetic field \(B\), the NMV will experience a torque that causes it to precess about \(B\).

\[ \frac{dM}{dt} = \gamma M \times B \]  

If \(B\) is a static magnetic field along the z-axis \((B = B_0 \hat{k})\), the precession seen in Figure 2.4 can be described with the solution set

\[ M_x'(t) = M_x'(0) \cos \omega_0 t + M_y'(0) \sin \omega_0 t \]
\[ M_y'(t) = -M_x'(0) \sin \omega_0 t + M_y'(0) \cos \omega_0 t \]
\[ M_z(t) = M_z(0) \]  

\(^2\)The longitudinal direction is aligned with the direction of the external magnetic field.

\(^3\)The transverse direction is perpendicular to the direction of the external magnetic field.
CHAPTER 2. THE PHASE CONTRAST PULSE SEQUENCE

(a) Nuclei oppose or align with an external magnetic field \((B_0)\). The distribution favours the spin up over the spin down state and they precess at the same frequency. The vector sum of all magnetic moments equates to a weak net magnetisation about \(B_0\).

(b) When an RF pulse \((B_1)\) set at the Larmor frequency \((\omega_0)\) is applied transverse to the \(B_0\) axis, it (i) evens the distribution between spin states and (ii) causes the nuclei to simultaneously precess about \(B_1\), which results in a weak net magnetisation in the transverse plane.

Figure 2.5: Net magnetisation (adapted from [1])

where \(\omega_0 = \gamma B_0\). Similarly the rotation seen in Figure 2.5 can likewise be described by including the RF pulse \((B_1)\) rotating perpendicular to the external magnetic field such that \(B = B_1 \cos \omega_0 t \hat{i} + B_1 \sin \omega_0 t \hat{j} + B_0 \hat{k}\). The solutions are

\[
\begin{align*}
M_x'(t) &= M_o \sin \omega_1 t \sin \omega_0 t \\
M_y'(t) &= -M_o \sin \omega_1 t \cos \omega_0 t \\
M_z(t) &= M_o \cos \omega_1 t
\end{align*}
\]  

(2.9)

where \(\omega_1 = \gamma B_1\) and the initial condition \(M(0) = M_o \hat{k}\).
2.2. MR BASIC PRINCIPLES

The rotating frame of reference

These solutions and diagrams use the laboratory frame of reference \((x'y'z)\). Allowing the transverse plane \((x'y')\) to rotate with an angular frequency \(\omega\) about the longitudinal axis \(z\) simplifies the description. The NMV can be considered to precess about an effective magnetic field \(B_{\text{eff}} = (B_0 - \frac{\omega}{\gamma}) + B_1 i\). When \(\omega\) is chosen to equal \(\gamma B_0\) then in the rotating frame of reference \((xyz)\) the application of an RF pulse \(B_1\) along the \(x'\) axis causes the vector sum to precess solely about \(B_1\) [31], Figure 2.6.

\[
\alpha = \gamma B_1 t_{rf} \quad (2.10)
\]

The precession about \(B_1\) is many magnitudes smaller than about \(B_0\) (Hz vs MHz), hence it equates to a simple rotation about the \(y\) axis where \(t_{rf}\) is the duration of the RF pulse.

The flip angle \((\alpha)\) of a RF pulse relates to how much of the NMV is flipped into the transverse plane [39]. A 90° RF-pulse flips all of the longitudinal magnetisation into the transverse plane.

2.2.3 Detecting a signal

If the NMV is aligned longitudinally it is not detectable; in the transverse plane it is [1]. Through utilising Faraday’s law\(^4\) an induced signal known as a free

\(^4\)A changing magnetic field will induce a small voltage (emf) to be induced in a coil perpendicular to that field.
induction decay (FID), Figure 2.7, can be picked up in a coil placed around (body coil) or on top (surface coil) of the object. [31].

Figure 2.7: MR images are interested in measuring the frequency, phase and magnitude of the FID signal. The Fourier transform of the real and imaginary components yields the magnitude and phase of a FID signal. (adapted from [31]).

2.2.4 Relaxation Mechanisms

Tissues are characterised by the average time it takes to release the absorbed RF energy. Relaxation forms the basis for creating an anatomical MR image of different contrasts [1; 2]. Two relaxation times are used to measure the time interval for spins’ to spontaneously release their energy.

$T_1$ relaxation

Spin to lattice or $T_1$ relaxation measures the time taken for the longitudinal magnetisation ($M_z$) to return to 63% of its original value $M_o$ [2; 31; 1; 54]. It describes how quickly the spins give up their energy to return to their original equilibrium configuration. The $T_1$ relaxation curve, Figure 2.8, shows that after a 90° RF pulse the spins are equally distributed and the longitudinal magnetisation $M_o$ is flipped into the transverse plane. Over time, the spins spontaneously release their energy to the surroundings (the lattice) returning the spin state distribution to equilibrium [54] and the longitudinal magnetisation exponentially grows back towards $M_o$. $T_1$ is the time constant that describes the rate of growth.

$$M_z(t) = M_o(1 - e^{-\frac{t}{T_1}})$$ (2.11)
2.2. MR BASIC PRINCIPLES

(a) $T_1$ relaxation

(b) $T_2^*$ relaxation

Figure 2.8: $T_1$ relaxation refers to the time constant for the recovery of longitudinal magnetisation and $T_2^*$ relaxation refers to the time constant for the loss of transverse magnetisation.

$T_2$ vs $T_2^*$ relaxation

$T_2$ relaxation measures the time taken for the NMV’s transverse magnetisation ($M_{xy}$) to decay to 37% of its original value. The decay is due to the loss of the phase coherence, gained from application of the RF pulse. Spin to spin relaxation or true $T_2$ relaxation is where the energy is transferred between two spins that are within close proximity. The transferred energy is retained instead of being released to the lattice and can occur multiple times as long as $\omega_0$ remains the same [31; 1; 54; 2]. During this exchange process intramolecule and intermolecule vibrations and rotations causes $\omega_0$ to fluctuate and results in an irreversible loss of phase coherence reducing the transverse magnetisation.

Local differences cause the spins to experience slightly different magnetic fields and different Larmor frequencies [54]. The different Larmor frequencies increases the loss of phase coherence and hence transverse magnetisation. The combined loss of phase coherence due to true $T_2$ and inhomogeneities is called $T_2^*$ relaxation, Figure 2.8(b), and describes the decay envelope of the FID curve, Figure 2.7.

$$M_{xy}(t) = M_{xy0} e^{-t/T_2}$$

(2.12)

---

*Due to main field inhomogeneities, magnetic susceptibilities and imaging gradients.*
2.3 K-space

Any image can be decomposed into sinusoidal components that describe the repeating structures within an image. The representation of these spatial frequencies is known as K-space. Transformation from the image domain to K-space is performed using the two-dimensional discrete Fourier transform \((2D-\mathcal{F}T)\) and from K-space to image space by applying the inverse \(2D-\mathcal{F}T\), Figure 2.9.

Each pixel in the K-space image contributes to every pixel in the original image. Low spatial frequencies, the centre of K-space, contain global information about the image and are predominately responsible for the image’s rough shape, orientation and contrast. The fine edges and sharp features of an image are contained in the high frequency components, the periphery of K-space, Figure 2.9 [31].

2.3.1 K-space’s mathematical definition

A MR image is acquired in K-space. In PC imaging, K-space is commonly mapped using Cartesian image readout gradients. The process is analogous to reading a book where slice excitation is the identification of an individual page, phase encoding chooses a line and frequency encoding reads it [2].

The FID, Figure 2.7, oscillates close to the Larmor frequency \(\omega_0\).

\[
S(t) = S_0 e^{-\frac{t}{T^*}} \cos \omega t
\]  

(2.13)

To view the induced signal in the rotating frame of reference the oscillation \((\cos \omega t)\) needs to be removed through signal demodulation. Demodulation is where the measured signal is electronically multiplied by two reference sinusoid and cosinusoid signals, oscillating at the transmit frequency \((\omega_{rf})\), to obtain a real and imaginary representation of the induced signal [33; 39]. The demodulated signal from the MR echo can be written as

\[
S_R(t) = M_{xy}(x, y) \cos(\omega - \omega_{rf})t
\]

(2.14)

\[
S_I(t) = M_{xy}(x, y) \sin(\omega - \omega_{rf})t
\]

(2.15)

where \(M_{xy}(x, y)\) is the integral of the NMV’s transverse component. The demodulated real and imaginary signals can be combined into a complex representa-
2.3. K-SPACE

Original image

K-space image

Fourier transform pairs

Low pass filter
Preserving central K-space maintains the image’s global information

High pass filter
The periphery of K-space controls the image’s edges and fine details

Figure 2.9: The effect of removing high and low spatial frequencies in K-space has on an image.

So, given Larmor’s Eq. 2.4, the imaging gradients \( B = G_x x + G_y y \), and the fact that the MR signal from one line of K-space is the summation of all the individual spins \( \text{NMV} \), (Figure 2.13), Eq. 2.16 can be rewritten as [33]

\[
S_Z(t) = \int M_{xy}(x, y)e^{-i(x\gamma \int_0^t G_x(t) \, dt + y\gamma \int_0^t G_y(t) \, dt)} \, dx \, dy
\]  

(2.17)
CHAPTER 2. THE PHASE CONTRAST PULSE SEQUENCE

Following the substitutions of \( k_x = \gamma \int_0^t G_x(t) \, dt \) and \( k_y = \gamma \int_0^t G_y(t) \, dt \) this becomes [33]

\[
S_Z(k_x, k_y) = \int M_{xy}(x, y) e^{-i(k_x x + k_y y)} \, dx \, dy
\]  
(2.18)

Eq. 2.18, the mathematical definition of K-space, is simply the Fourier transformation of the NMV with respect to the applied magnetic gradients.

Rotating an image

In pulse sequence design the scanner can be thought of as an RF transmitter; an analogue to digital converter (ADC) that digitises the FID signal from the receive coils; and three orthogonal logical gradient axes that detail the slice select \((G_z(t))\), phase encoding \((G_y(t))\), and frequency encoding or readout \((G_x(t))\) magnetic gradient pulses. The gradients are generated by physical coils which, when activated, add or subtract from the main magnetic field \((B_0)\) in a linear manner. Gradients operate around the isocentre\(^6\) of the scanner and are measured in \(mT/m\). Different image orientations are achieved by applying a specific rotation matrix to transform the instructions from the logical gradient axes to the scanner’s magnetic gradient axes prior to acquisition. Sequences can be designed and discussed as if they are always imaging on the logical axes.

2.3.2 Slice excitation

Slice selective gradient

Slice excitation takes advantage of the spins’ dependency on the magnetic field. The main magnetic field is made to vary linearly by switching on the slice select magnetic gradient, Figure 2.10. The spins’ precession becomes dependent on position \( \omega_0 = \gamma(B_0 + G_z z) \). A slice of spins of a desired thickness \((\Delta z)\) can be excited by simultaneously playing out an RF pulse of a given bandwidth \((\Delta \omega_{RF})\) [1; 33; 39].

\[
\Delta \omega_{RF} = \frac{\gamma}{2\pi} G_z \Delta z
\]  
(2.19)

\(^6\)The centre point of the external magnetic field and the fulcrum of the magnetic field gradients.
2.3. K-SPACE

An ideal rectangular slice profile requires the envelope of the RF pulse envelope to be an infinite SINC function\(^7\). Obviously, this is impossible. The SINC RF pulse must be truncated to a finite length \([39]\).

To save time in PC imaging, only a central lobe is used. Consequently, slice profiles inherently suffer from Gibbs ringing. Gibb's ringing causes a series of excitation lines to appear parallel to any abrupt changes in the slice profile, because of the overshoot of the Fourier series components that occurs at the discontinuous first derivative on the margin of the SINC RF pulse envelope. This can be partly avoided by apodizing the SINC pulse with either a Hanning\(^8\) or Hamming\(^9\) filter \([39]\).

The RF pulse's flip angle, Eq. 2.10, determines the strength and duration of the slice select gradient. At the magnet's isocentre the carrier frequency of the RF pulse is the Larmor frequency. Off-centre excitation can be achieved by varying the carrier frequency as dictated by the centre of the desired slice \([33]\).

The isodelay and the refoocussing gradient

An important parameter of a slice excitation RF pulse is its isodelay time. The slice select gradient causes the spins to precess at slightly different frequencies. The result is that a RF pulse played out along the \(x\) axis will not result in the spins aligning with the \(y\) axis. Instead there will be a phase dispersion about the \(y\) axis. The isodelay time is the effective dephasing time that results in the phase dispersion. The isodelay point occurs at the peak of a symmetric central lobe RF pulse \([39]\).

The magnetisation behaves as if it was instantaneously flipped into the transverse plane \([55]\), Figure 2.10(\(t_0^-\)). At the isodelay point the spins are all in phase (\(t_0^+\)). During the remainder of the slice select gradient, their varying precessional frequencies causes a gradual fanning out of the spins (\(t_1\)). The transverse magnetisation loses coherency, reducing the potential strength of the MR signal. This can be mitigated by applying a second gradient pulse with opposite polarity causing the spins to refoocuss. Spins that were precessing slightly faster in the slice select gradient now precess slightly slower in the refoocussing gradient and

\(^7\)A SINC pulse is the Fourier transform of a top hat (rectangular) function.
\(^8\)A Hanning filter ensures a continuous first derivative if the envelope is symmetric.
\(^9\)A Hamming filter smoothly reduces the first derivative to zero at the margins.
CHAPTER 2. THE PHASE CONTRAST PULSE SEQUENCE

Figure 2.10: The simultaneous application of a magnetic gradient, that causes the spins to precess as a function of position, and an RF pulse with a specific bandwidth results in a slice of spins to be excited. The slice select gradient also results in a dephasing of the spins (see text), a second gradient is required to rephase the spins after excitation.

vice versa \((t_2)\). Correct refocussing at the end \((t_3)\) of the refocussing gradient is achieved by equalising the area between these two gradients pulses.

2.3.3 Phase encoding

In our book analogy, selective slice excitation provides a page of spins, phase encoding gets the line.

As discussed previously during a gradient pulse the spins’ precession frequency varies according to their position. When the gradient is turned off the spins return to their precessional frequency about \(B_0\); knowledge about their previous frequency is retained in the form of a phase shift [1], Figure 2.11. If a phase encoding gradient was applied that resulted in a phase variation of \(5 \times 6\pi\) across a large column of water then the summation of those spins would cancel: we would
get no MR signal. If the column of water was instead evenly compartmentalised by placing five solid blocks that give no signal then the water compartments phase would constructively add to give a strong signal. The MR signal is sensitive to repetitive patterns in the object of the same spatial frequency.

![Figure 2.11: A phase encoding gradient causes the spins phase to vary across the object at a specific frequency. If the object does not vary in that direction the signal from individual blocks cancel and we obtain no signal; however, regional variations of tissues with strong and no (or weak) signal at that frequency constructively combine and we obtain a detectable signal.](image)

In practice, the object’s many spatial frequencies or phase encoding frequency \((k_y)\) must be interrogated. This is achieved by stepping through \(N_y\) lines of K-space where \(\Delta k_y\), the phase encoding step size, is defined as [39]

\[
\Delta k_y = \frac{1}{\text{FOV}_y} = \frac{1}{N_y \Delta y} 
\]  (2.20)

When no phase encoding gradient is applied, the signal represents information from the whole object and is termed the zero spatial frequency, \(k_y = 0\).

Normally the number of phase encoding lines is chosen to be symmetric about \(k_y = 0\). The area of K-space examined becomes \((N_y - 1)\Delta k_y\) and the maximum spatial frequency investigated equates to

\[
k_y,\text{max} = \frac{1}{2} (N_y - 1)\Delta k_y 
\]  (2.21)

The spatial resolution in the phase direction \(\Delta y\) is a function of the maximum...
spatial resolution investigated \( k_{y,\text{max}} \),
\[
\Delta y = \frac{1}{N_y \Delta k_y} = \frac{N_y - 1}{2N_y k_{y,\text{max}}}
\] (2.22)

The gradient area of the maximum phase encoding lobe is specified as [39]
\[
A_{y,\text{max}} = \frac{2\pi k_{y,\text{max}}}{\gamma}
\] (2.23)

Spatial Aliasing due to Phase encoding

The discrete 2D-\( \mathcal{F} \) causes the object to be replicated in the phase direction. If the number of K-space lines or field of view (FOV) are chosen so that \( \Delta k_y \) is too large then this may cause the object to wrap in on itself. This is known as spatial aliasing [2], Figure 2.12.

![Figure 2.12: Spatial aliasing occurs when the spacing between spatial frequency \( \Delta k_y \) is too large causing the object to wrap in on itself.](image)

In PC imaging some spatial aliasing is acceptable provided the wrapped objects do not coincide with the region of interest. The Nyquist criterion to avoid spatial aliasing requires the encoding step size satisfy
\[
\Delta k_y \leq \frac{1}{F O V_y}
\] (2.24)

which suggests the maximum K-space sampling extent is related to the pixel size
\[
N_y \Delta k_y = \frac{1}{\Delta y}
\] (2.25)
2.3.4 Frequency encoding

In our book analogy, slice selection chose the page, phase encoding the line, now we must read it.

Conceptually, repeating a phase encoding gradient to bin individual spatial frequencies is possible but time consuming [1; 2]. Instead, if the transverse magnetisation was measured simultaneously with a gradient pulse, the frequency encoding or readout gradient, the MR signal would become a combination of sinusoids corresponding to each spins precessional frequency [31]. Taking the Fourier transform of the time domain signal enables the spins to be binned according to their spatial (precessional) frequencies, Figure 2.13.

![Diagram](image)

Figure 2.13: A frequency encoding gradient generates a location dependence for the spins’ precessional frequency that enables the Fourier transform to distinguish their position.

In the section of slice selection, we showed that during the slice select gradient the spins dephased relative to each other. The dephasing causes a smearing of the transverse magnetisation and a subsequent loss of signal. A similar loss of signal would occur due to the readout gradient. To compensate, the reverse of the slice select and refocussing pair is performed in the read direction.

A prephasing gradient causes the spins to dephase prior to the readout gradient,
so that the spins refocus during image acquisition. The envelope of the MR signal grows as the spins phase becomes more coherent, peaking when they are in phase, before decaying again—this is called an echo. The time taken between the centre of the RF excitatory pulse and the peak of the echo is known as the echo time (TE) [33; 39].

Once the readout gradient is determined, the prephasing gradient lobe can then be determined.

**Gradient vs spin echo**

A gradient echo sequence reverses the polarity of the pre-focussing gradient to refocus the spins. A spin echo sequence places a 180° refocussing RF pulse in between the pre-focussing and readout gradients. The spin echo pre-focussing gradient has the same polarity as the readout gradient. If the spins were precessing faster prior to the refocussing pulse, the 180° refocussing pulse makes them appear as if they were precessing slower. They begin to refocus in the readout gradient forming the echo. The main difference between these methods is that in a spin echo the dephasing due to field inhomogeneities can be recovered. The loss of transverse magnetisation is from true $T_2$ relaxation rather than gradient echo’s $T_2^*$ relaxation [31; 1].

The definition of the readout gradient’s area is related to the number of K-space data points along the readout direction ($N_x$), the receiver bandwidth ($\pm BW_{ro}$), the field of view ($FOV_x$) and the gyromagnetic ratio. For a Cartesian readout gradient, the duration ($T_{ro}$) is defined by [39]

$$T_{ro} = \frac{N_x}{2 BW_{ro}}$$  \hspace{1cm} (2.26)

and the amplitude ($G_{x,ro}$) can be derived from the desired $FOV_x$ given the frequency encoding step size ($\Delta k_x$)

$$\Delta k_x = \frac{1}{N_x \Delta x} = \frac{1}{FOV_x}$$  \hspace{1cm} (2.27)

$$\Delta k_x = \frac{\gamma G_{x,ro} T_{ro}}{2\pi N_x}$$  \hspace{1cm} (2.28)

$$G_{x,ro} = \frac{4\pi BW_{ro}}{\gamma FOV_x}$$  \hspace{1cm} (2.29)
2.3. K-SPACE

Figure 2.14: In a spin echo sequence, signal loss due to $T_2^*$ relaxation is recovered by refocussing the spins with a $180^\circ$ RF pulse: In a gradient echo sequence, the reversal of the pre-phase gradient’s polarity means signal loss due to $T_2^*$ relaxation can not be recovered as different inhomogeneities are experienced.

The pixels at the edge of the FOV$_x$ are precessing at the Nyquist frequency.$^{10}$ To avoid digitisation of higher frequencies, the MR signal is passed through a low pass filter prior to digitisation. The readout gradient is therefore not susceptible to spatial aliasing [31].

2.3.5 Populating K-space

Partial Fourier—The asymmetric echo and zero filling

The Fourier transform of a real object is Hermitian, the real part is symmetric and the imaginary part is antisymmetric about the centre of K-space [39].

$$S(-k_x, -k_y, -k_z) = S^*(k_x, k_y, k_z)$$  \hspace{1cm} (2.30)

To reconstruct a real object only half of K-space is needed in either the phase or frequency direction. Nevertheless, K-space data is normally collected symmetrically about the centre because unwanted phase shifts from motion, resonance

$^{10}$The Nyquist frequency represents the greatest frequency that can be unambiguously determined; it is typically half the sampling frequency.
frequency offsets, hardware delays, eddy currents, and receive $B_1$ inhomogeneities cause the reconstructed object to be complex.

In cardiac magnetic resonance (CMR) it is very popular to reduce the total scan time by asymmetrically sampling K-space, at the expense of a worse signal to noise ratio (SNR). To reduce the unwanted phase shifts, some data is acquired in the under sampled half of K-space [39], Figure 2.15. For non-PC imaging the spatial resolution is not compromised when Homodyne processing\textsuperscript{11} [39] is utilised.

Homodyne processing does not preserve the phase information. Phase sensitive reconstruction methods rely on zero filling to replace the non measured data. The low spatial frequencies in the partially sampled regions of K-space give a relatively faithful representation of the object’s phase. Although the truncation and zero filling of K-space data does increase Gibbs ringing near sharp edges, the phase of large structures should be preserved [39].

In the PC sequences used in this thesis, partial Fourier acquisition was implemented in the frequency encoding direction with an asymmetric echo. An asymmetric echo has an additional advantage that it reduces the gradient moments (Section 2.4), which is beneficial for reducing motion and flow artefacts. The asymmetry of the echo is defined by the partial Fourier fraction: the ratio between the partially acquired K-space line and the full K-space line required to completely cover K-space with the same spatial resolution. Typically in PC imaging a fractional echo between $70 - 80\%$ is required to ensure image quality is maintained [39].

Rectangular FOV vs reduced matrix size

Anatomical regions do not share similar dimensions. They are often not best covered by a square FOV but a rectangular FOV. If the phase encoding axis is aligned with the smaller dimension, then it is possible to reduce the number of phase encoding points $N_y$ relative to frequency encoding points $N_x$ without sacrificing spatial resolution [39]. The highest frequency component $k_{\text{max},y}$ is held constant to maintain spatial resolution. The effect of reducing the FOV\textsubscript{y} is a larger spacing between K-space lines $\Delta k_y$. The reduced number of K-space lines results in a faster scan time at the cost of a reduced SNR.

\textsuperscript{11}Exploitation of the Hermitian property.
2.3. K-SPACE

Figure 2.15: The amount of K-space (asymmetric echo, reduced K-space lines) that needs to be acquired can be reduced by using the Hermitian principle and zero filling. If the object is rectangular, the FOV$_y$ can be reduced at the expense of the SNR, whilst still avoiding spatial aliasing.

Another method to reduce the scan time is to reduce the number of K-space lines acquired, phase under-sampling, whilst keeping $\Delta k_y$ fixed. The effect is to reduce the maximum spatial frequency $k_{y,\text{max}}$ investigated Eq. 2.22. This decreases the spatial resolution but gains a slight increase in the SNR.

Both techniques zero pad the raw K-space matrix to obtain a power of two so the discrete Fast Fourier transform can be utilised. Zero padding is equivalent to interpolating the image. The resolution of the final image appears greater; however, no new signal has in fact been added [39].
2.4 Sensitivity to velocity and flow

During slice excitation and the readout gradients, the spins’ precess at different frequencies depending on their position in the slice. This causes the transverse magnetisation to fan out and requires it to be refocussed. What would happen if those spins had also moved during the gradient duration?

2.4.1 Phase accrual: The qualitative description

Spins precess according to their current position in the gradient. When spins move position their precession changes. In a bi-polar gradient, this results in the spins accruing phase relative to a stationary spin. For example Figure 2.16 shows three spins who start at the same location (isocentre) but are travelling at different velocities, \(0\), \(\frac{-v}{2}\), and \(v\), during a bi-polar gradient.

![Diagram of phase accrual](image)

Figure 2.16: The different precessional frequencies, due to the application of a bi-polar gradient, experienced by a moving spin is realised as a phase shift relative to a stationary spin.

At \(t_0\) all the spins are in phase. In the rotating frame of reference, the stationary spins do not rotate throughout the application of the gradient waveform. During the first positive gradient lobe, the spins travelling at \(v\) move away from their initial location to experience a larger magnetic field, therefore their precessional frequency increases. In the rotating frame of reference this is realised as a phase accrual relative to the stationary spins \((t_1\) and \(t_2)\). Similarly, spins travelling at
2.4. SENSITIVITY TO VELOCITY AND FLOW

\( -v \) experience a weaker magnetic field, precess slower and appear to lose phase relative to the stationary spins.

To remove any phase accrual due to position a second gradient lobe of equal area but opposite polarity is played out. The spins now either lose \((v)\) or gain \((-v)\) phase relative to the stationary spin \((t_3)\). At the end of the bi-polar gradient lobes the phase accrued by the spins is proportional to their velocity \((t_4)\).

2.4.2 Phase accrual: The quantitative description

Mathematically, phase accumulation \((\phi(t))\) can be calculated by investigating the gradient moments [39].

\[
\phi(t) = \gamma \int_0^t G(t)x(t)\, dt = \gamma \left( m_0 x + m_1 \left( \frac{dx}{dt} \right) + \frac{1}{n!} m_n \left( \frac{d^n x}{dt^n} \right) \right)
\]  (2.31)

where

\[
m_0 = \int_0^t G(t)\, dt
\]

\[
m_1 = \int_0^t G(t)t\, dt
\]

\[
m_2 = \int_0^t G(t)t^2\, dt
\]

\[
\ldots \ldots
\]

The bipolar gradient from Figure 2.16 has equal gradient lobe areas (a ratio of 1:1), \(m_0\) equals zero. When this condition is satisfied the gradient is said to be position compensated or 0th order moment nulled [39]. This can be extended further to compensate for velocity \((m_1 = 0)\) by repeating a bi-polar gradient of opposite polarity to form a 1:2:1 tri-polar gradient. When repeated again this forms a 1:3:3:1 gradient lobe waveform that will compensate for acceleration \((m_2 = 0)\); and so forth to null any moment, Figure 2.17 [39].
2.4.3 Velocity encoding

The calculation of the $0^{th}$, $1^{st}$ and $2^{nd}$ order moment for each waveform in Figure 2.17 shows that the nulling of a particular moment leaves the waveform sensitive to all higher moments. In PC velocity mapping the spins are assumed to be moving at a constant velocity. Any phase accrued ($\phi$) is solely due to velocity and can be determined according from Eq. 2.31 to be

$$\phi = \gamma m_1 v$$ \hspace{1cm} (2.32)

In a MR image the spins accumulate phase from other sources (e.g. $B_0$ inhomogeneities) Figure 2.17. PC imaging removes the spins’ inherent phase with a second acquisition that uses a different velocity encoding$^{12}$ e.g. a tri-polar velocity compensated waveform or another bi-polar gradient with opposite polarity, Figure 2.18. The velocity sensitivity is determined by the change in first order moment between the two gradient waveforms ($\Delta m_1$) \cite{39}.

$$\phi = \gamma |\Delta m_1| v$$ \hspace{1cm} (2.33)

Within a PC sequence’s repetition time (TR), the time between the centre of the first RF pulse in a pulse sequence and the repetition of that same pulse in a successive repetition of the same sequence, two acquisitions of the same K-space line is performed, each one with a different velocity encoding.

---

$^{12}$It is possible to remove the inherent phase using surrounding stationary tissue; however, these approaches have limited application around the heart where there is little stationary tissue nearby.
2.4. SENSITIVITY TO VELOCITY AND FLOW

Encoding schemes

Velocity encoding can be applied to any of the three orthogonal axis either individually or simultaneously. The preferred method for imaging aortic stenosis jets is through-plane velocity encoding, where the velocity encoding is placed along the slice select axis. Consequently, further description will focus on through-plane velocity sensitive sequences.

Three different schemes have been proposed: one-sided, two-sided and minimumTE encoding. In one-sided encoding one of the acquisitions is velocity compensated ($m_1 = 0$) and the other produces the desired velocity sensitivity ($\Delta m$), Figure 2.18. In the two-sided encoding the first order moment is symmetric $m_1 = \pm \frac{1}{2} \Delta m$, Figure 2.18. To save time these gradients are combined with the refocussing lobe from slice excitation, Figure 2.2. This allows the two-sided approach to be optimised so that the TE is minimised by relaxing the symmetric $m_1$ constraint [55].

Figure 2.18: Velocity encoding schemes (adapted from [39]).

In practice the scheme used often depends on how the anatomical magnitude image is created. If created from a single acquisition, the velocity compensated acquisition from the one-sided approach is desired as it is more robust to flow artefacts. If created from both acquisitions, the two-sided approach is a better choice as the flow artefacts are comparable between the sequences. The minimum TE approach can be used if the overriding consideration is to reduce the scan time to achieve a suitable breath hold.

The pulse sequence in Figure 2.2 uses the velocity compensated acquisition to reconstruct the anatomical magnitude image. This approach is also considered to reduce the mis-location of spins due to velocity/flow induced phase accrual.

\[\text{For specific calculation of the gradients we refer the reader to the paper by Bernstein et al [55].}\]
2.5 Motion artefact suppression

Patient breathing, cardiac motion and blood flow can cause motion artefacts, or ghosting, where the moving structure appears many times in the image. Motion artefacts only appear along the phase encoding axis. Physiological motion is slow in comparison to frequency encoding, where successive points are effectively measured sequentially, but is fast compared to consecutive points in the phase encoding lines. Through physiological motion, the anatomy may incur a different phase encoding and appear in a different position.

2.5.1 Respiratory motion

Breath-hold and Segmented K-space acquisition

The most effective method for reducing respiratory motion is to reduce the total scan time $T_{\text{scan}}$ so that the patient can hold their breath throughout the acquisition.

$$T_{\text{scan}} = N_{\text{ave}} \times N_{\text{slice}} \times N_y \times \frac{TR}{vps}$$  \hspace{1cm} (2.34)

where $N_{\text{ave}}$ is the number of averages, $N_{\text{slice}}$ the number of slices, $N_y$ the number of K-space lines, $TR$ is the repetition time and $vps$ the views per segment.

In PC imaging it is normal to only collect a cine from one slice and with only one average. If only one K-space line for each image was acquired per heart beat we would require $N_y$ heart beats which may result in scan time greater than one minute. Too long for any person to hold the breath comfortably. If we instead acquired several lines per image per heartbeat, i.e. a segment of K-space, we could reduce the overall scan time by sacrificing the true temporal resolution or temporal footprint $T_{fp}$ of the pulse sequence

$$T_{fp} = vps \times TR$$  \hspace{1cm} (2.35)

Reducing $T_{\text{scan}}$ to less than 15s creates a suitable breath-hold duration that is achievable by most patients.
2.5. MOTION ARTEFACT SUPPRESSION

Free Breathing

Alternatively, respiratory gating can be used. A bellows can be strapped around the patients chest so that as they breathed the changing volume could be used to create a respiratory waveform. In a similar process to cardiac triggering (Section 2.5.2), the waveform can be monitored to ensure that the reconstructed K-space data has the ribcage in a similar position.\(^{14}\)

2.5.2 Cardiac triggering

The electrocardiogram, Figure 1.3, can be used to synchronise the pulse sequence to the patient’s cardiac cycle.\(^ {15}\) Cardiac motion artefacts are minimised by ensuring that each K-space data set comes from the same phase of the cardiac cycle assuming that the tissue/blood is moving with the same velocity, acceleration, jerk and other higher order motions.

A PC pulse sequence’s TR is much less than the ECG’s R-R interval, allowing a PC cine to be built up over a series of heart beats (Figure 2.19). The QRS wave in the ECG can be used to indicate the start and end point of the cine acquisition.

Prospective triggering

In prospective triggering the user defines an acquisition window that stipulates the available imaging time and the number of desired frames. Once the QRS wave is detected the pulse sequence is repeatedly played out acquiring sequential lines of K-space until all the desired frames are collected. The scanner then waits until the next QRS wave to acquire the next segment of K-space. In prospective triggering if the acquisition window is set too long it is possible to skip a heart beat, thereby lengthening the breath-hold.

\(^{14}\)Other respiratory motion reduction methods are available such as respiratory compensated phase reordering and (recently) navigator echoes.

\(^{15}\)Other triggering mechanisms are also possible, for example peripheral pulse wave triggering (measurement of blood flow in the finger), but their signals are delayed and generally not as reliable as the ECG. Therefore they are normally only used as a backup.
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Figure 2.19: Prospective and retrospective cardiac triggering using \((vps = 4)\) segmented K-space acquisition.

**Retrospectively gated**

A retrospectively gated pulse sequence is continuously played out during the R-R interval to acquire sequential lines of K-space whilst recording the time from the ECG trigger at which they were acquired. The time stamps are subsequently used to reconstruct a user-specified number of frames (see Figure 2.5.2, often with the aid of an arrhythmia algorithm to detect false triggers due to gradient noise or patient arrhythmia.

**View sharing**

One image is created for each segment of K-space acquired over the heart beat. Additional intermediate images can be created by combining K-space data from successive images. For example, given two successive images obtained using 4 lines (or views) per segment \((vps)\) of K-space, a second intermediate image could be constructed using the last 3 lines from the first segment and the first line of the second segment\(^{16}\). This means a total of \(vps - 1\) intermediate images can be created. But due to the large amount of cardiac images produced, each scan is commonly restricted, ideally, to one intermediate phase located halfway in time between the original images [39].

\(^{16}\)This approach follows similar principles to those utilised in 2D echocardiography, Figure 1.5.2.
Note: There is an important distinction between the temporal footprint versus the temporal resolution of a cine acquisition. The temporal footprint of the sequence refers to the true temporal resolution of the measured K-space data. The temporal resolution of a sequence is the time between the resultant images once retrospective reconstruction and view sharing have been performed.

2.5.3 Motion artefacts from flow

Motion due to blood flow has two effects: a) the increased signal within a blood vessel due to the inflow of fully magnetised spins and b) the velocity induced phase effects which can decrease blood signal and/or create ghosting of arteries and veins in the phase encode direction.

Black blood versus bright blood imaging

In gradient echo sequences blood appears bright. This is due to the replenishment of fully magnetised spins. Since the TR is much shorter than the T1 relaxation times of most soft tissues, the spins’ longitudinal magnetisation is not able to fully recover. Instead the longitudinal magnetisation reaches a steady state over the scan. Flowing blood results in a fresh inflow of fully magnetised spins. These spins have a larger longitudinal magnetisation relative to stationary tissue and appear bright (have more signal). On the other hand blood in spin echo sequences appears black. Since, the blood has moved out of the imaging slice before the 180° refocussing pulse is applied, there will be no excited spins available to produce a signal.

The PC sequences used to image fast moving blood such as in aortic stenosis jets are all gradient echo sequences. Blood should appear bright.

2.5.4 Flow compensated imaging gradients

The pre-focussing readout gradient used in image readout is typically designed to satisfy the condition $m_0 = 0$ at TE. Signal loss due to the spins position is prevented. Signal loss due to moving or flowing spins is not. A flow compensated pre-focussing gradient ensures that at the centre of the echo both the 0th, $m_0 = 0$, and 1st, $m_1 = 0$, moments are nulled (Figure 2.20). Though the phase encoding
axis can be similarly nulled this increases TR/TE, and makes breath hold cardiac imaging difficult.

Figure 2.20: The phase contrast pulse sequence diagram with gradient moments superimposed.
2.6 Image reconstruction

The inverse $2D-\mathcal{F}T$ of K-space results in images with real and imaginary parts. Magnitude images, the recognisable anatomical MR images shown thus far (Figures 1.17, 1.18, 2.9 and 2.9), are formed by taking the complex magnitude of the real and imaginary parts. The phase of the real and imaginary parts, normally discarded, is used in PC imaging to create the velocity map, Figure 1.18. The ability to measure velocity whilst maintaining the anatomical and positional information is what is so beneficial in PC imaging.

Two different methods can be used to calculate phase: complex difference reconstruction and phase difference reconstruction. In this thesis only phase difference reconstruction has been employed. Complex phase difference uses the law of cosines to reconstruct the image, it does not take on negative values. The loss of directional information does not allow the quantification of flow, hence phase difference reconstruction is preferred in the quantitative imaging of aortic stenosis jets.

2.6.1 Phase difference reconstruction

In two-sided encoding, the acquisition of a bipolar velocity encoding gradient and a subsequent acquisition with the inverse bi-polar gradient results in two phase images. The spins have accrued phase proportional to their velocity as well as the inherent phase shift due to imaging gradients and $B_0$ inhomogeneities, and gradient eddy currents. Subtraction of these two phase shifts would remove the inherent phase shifts and reveal the phase shift due to velocity, Figure 2.21.

In practice, phase difference reconstruction is performed with a per-pixel arctangent operation. After the inverse $2D-\mathcal{F}T$ of the two acquired images we denote a particular pixel from each image in its complex form:

\[
\begin{align*}
Z_1 &= x_1 + iy_1 = C_1e^{i\phi_1} \\
Z_2 &= x_2 + iy_2 = C_2e^{i\phi_2}
\end{align*}
\] (2.36)

The phase difference for this pixel can be calculated by

\[
\Delta\phi = \arctan\left(\frac{y_1}{x_1}\right) - \arctan\left(\frac{y_2}{x_2}\right) = \phi_1 - \phi_2
\] (2.37)
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The subtraction of phasors from opposing bi-polar gradients results in a phase difference that is proportional to velocity.

![Diagram of phase subtraction](image)

Figure 2.21: The subtraction of phasors from opposing bi-polar gradients results in a phase difference that is proportional to velocity.

The two arctangent operations are computationally expensive and introduce phase wraps\(^\text{17}\), Figure 2.22. To improve computational efficiency and reduce phase wraps it is advantageous to perform the subtraction in the complex domain to form a complex ratio that uses only one arctangent operation.

\[
\Delta \phi = \angle \left( C_1 e^{i\phi_1} - C_2 e^{i\phi_2} \right) = \arctan \left( C_1 C_2 e^{i(\phi_1 - \phi_2)} \right) = \arctan \left( \frac{Z_1}{Z_2} \right) \quad (2.38)
\]

2.6.2 Aliasing velocity

The calculation of Eq. 2.37 and Eq. 2.38 on a computer is performed with the four-quadrant arctangent operator (ATAN2). The ATAN2 function investigates the signs of the numerator and denominator to determine the value’s quadrant.

\(^\text{17}\) Phase wraps are occur at an abrupt transition between \(\pi\) and \(-\pi\).
2.6. IMAGE RECONSTRUCTION

to increase the dynamic range of the phase image from $\pm \frac{\pi}{2}$ to $\pm \pi$. If after the phase difference reconstruction the spin velocity resulted in a phase shift greater than $\pm \pi$ then it would be wrapped back or aliased, Figure 2.23. The aliasing velocity or maximal encoding velocity ($V_{\text{enc}}$) is by definition the velocity along the gradient direction that results in a phase difference of $\pm \pi$. From Eq. 2.32

$$V_{\text{enc}} = \frac{\pi}{\gamma |\Delta m_1|}$$

(2.39)

It is possible to restore aliased pixels back to their true values by a process called phase unwrapping. In the thesis, phase unwrapping, when required, is performed using the “Robust two dimensional weighted phase unwrapping algorithm” developed by Ghiglia and Romero [56]. This is just one of many possible phase unwrapping algorithms available. Because phase unwrapping is not a focus of this thesis, we refer the reader to the paper for detail [56].

![Figure 2.23](image)

Figure 2.23: Velocity aliasing occurs when the actual phase difference is greater than the measurable range, $\pm \pi$. The true phase can be recovered by adding the correct multiple of $2\pi$.

2.6.3 Unwanted background phase errors

Even after performing the phase difference calculation there remains unwanted phase errors, principally due to gradient eddy currents and concomitant gradients.
CHAPTER 2. THE PHASE CONTRAST PULSE SEQUENCE

Eddy currents

Unwanted gradient eddy currents are generated by the electrical fields induced by the time varying parts of the gradient waveform (Faraday’s Law), e.g. the ramp up and ramp down of a trapezoidal waveform, in the conducting objects in the scanner. A magnetic field is induced to oppose the changing electrical field generated by the eddy currents (Lenz’s Law). The size of the eddy currents are dependent on the amplitude and duration of the ramp. The eddy currents from each ramp act to distort the desired gradient waveform 2.40. Eddy currents are commonly classified into $B_0$ eddy currents ($e_{B_0}$) and linear eddy currents ($e_l$)

$$B(x, G(t), t) = G(t) \cdot x + e_l(G(t)) \cdot x + e_{B_0}(G(t)) + e_{other}(x, t) \quad (2.40)$$

where $e_{other}$ is the eddy currents resulting from other sources [57].

$B_0$ eddy currents manifest themselves as an unwanted phase shift between the two PC acquisitions. Linear eddy currents cause a mismatch between the applied Larmor frequency and the Larmor frequency experienced within the slice [57]. The time dependence of an eddy current is best described using exponential functions and is characterised by time constants and amplitudes. The time constants describe the build up and decay of a gradient eddy current and can range from a few micro seconds to hundreds of seconds.

Eddy current compensation is vital for many advanced sequences. The opposite polarity of the ramps mean eddy currents partially cancel, Figure 2.24. The extent of cancellation depends on the gradient waveform’s plateau, and the decay rate of the eddy current. Ramp balancing can be used as one form of eddy current compensation, but eddy current compensation is generally better dealt with in four ways:

1. **Shielded gradient coils**: Eddy currents are normally established in the conducting structures outside the gradient coil. A secondary (outer) shield coil is employed to oppose the primary (inner) coil. These coils are designed so that the fringe field\(^{18}\) rapidly decays to zero minimising any induced eddy currents in the conducting structures.

2. **Waveform pre-emphasis**: Control theory is used to characterise the induced eddy currents of the gradient hardware. A model of the eddy currents can be used to modify the input of the ideal gradient waveform or

\(^{18}\)The net field outside a gradient coil or the magnet bore itself.
to design high pass filters that modify the waveform so the realised gradient waveform is a better representation of the expected waveform.

3. **Gradient derating**—for gradients where a specific area is required rather than a specific amplitude it is possible to reduce eddy currents by reducing the gradient amplitude. Reducing the slew rate whilst maintaining a fixed amplitude is not normally as effective as reducing the amplitude because the rate of eddy current build up is proportional to the ramp’s duration i.e. a lower slew rate has more time to build up a significant eddy current. If the eddy current’s time constant is much longer than the ramp time the strength of the eddy current increases almost linearly with time.

4. In general, the shielded gradients, waveform pre-emphasis and gradient derating are adequate mechanisms for suppression of eddy current effects. Some very advanced imaging techniques are particularly sensitive to eddy currents. These techniques normally rely on application specific calibrations during image acquisition or reconstruction. These can include attempting to measure eddy currents during the scanning procedure.

![Diagram of waveform distortion](image)

**Figure 2.24:** Distortion of a trapezoid waveform due to eddy currents and the effects of reducing the gradient strength and slew rate on the eddy currents (schematic representation adapted from [39]).

In PC imaging the final approach to background phase correction due to eddy currents, if required, is to obtain an average estimate of the residual background phase by selecting stationary tissue around the vessel and subtracting it from vessel. The variation in background phase is approximately linear (Chapter 6). However, in cardiac imaging there is no stationary tissue around the heart.
Concomitant gradients

The second major contributor to background phase errors are concomitant magnetic fields. According to the Maxwell equations,\textsuperscript{19} when the linear magnetic field gradient \( G_x \) is activated with the intention of causing a linear variation in \( B_z \) with respect to \( x \), it unavoidably produces a variation of \( B_z \) with respect to \( z \). This causes the NMV to deviate from the direction of \( B_0 \) and results in the magnetic field exhibiting higher order spatial dependence.

In contrast to eddy current induced fields, concomitant gradient fields are due to a fundamental magnetic property. They exist only when there is a gradient switched on and disappear immediately when it is switched off. The concomitant magnetic field \((B_c)\) can be described analytically by [58]:

\[
B_c(x, y, z, t) = \frac{1}{2B_0} \left( G_x^2 z^2 + G_y^2 z^2 + G_2^2 \frac{x^2 + y^2}{4} - G_x G_z xz - G_y G_z yz \right) \tag{2.41}
\]

The concomitant phase can cause a number of artefacts, geometric image distortion, ghosting intensity loss, blurring and shading. In the case of PC image it gives rise to a concomitant phase difference error \( \Delta \phi_c \)

\[
\Delta \phi_c(x, y, z) = \phi_{aq1}^c(x, y, z) - \phi_{aq2}^c(x, y, z) \tag{2.42}
\]

There are two principle strategies for removing concomitant gradients:

1. removal of the source of the concomitant gradient within the pulse sequence
2. phase correction applied in the imaging domain.

A PC sequence can be designed so that the self-squared terms in Eq. 2.41 can be removed, e.g. by using the two-sided encoding scheme, and the cross terms eliminated by ensuring there is no overlap of gradients between axis. Unfortunately, this method and other pulse sequence based strategies do so at the expense of the TE. Alternatively, the second approach, applied in the PC sequences discussed in this thesis, explicitly calculates the expected phase due to the applied gradients for each position in the image [58]. The concomitant gradient phase errors

\textsuperscript{19}The complete set of laws governing electromagnetism: Gauss’ law; Gauss’s law for magnetism; Faraday’s law of induction; the Ampère-Maxwell equation; and Lorentz’s law.
should be corrected prior to the arctangent operation. Eq. 2.37 is modified to become:

$$\Delta \phi_{corr} = \arctan \left( \frac{\Im (Z_1 Z_2^*) e^{-i \phi_e}}{\Re (Z_1 Z_2^*) e^{-i \phi_e}} \right)$$

(2.43)

This approach has the additional advantage that the concomitant gradients’ non-linear spatial dependence is removed, enabling any residual linear eddy current based background phase to be more easily removed.

**Gradient non-linearities**

Additional background phase errors are introduced from gradient non-linearities. In non-PC imaging, these non-linearities lead to image distortion at the edges of an image, which can be unwrapped through the application of a spatial “distortion correction filter” during image reconstruction. In PC imaging the non-linearities lead to local changes in the strength and direction of the velocity encoding that leads to a non-linear background phase errors which worsens at a larger distance from the isocentre. These errors are not corrected by the spatial distortion correction filter and may require additional correctional. Fortunately the non-linearities close to the isocentre, where PC imaging is performed, are small.

**2.6.4 Phase difference image reconstruction algorithm**

In addition to these PC specific reconstruction techniques other general corrections are also applied:

1. Windowing and sign alternation;
2. Multicoil combination;
3. Image warping; and
4. Rectangular FOV processing.

A complete discussion is outside this thesis but the flowchart, Figure 2.25, summarises the reconstruction steps.
Figure 2.25: Phase correction algorithm (adapted from [39]).
2.7 Gradient spoiling

At the end of the pulse sequence’s TR, residual transverse magnetisation may still remain. If not correctly eliminated, the residual transverse magnetisation may interfere with the next acquisition. Gradient spoiling is where a gradient, typically located at the end of a sequence, spoils or kills the unwanted MR signal. The area of the spoiler gradient is typically large enough in ensure that all the spins that make up the transverse magnetisation are completely dephased.

The minimal gradient area required to spoil the unwanted transverse magnetisation is typically determined by experiment. The area of the spoiler can be incrementally increased by either modifying its gradient or amplitude until the observed image artefacts are removed. Normally a $2\pi$ minimum phase dispersion is required across the voxel.

The concomitant gradients described previously make it unnecessary to apply spoiling gradients on every axis. It is normally placed along the axis that results in the largest phase dispersion or has the lowest duty cycle to avoid overheating of the gradient amplifiers. It is also advantageous to choose the same polarity as the readout gradients. This ensures that the phase accumulation due to the readout gradient constructively adds to the dephasing. But, as with any gradient, gradient spoilers can introduce eddy currents that do not fully decay prior to the next acquisition and which can lead to other artefacts.

The PC sequence in Figure 2.2 applies gradient spoiling along the slice select axis.
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2.8 Encasing the spins in a voxel

Thus far we have eluded to but not introduced the voxel. Though a PC image appears two dimensional, it must be remembered that the magnitude and the phase of each pixel are actually 2D representations of all the spins’ within a 3D volume, a voxel.

*Note throughout the remainder of the thesis we will refer to the voxels of an MR image, rather than pixels, to enforce in the reader the importance of considering the source of the MR signal as a 3-D volume.*

2.8.1 The source of noise

Noise in MR images is primarily due to random voltage fluctuations in the receive coil and the sample’s electrical and magnetic field \((emf)\). Other sources of contamination such as digitisation error or ghosting artefacts due to moving spins are considered to be minimised in an ideal PC sequence. The variance of the noise fluctuations is equivalent to the thermal noise or the measured noise \(\sigma^2_m\) and is proportional to the temperature \((T)\), the resistance \((R = R_{\text{body}} + R_{\text{coil}} + R_{\text{electronics}})\) and the sampling bandwidth \((BW_{\text{ro}})\) of the receive coil.

\[
\sigma^2_m = (emf_{s,\text{noise}} - emf_{s,\text{noise}})^2 \propto 4kT \cdot R \cdot BW_{\text{ro}} \quad (2.44)
\]

The random measured fluctuations appear as *white noise*\(^{20}\) and can equate to the sum of the variances from the body, receive coil and the scanner’s electronics, all of which are considered to be statistically independent.

\[
\sigma^2_m (k) = \sigma^2_{\text{body}} (k) + \sigma^2_{\text{coil}} (k) + \sigma^2_{\text{electronics}} (k) \quad (2.45)
\]

In most circumstances the temperature and the resistance of the body, coil and electronics can be considered not to vary. Thereby the variation in noise of any K-space point is principally determined by the \(BW_{\text{read}}\).

---

\(^{20}\)White noise exhibits equal power across all frequencies, has a mean of zero and a standard deviation equal to the root mean squared (RMS) value.
2.8. ENCASING THE SPINS IN A VOXEL

Averaging: Multiple acquisitions and the voxel

The SNR of the measured signal \( s_m(k) \) can be effectively increased by adding multiple K-space lines from additional acquisitions \( N_{acq} \).

\[
s_{m,\text{ave}}(k) = \frac{1}{N_{acq}} \sum_{i}^{N_{acq}} s_{m,i}(k) = \frac{1}{N_{acq}} (N_{acq} s_m(k)) = s_m(k) \tag{2.46}
\]

Long term averaging is where all K-space lines for all scans are acquired sequentially before performing signal averaging. Short term averaging is where signal averaging is performed over each line of K-space. If we assume the measured signal is the same and that the noise from each acquisition can be considered to be statistically independent, then the variance of the noise adds in quadrature.

\[
\sigma_{m,\text{ave}}^2(k) = \frac{1}{N_{acq}^2} \sum_{i}^{N_{acq}} \sigma_m^2(k) = \frac{\sigma_m^2(k)}{N_{acq}} = \frac{\sigma_m(k)}{\sqrt{N_{acq}}} \tag{2.47}
\]

The SNR of the measured K-space signal becomes:

\[
SNR(k) = \sqrt{N_{acq}} \frac{s_m(k)}{\sigma_m(k)} \tag{2.48}
\]

Analogous to reducing \( \sigma_m^2(k) \) by repeated acquisitions of K-space, the image noise \( \sigma_o \) of a voxel is a combination of all the K-space points acquired. Increasing the number of K-space points by a factor of \( a \) would decrease the noise by a factor of \( \frac{1}{\sqrt{a}} \), which can be generalised to

\[
\sigma_{m,\text{voxel}}^2 = \frac{\sigma_m^2}{N_x N_y} \tag{2.49}
\]

2.8.2 The voxel’s signal to noise ratio

The voxel signal magnitude \( S \) of a homogeneous volume element \((\Delta x, \Delta y, \Delta z)\) for proton imaging (Eq. 2.6) is given by

\[
S = \frac{\gamma^3 h^2}{\pi^2 k_B T} B_0^2 B_\perp p \Delta x, q \Delta y, r \Delta z \cdot \Delta x \Delta y \Delta z \tag{2.50}
\]

where \( \hat{\rho} \) is the effective spin density. Combining this with equations 2.44 and 2.49 we can determine the dependence of SNR on the imaging parameters:

\[
SNR_{\text{voxel}} \propto \frac{\Delta x \Delta y \Delta z \sqrt{N_{acq}}}{\sqrt{\frac{BW_{\text{read}}}{N_x N_y N_z}}} \tag{2.51}
\]
CHAPTER 2. THE PHASE CONTRAST PULSE SEQUENCE

After image reconstruction of a PC velocity image, areas of low SNR, such as air, appear dark in the magnitude image. The signal is restricted to the lower bounds of the dynamic range. In contrast, areas of low SNR in the phase image span the entire dynamic range and results in a characteristic salt and pepper noise. This means that the SNR of the phase estimate of moving tissue \( SNR_{\Delta \phi} \) is also dependent on the \( V_{\text{enc}} \).

\[
SNR_{\Delta \phi} \propto SNR_{\text{mag}} \left( \frac{|v|}{V_{\text{enc}}} \right)
\]

(2.52)

Though changing any of these parameters can alter the SNR, it is necessary to check the interrelations that exist. For example, halving the image domain’s spatial resolution \( \Delta y \) by decreasing the \( FOV_y \) while holding \( N_y \) constant halves the expected SNR. On the other hand halving \( N_y \) and holding \( FOV_y \) fixed only results in SNR decreasing by a factor of \( \sqrt{2} \) but at the expense of doubling the scan time, Table 2.1.

Similarly, Table 2.2, if \( N_x \) in the readout is halved then the gradient readout duration may also halve, reducing the overall scan time. This incurs an increase in SNR of \( \sqrt{2} \). But, if the acquisition time was fixed, halving the bandwidth and the amplitude of the gradient instead, the SNR is increased by a factor of 2.

The manipulation of PC image parameters, to either change the dynamic range, resolution or speed up the overall scan time, must always consider the interrelations and their expected effect on the SNR.

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>( \Delta y )</th>
<th>( N_y )</th>
<th>( FOV_y )</th>
<th>( \Delta k_y )</th>
<th>( SNR )</th>
<th>( T_{\text{scan}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>( \Delta y_o )</td>
<td>( N_o )</td>
<td>( FOV_o )</td>
<td>( \Delta k_o )</td>
<td>1</td>
<td>( T_o )</td>
</tr>
<tr>
<td>Double ( N_y ), fix ( FOV_y )</td>
<td>( \frac{\Delta y_o}{2} )</td>
<td>2( N_o )</td>
<td>( FOV_o )</td>
<td>( \Delta k_o )</td>
<td>( \frac{1}{\sqrt{2}} )</td>
<td>2( T_o )</td>
</tr>
<tr>
<td>Half ( FOV_y ), fix ( N_y )</td>
<td>( \frac{\Delta y_o}{2} )</td>
<td>( N_o )</td>
<td>( \frac{FOV_o}{2} )</td>
<td>( \Delta k_o )</td>
<td>( \frac{1}{\sqrt{2}} )</td>
<td>( T_o )</td>
</tr>
<tr>
<td>50% K-space line reduction</td>
<td>( 2\Delta y_o )</td>
<td>( \frac{N_o}{2} )</td>
<td>( \frac{FOV_o}{2} )</td>
<td>( \Delta k_o )</td>
<td>( \sqrt{2} )</td>
<td>( \frac{T_o}{2} )</td>
</tr>
<tr>
<td>50% Rectangular FOV</td>
<td>( \Delta y_o )</td>
<td>( \frac{N_o}{2} )</td>
<td>( \frac{FOV_o}{2} )</td>
<td>2( \Delta k_o )</td>
<td>( \frac{1}{\sqrt{2}} )</td>
<td>( \frac{T_o}{2} )</td>
</tr>
</tbody>
</table>

Table 2.1: Changing SNR, \( T_{\text{scan}} \) and K-space coverage in the phase direction.

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>( \Delta x )</th>
<th>( N_x )</th>
<th>( FOV_x )</th>
<th>( G_x )</th>
<th>( BW_{ro} )</th>
<th>( SNR )</th>
<th>( T_{\text{ro}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>( \Delta x_o )</td>
<td>( N_o )</td>
<td>( FOV_o )</td>
<td>( G_o )</td>
<td>1</td>
<td>( T_{aq} )</td>
<td></td>
</tr>
<tr>
<td>Half ( N_x )</td>
<td>( 2\Delta x_o )</td>
<td>( \frac{N_o}{2} )</td>
<td>( FOV_o )</td>
<td>( G_o )</td>
<td>1</td>
<td>( \sqrt{2} )</td>
<td>( \frac{T_{aq}}{2} )</td>
</tr>
<tr>
<td>Half ( N_x ) and ( BW )</td>
<td>( 2\Delta x_o )</td>
<td>( \frac{N_o}{2} )</td>
<td>( \frac{FOV_o}{2} )</td>
<td>( \frac{G_o}{2} )</td>
<td>( \frac{1}{2} )</td>
<td>( 2 )</td>
<td>( T_{aq} )</td>
</tr>
</tbody>
</table>

Table 2.2: Changing SNR, \( T_{\text{scan}} \) and K-space coverage in the frequency direction.
2.9 Where to go for more

In this chapter we have given an overview of the main underlying principles required to explain the key concepts of a PC pulse sequence.

The main concepts to take forward are:

1. the voxel signal is formed from the summation of the individual spins;
2. the velocity encoding and compensation assumes a constant velocity;
3. the TE defines the time from the centre of excitation to the peak of the echo;
4. and importantly any manipulation of the sequences image parameters to affect resolution scan time or the dynamic range inherently affect the SNR.

To obtain a better understanding, including a detailed mathematical description, we refer the reader to several different texts. We suggest:

- Callaghan’s “Principle of Nuclear Magnetic Resonance Microscopy” [54] for a thorough description of the quantum mechanics and the effects of spin motion;
- McRobbie et al’s “MRI: From Picture to Proton”,
- Brown et al's “MRI: Basic Principles and Application”,
- Bushong’s “Magnetic Resonance Imaging: Physical and Biological principles”

for an introduction to MR physics at the clinical level, explanations about image contrast and MR’s applications; and

- Haacke et al’s “Magnetic resonance imaging: Physical principles and sequence design”,
- Bernstein et al’s “Handbook of MRI pulse sequences”

for a more rigorous description of the MR physics and the practical implementation of the sequences.
No amount of experimentation can ever prove me right; a single experiment can prove me wrong.

Albert Einstein

3

In-vitro examination of phase contrast errors

3.1 Introduction

Phase contrast (PC) measurement of stenotic jets has been previously studied. In-vitro experiments conducted by Stahlberg et al [59] and Sondergaard et al [44] in 1992 investigated the influence of image parameters on PC measurements of mean velocity in steady (non-pulsatile) flow. The stenotic jets had velocities up to 480 cm/s. They found that PC measurements in stenotic jets were not completely reliable. PC estimations of stenotic valve area had an error of 24% and flow rate, 28%. Higher order motion such as acceleration increased intravoxel dephasing leading to signal loss and errors in velocity quantification [60]. Shortening the echo time (TE) reduced the intravoxel dephasing due to higher order motion.

Subsequent in-vivo data was limited to less than jets of 200 cm/s [61], Figure 1.21. The more recent studies that show “good agreement,” must assume (and some acknowledge [42]) that the TE is short enough to be relatively free from higher order motion errors. The results of our own study, Figure 1.20, does not share a similar “good agreement.” We hypothesise that errors may have been missed or overlooked in other studies due to their limited size or restriction to patients with mild or moderate aortic stenosis.

Since Stahlberg’s and Sondergaard’s work, significant advancements in magnetic resonance (MR) hardware have occurred. Yet, there have been no subsequent in-vitro studies investigating the ability of PC to accurately measure jet velocities and flow in the presence of a stenosis. To investigate these discrepancies, we
constructed an experimental MR pipe phantom\textsuperscript{1} to replicate stenotic and non-stenotic flows \textit{in-vitro}. A series of experiments was performed to confirm the findings of the \textit{in-vivo} data and to investigate the relationships between signal loss, TE and accuracy of PC in turbulent jets using currently available clinical hardware and pulse sequences.

\footnote{A phantom refers to a model of the human body or its parts.}
3.2 Experimental Design

In a patient experiment there are many different sources of error. To better isolate the causes of the error it is often more informative to design an experimental apparatus that replicates the \textit{in-vivo} situation. \textit{In-vitro} experiments using a phantom are an excellent method for the systematic investigation of errors in a controlled environment. But, they require careful consideration to ensure that the experiment is a good representation of the problem.

3.2.1 Constructing the phantom

Specifications

Two phantoms were required. The first, a non-stenotic phantom, aimed to verify the ability of PC to measure turbulent flow and velocities that are comparable to those measured in aortic stenosis jets. The second, a stenotic phantom, planned to recreate the high velocity stenotic jet. The phantoms were required to:

1. be anatomically consistent, the aorta’s diameter ranges between $2 - 3cm$ \cite{7}
2. produce velocities greater than $5m/s$
3. ensure fully developed flow at the image plane
4. simulate the full range of aortic valve area (AVA) (normal to severe)
5. provide a continuous estimate of flow
6. produce the equivalent constant physiological flow rate of $300 - 500mL/s$
   (calculated assuming an average stroke volume (SV) of $100mL$ and a systolic duration of 200-300ms);
7. be MRI compatible, easily maintained, and reproduced.

The phantoms

Stenotic flow was simulated by a pipe network consisting of two straight $1.2m$
long PVC pipes (internal diameter, $d_I = 28mm$) connected by a thin circular plate ($< 3mm$ thick) with a concentric circular orifice.
CHAPTER 3. **IN-VITRO EXAMINATION OF PHASE CONTRAST ERRORS**

A thin orifice plate \(^2\) is a common method for measuring flow and produces a similar high velocity jet to what is seen *in-vivo*. A circular shaped sharp edged orifice's coefficient of contraction, the ratio of the orifice and vena contracta \(^3\) area, is approximately 0.63. The orifice diameters vary from 8mm-20mm covering the full severity range 0.32 – 2.00 cm\(^2\) (Table 1.3).

Non-stenotic flow could be examined either in a straight 2.4m long plastic pipe \((d_I = 17mm)\) or by placing a spacer plate (no constriction i.e \(d_I = 28mm)\) in the stenotic phantom. All phantoms exceed the entrance length criteria for turbulent flow \((L = 4.4Re^{1/6}d_I)\) ensuring fully developed flow at the image plane. Wooden supports secure the phantom at the centre of the scanner's bore. The orifice plate is surrounded by saline bags during imaging.

The pipe network

Flow around the closed circuit, Figure 3.1, (including a 120L reservoir located outside the 5 Gauss line \(^4\)) was achieved with a self priming centrifugal pump that can achieve a maximum head of 530kPa and a maximum flow rate of \(\approx 1200mL/s\). Figure 3.2 shows, assuming the orifice plate and total length pipe cause the main pressure losses, the system characteristic of the stenotic phantom system for various orifice plates. With orifice plates greater than 12mm, the system is capable of circulating water to the maximum flow rate. With the 8mm orifice a flow rate of \(\approx 900mL/s\) is possible, which is in excess of the desired equivalent constant flow rate.

Continuous flow measurement was provided by an electromagnetic flow meter (Endress + Hauser GmbH, Lörrach, Germany) \(^5\), located in the flow circuit but

---

\(^2\)The Gorlin equation (1.13) used to evaluate AVA with catheterisation is a simplified adaptation of the orifice plate flow meter formula: \(Q = C_dE\pi d^2\sqrt{\frac{2(P_1-P_2)}{\rho}}\). The expansion coefficient \((E)\), accounts for the change in density of a fluid as it expands, and the coefficient of discharge \((C_d)\), the ratio of the actual to the ideal discharge, are dependent on the geometry and Reynolds number of the flow meter. The Gorlin coefficient \((K)\) lumps these terms together with the \(\sqrt{\frac{2}{\rho}}\) term. One explanation for the loss of accuracy experienced by catheterisation at low flow rates is that the calibration of the Gorlin constant is no longer valid.

\(^3\)Minimal cross-sectional area of forward flow, Section 4.2.2.

\(^4\)This is the safety line that marks where the magnets fringe field drops below 5 gauss.

\(^5\)\(Q = AU_f\) where \(A\) is cross-sectional area and \(U_f\) the mean flow velocity calculated from the induced velocity \(V = BL_eU_f\) with \(B\) equal to the flow meters magnetic field and \(L_e\) is the electrode spacing.
3.2. EXPERIMENTAL DESIGN

(a) Floor layout

(b) Phantom place into the bore of the magnet

(c) Pump with pressure buffer

(d) Electromagnetic flow meter board

Figure 3.1: Phantom layout and picture of various components of the phantom setup.
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(a) System characteristic

(b) Flow meter accuracy

Figure 3.2: The phantom’s system characteristic for various orifice plates shows the available flow rate range and the flow meter’s accuracy corresponding to that range.

outside the 5 Gauss line, Figure 3.1.

The flow meter was calibrated, by the manufacturers, against three master flow meters in accordance with standards set by the Swiss Accreditation Service and had a stated accuracy in the desired flow range of 0.53% – 0.57%, Figure 3.2. The flow meter’s 4 – 20 mA current output (resolution 1.5 µA) is sampled over a 312Ω resistor at a sampling rate of 100 Hz with a 12 bit, M6221 National Instruments data acquisition card) using Labview v6.1. The signal is averaged to give an independent gold standard measurement of flow over the entire scan. The dynamic range of the output was set to 1.5 times the desired flowrate during experimentation.

**Sequence set-up**

All *in-vitro* experiments were conducted on a Siemens 1.5T Avanto scanner capable of higher gradient strengths and slew rates than the Symphony scanner used to acquire the ZEST data (45 mT/m and 200 mT/m/ms respectively vs 35 mT/m and 125 mT/m/ms). The breath-hold retrospectively gated velocity encoding pulse sequence acquired 15 phases; using an artificial electrocardiogram trace for triggering. Typical image parameters are given in Table 3.1, these parameters are held fixed unless otherwise stated.
3.2. EXPERIMENTAL DESIGN

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Standard sequence</th>
<th>Modified sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE (ms)</td>
<td>3.3, 4.0, 4.8</td>
<td>2.2, 2.0</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>22</td>
<td>14.8, 14.8</td>
</tr>
<tr>
<td>Lines / Segment</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>No. of Frames</td>
<td>25</td>
<td>25, 25</td>
</tr>
<tr>
<td>RF pulse duration (µs)</td>
<td>1000</td>
<td>500, 500</td>
</tr>
<tr>
<td>Flip angle (α) (deg)</td>
<td>15</td>
<td>30, 30</td>
</tr>
<tr>
<td>Δz (mm)</td>
<td>8</td>
<td>8, 8</td>
</tr>
<tr>
<td>FOV&lt;sub&gt;x&lt;/sub&gt; (mm)</td>
<td>300</td>
<td>300, 300</td>
</tr>
<tr>
<td>Asymmetric echo (%)</td>
<td>70</td>
<td>70, 70</td>
</tr>
<tr>
<td>BW&lt;sub&gt;r&lt;/sub&gt; (Hz)</td>
<td>170</td>
<td>490, 490</td>
</tr>
<tr>
<td>Δx (mm)</td>
<td>1.17</td>
<td>1.17, 1.56</td>
</tr>
<tr>
<td>FOV&lt;sub&gt;y&lt;/sub&gt; (%)</td>
<td>75</td>
<td>75, 75</td>
</tr>
<tr>
<td>Phase under sampling (%)</td>
<td>65</td>
<td>65, 65</td>
</tr>
<tr>
<td>Δy (mm)</td>
<td>1.80</td>
<td>1.80, 2.40</td>
</tr>
<tr>
<td>V&lt;sub&gt;enc&lt;/sub&gt; (cm/s)</td>
<td>&gt; 150</td>
<td>&gt; 150, &gt; 150</td>
</tr>
<tr>
<td>G&lt;sub&gt;max_flow&lt;/sub&gt; (mT/m)</td>
<td>13/10/10</td>
<td>26/20/20</td>
</tr>
</tbody>
</table>

Table 3.1: Typical image parameters used for investigating aortic stenosis.

3.2.2 Phantom validation

To validate the experimental set-up, the non-stenotic \( d_l = 28 \text{mm} \) phantom was imaged at 4 different maximal encoding velocities (\( V_{enc} \)) (250, 500, 750 and 999 cm/s). The slice was orientated axially and positioned at isocentre. The flow rate was varied from 300 – 1200 mL/s. Good agreement was observed, with an average absolute error of 1.4%, 1.6%, 2.4%, 2.2%<sup>6</sup> respectively. The linear regression had an average \( R^2 \) value of 1, Figure 3.3.

The stenotic phantom with a 12mm orifice plate set at isocentre was imaged \( \approx 35 \text{mm} \) up and downstream and the desired flow rate was set to 400 mL/s. From Table 3.2, the PC estimate of flow correctly estimated the flow upstream of the orifice but, as expected, underestimated the flow downstream in the stenotic jet.

<sup>6</sup>The resistor’s value was set at 316Ω, subsequent experiments used a measured resistance, \( \approx 312 \Omega \), obtained from a calibration at zero flow.
3.2.3 Experimental protocol and analysis methods

Analysis was performed using Matlab\textsuperscript{7} and GNU Octave v3.0\textsuperscript{8}.

Effect of area

The PC estimate of flow was calculated from the numerical integration of velocities\textsuperscript{9} \((V_{\text{voxel},i})\) across the vessel.

\[
Q = \sum_{i=1}^{N_{\text{voxel}}} V_{\text{voxel},i}A_{\text{voxel}} = N_{\text{voxel}}A_{\text{voxel}}\bar{V}_{\text{phantom}}
\]  

The number of edge voxels included affects the flow estimate, Figure 3.4. To remove the influence of variations in area from the flow calculations, a circular mask was created from a fixed contour using the known diameter of the pipe. Voxels with more than 50\% of their area contained within the contour were included in the mask. Peak velocity was obtained using no neighbourhood averaging.

\textsuperscript{7}Math-Works, South Natick, MA, USA.
\textsuperscript{8}An open-source alternative initiated by the Department of Chemical Engineering, University of Wisconsin, Madison, Wisconsin.
\textsuperscript{9}For simplicity, when referring to the fluid the velocity is symbolised as \(U\), and when referring to the velocity obtained from PC it is symbolised as \(V\).
3.2. EXPERIMENTAL DESIGN

Figure 3.4: demonstrates the sensitivity to the inclusion of removing edge voxels. Smaller areas lead to an underestimation of flow larger areas an overestimation. A fixed contour using knowledge about the known diameter of the pipe was utilised to remove the area’s influence from the flow calculations.

Choice of VENC

To determine an appropriate Venc or dynamic range of the PC image, the Venc was varied from \(1.15 - 13\) times the expected average velocity in the non-stenotic \(d_I = 28\)mm phantom. The flow rate kept constant at \(400mL/s\); the image plane was orientated axially and positioned at isocentre; and the lowest Venc was chosen to validate the unwrapping algorithm’s ability to remove aliased voxels.

Figure 3.5: Successful unwrapping of aliased velocity profiles in plug flow and a the jet.

Figure 3.5 proves the unwrapping algorithm successfully recovers aliased voxels in the phantom. Figure 3.6 shows that as the Venc becomes too large the PC
estimate’s flow error increases. The increased standard deviation in the peak velocity and flow errors when the ratio of peak velocity to Venc was low is consistent with a decrease in the SNR, Eq. 2.52.

Similar experiments were conducted in the stenotic experiment with four flow rates (100, 200, 300 and 500mL/s). Though aliasing occurred, it could be successfully unwrapped at low flow rates (< 300mL/s, Figure 3.5), the aliasing that lead to the severe underestimation at a flow rate of 500mL/s could not be, Figure 3.7.

From these preliminary experiments it was considered important to maintain a consistent dynamic range that avoids aliasing. It was determined, from experience, that the Venc needed to be adjusted in the stenotic phantom experiments by

\[ V_{\text{enc}} = \text{roundup}_{50}(1.5\bar{U}_{E,O}) \]  \hspace{1cm} (3.2)

and in the non-stenotic and upstream stenotic experiments by

\[ V_{\text{enc}} = \text{roundup}_{50}(2\bar{U}_{E,P} + 50) \]  \hspace{1cm} (3.3)

where \( \bar{U}_{E,P} \) is the expected average velocity in the pipe and \( \bar{U}_{E,O} \) is the expected average velocity at the orifice. The Venc was rounded up to the nearest increment of 50.
Residual Background phase correction

Residual background phase varied spatially across the image (Section 2.6.3). Though an individual voxel’s velocity/phase error may be small (1%), these errors accumulate during the integration required to calculate flow. Because the phantom compares flows, residual background phase correction becomes an important consideration. Subsequent data were all phase corrected by manually identifying two near regions in saline bags placed either side of the phantom, Figure 3.4.

Figure 3.6 shows that correction improved the flow estimate in the non-stenotic phantom with only a marginal effect on the peak velocity. In the stenotic phantom, background phase correction (and unwrapping) did not exhibit any significant improvement, which implies there were other causes for the error, Figure 3.7.

Relative SNR

The signal to noise ratio (SNR) depends not only on the image parameters, but also on the inflow of fresh spins (Section 2.5.3). To compare between acquisitions the signal intensity (SI) was normalised against stationary tissue. For each image
CHAPTER 3. IN-VITRO EXAMINATION OF PHASE CONTRAST ERRORS

series a relative signal intensity (RSI) across the phantom’s ($RSI_P$) region of interest (ROI) and for each individual voxel ($RSI_{voxel}$) was defined as

$$RSI_P = \frac{SI_P}{SI_S}$$ (3.4)  
$$RSI_{voxel} = \frac{SI_{voxel}}{SI_S}$$ (3.5)

Where $SI_P$, $SI_{voxel}$, and $SI_S$ are the average signal intensities, over all frames, across the phantom’s ROI, for each individual voxel and for stationary tissue, identified in the adjacent saline bags, respectively.

Signal enhancement occurs if SI is brighter ($RSI > 1$) than stationary fluid; signal loss occurs if SI is darker ($RSI < 1$) relative to stationary fluid.

**Velocity reliability**

The use of non-pulsatile flow means that each frame measures the same velocity/flow. This makes it possible to average all frames and to calculate the standard deviation of the ROI and each voxel over the frames. This standard deviation is used as a measure of the velocity estimate’s reliability. A normalised standard deviation ($\sigma_N$) was calculated by taking the velocity estimate’s standard deviation over the frames for each voxel in the ROI ($\sigma_{voxel}$) and dividing it by the average voxel’s standard deviation in the stationary saline bag ($\sigma_S$).

$$\sigma_N = \frac{\sigma_{voxel}}{\sigma_S}$$ (3.6)

### 3.2.4 Sequence modification

To reduce the TE beyond what is possible with the standard PC sequence, the sequence was modified to utilise the improved performance available on the Avanto scanner. To enable a TE 2.2ms: the duration of the RF excitation pulse was halved from 1000$\mu$s to 500$\mu$s; the maximum amplitude of the flow gradient was increased from $13/10/10mT/m$ to $26/20/20mT/m$ (Read/Phase/Slice); and the readout bandwidth was increased from $170 - 488Hz$ Table 3.1. To further reduce the TE to 2.0ms, the base matrix size ($N_x$) could be reduced from 256 to 192 and the slice thickness dropped to 5.5mm.
3.3 Experimental results

3.3.1 Non-stenotic phantom

The first experiment aimed to verify the ability of PC to measure high velocity, high Reynolds ($Re$) flows. The non-stenotic phantom ($d_I = 17\,mm$) was used to examine flow rates of $100 - 1100\,mL/s$ (theoretical plug flow average velocities of $44 - 485\,cm/s$, $Re$ of $7,200 - 78,000$). Two different TEs were tested, $4.8\,ms$ (as used *in-vivo*) and $3.3\,ms$, the sequence’s minimum TE on the Avanto.

![Figure 3.8](image)

(a) Figure 3.8: In a non-stenotic phantom the PC estimate of flow exhibits good agreement with the flow meter (a), even though the RSI shows signal loss at high flow rates (b).

Figure 3.8 plots the PC estimate of flow against the gold standard flow meter. Excellent agreement was shown at both TEs. The maximum error at TE $4.8\,ms$ was $2.5\%$ (average error±standard deviation $1.7 \pm 0.5\%, R^2 = 1.00$) and at TE $3.3\,ms$, $2.9\%$ (average error±standard deviation $1.9 \pm 0.7\%, R^2 = 0.99$). The RSI decreased as the flow rate increased. A RSI of 1, indicating no signal enhancement compared to stationary fluid occurred at a flow rate of $300\,mL/s$ ($Re = 21,000$). The peak velocity measured was $587\pm14\,cm/s$, which is comparable to continuous wave Doppler (Doppler) peak velocities in severe aortic stenosis.
3.3.2 Stenotic phantom

The recreation of Stahlberg and Sondergaard’s in-vitro experiments was performed on the \( d_t = 28 \text{mm} \) stenotic phantom with the 12mm orifice plate inserted. Their hypothesis was that shortening the TE reduces the higher order motion encoding [59]. TE was initially varied between 4.8, 4.0, and 3.3ms over the flow rate range \( 100 - 700 \text{mL/s} \) (average plug flow velocity at constriction \( 90 - 625.4 \text{cm/s} \)). All other imaging parameters were held constant and the image plane was orientated axially and located 35mm downstream of the orifice.

Figure 3.9 plots PC estimate of flow and RSI versus the flow meter for various TEs. Table 3.3 contains quantitative values for two flow rates. The data show the same trend as the in-vivo data, with increasing PC underestimation of flow at higher flow rates. This was paralleled by a steady decrease in RSI. At shorter TEs, both the RSI and errors improved. As either the flow rate or the TE increased, the standard deviations became larger, indicating greater variability in the measurement.

<table>
<thead>
<tr>
<th>Average predicted:</th>
<th>Flow rate (mL/s)</th>
<th>300</th>
<th>500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flow rate (mL/s)</td>
<td>V_{orifice} (cm/s)</td>
<td>266</td>
<td>447</td>
</tr>
<tr>
<td>V_{peak} (cm/s)</td>
<td>error (mL/s)</td>
<td>373 ± 44</td>
<td>-13 ± 9</td>
</tr>
<tr>
<td>V_{peak} (cm/s)</td>
<td>error (mL/s)</td>
<td>425 ± 49</td>
<td>-39 ± 12</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>4.8</td>
<td>4.0</td>
<td>3.3</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>4.8</td>
<td>4.0</td>
<td>3.3</td>
</tr>
</tbody>
</table>

Table 3.3: Measured peak velocities and the PC flow error from two flow rates.

3.3.3 Errors as a function of position

Image position in the jet was investigated by varying the position of an axial image plane between 5-180mm downstream of the orifice with TEs of 3.3ms at a flow rate of 400mL/s. A sagittal image with in-plane velocity encoding was acquired (at TE 3.3ms) to provide a longitudinal view of the jet for comparison with the axial studies, Figure 3.10. The flow was increasingly underestimated
3.3. EXPERIMENTAL RESULTS

Figure 3.9: Initially good agreement is maintained with the flow meter. When the flow rate (jet velocity) is increased the PC estimate of flow increasingly underestimates the flow meter (a). This is reflected in the decrease in RSI showing an increased signal loss. Shortening TE improves the RSI and consequently improves the accuracy of the PC estimate of flow.

up to 35mm (error < 10%), after which the underestimation doubled. The error was greatest 0 – 100mm downstream, beyond 100mm the error reduced.

The initial findings were consistent with Stahlberg’s and Sondergaard’s findings. The shorter TEs further improved the flow estimate at larger flow rates, Figure 3.9 and Table 3.3, and reduced the error’s dependency on position, Figure 3.10. The maximum error 2.8% occurred 140mm downstream of the constriction. The RSI increased in the modified sequence. It plateaued at low flow rates, demonstrating maximum velocity signal enhancement.

The displacement artefact in the sagittal image, Figure 3.10, where the largest velocities appear offset in relation to the narrowest point of the forward flow jet velocities, is due to the movement of spins during the time delay between the velocity encoding and readout gradients. In through plane encoding a similar effect may be observed, termed “spin mixing,” and is discussed in Chapter 4.
Figure 3.10: Flow error as a function of axial image position in the stenotic jet (400mL/s). The flow error at a TE of 3.3ms increases in the early part of the jet before decreasing as we move downstream. The error is worse at approximately 4 orifice diameters downstream of the orifice. Reducing the TE to 2.0ms removes the flow error. Note: the location of the velocities in the sagittal image are mis-registered because the spins have moved between excitation and readout.
3.4 Signal loss and intravoxel dephasing

3.4.1 Signal loss in the phantom

Investigation of the PC velocity and flow-compensated magnitude images at a flow rate of 500mL/s, Figure 3.11, clearly shows salt and pepper noise in the phase images and signal loss in the flow-compensated magnitude images at long TEs (4.8 and 4.0ms). Shortening the TE led to recovery of signal in the centre of the pipe, elimination of salt and pepper noise from the phase image, and an improvement in the error.

<table>
<thead>
<tr>
<th>TE (ms)</th>
<th>4.8</th>
<th>4.0</th>
<th>3.3</th>
<th>2.2</th>
<th>2.0(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error (%)</td>
<td>-166</td>
<td>-67</td>
<td>-25</td>
<td>-13</td>
<td>-8.8</td>
</tr>
</tbody>
</table>

\(^a\)At TE of 2.0ms a increased acquisition matrix is required

Figure 3.11: Magnitude and phase difference images in the stenotic-jet at a flow rate of 500mL/s and various TEs. Shortening the TE improves the signal in the flow compensated magnitude images and removes the salt and pepper noise from the phase difference images.

Plotting the velocity estimate’s standard deviation of each voxel (normalized relative to stationary spins) across all frames \(\sigma_N\) against the voxel’s \(RSI_{voxel}\) reveals a asymptotic relationship, Figure 3.12. As the \(RSI_{voxel}\) falls, there is a significant increase in variability in the velocity results. Shortening the TE (Figure 3.12(b)) or decreasing the flow rate (Figure 3.12(c)) causes the data to slide down this curve, indicating increased reliability of the results. Voxels with a \(RSI_{voxel}\) less than 1 suffer significant signal loss and the measured phase is too noisy to be considered reliable.
CHAPTER 3. \textit{IN-VITRO EXAMINATION OF PHASE CONTRAST ERRORS}

(a) All flow rates

(b) Flow rate = 500 mL/s

(c) TE = 4.8 ms

Figure 3.12: The normalised standard deviation ($\sigma_N$) (a measure of velocity variation) is very large at low RSI (a). Shortening TE (b) or reducing the flow rate (c) increases the RSI and this reduces the velocity variability.

The cause of the underestimation of flow in the phantom

The underestimation of flow in the stenotic pipe experiments was characterized by a decrease in RSI. The signal loss was associated with decreased reliability of the phase estimate in the centre of the jet, which in some cases resulted in random phase (salt and pepper) noise (Figure 3.11), and a loss of accuracy in the forward flow. The net flow begins to be dominated by the slower, more reliably estimated retrograde flow in the annulus surrounding the jet. Eventually as the forward jet flow is dominated by noise (noise has an average flow close to zero) the net flow may become negative as observed in the phantom results, Figure 3.9.
Shortening the TE reduced the signal loss and resulted in an improvement of the jet velocities that determine forward flow. TE 2.0ms was adequate for flow rates up to 600mL/s. The non-stenotic phantom showed no loss of PC accuracy at high velocity, high Reynolds flow despite considerable signal loss.\textsuperscript{10}

### 3.4.2 Signal loss in the ZEST trial data

<table>
<thead>
<tr>
<th>Patient</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error (%)</td>
<td>-55</td>
<td>-28</td>
<td>-81</td>
</tr>
</tbody>
</table>

Figure 3.13: The salt and pepper noise associated with signal loss was present in patients B and C. Patient A shows no salt and pepper noise; however, the magnitude image does suffer from signal loss. No patient showed any signal enhancement during systole.

\textsuperscript{10}The decreasing RSI with increasing flow rate in the non stenotic phantom was subsequently attributed to incomplete magnetisation. Section 4.3.1. The spins entering the phantom do not have adequate time to align with the external magnetic field prior to excitation. The amount of longitudinal magnetisation available to flip into the transverse plane is reduced, therefore the signal is weaker. This effect is greater at higher flow rates. Fortunately, this phenomenon does not occur in a patient.
Upon investigation of the flow-compensated magnitude and phase images, significant salt and pepper noise was present in the phase images for some patients (e.g. B and C in Figure 3.13), with SV errors of $-28\%$ and $-81\%$ respectively. This noise can have a similar appearance to aliasing. In fact, $15/31$ patients were initially considered to be aliased in the aortic root by the ZEST study analyst, although only $2$ patients had Doppler jet velocities greater than the $V_{\text{enc}}$ of $500\text{cm/s}$. Even though there was no salt and pepper noise in case (e.g. A in Figure 3.13), a significant SV error of $-55\%$ was still found. The corresponding flow-compensated magnitude images of all patients showed signal loss in the areas corresponding to the high velocities of the turbulent jet.

A measure of \textit{in-vivo} RSI was calculated (using the flow-compensated magnitude image) as the average signal intensity in the vessel lumen ($SI_{L}$) divided by the average signal intensity from the last $10$ frames in diastole ($SI_{S}$).

\[ RSI = \frac{SI_{L}}{SI_{S}} \]  

Diastolic blood may not be exactly stationary and the low reverse flow present could cause some signal enhancement relative to true stationary blood. The amount of inflow is difficult to predict because it will depend on the competency of the aortic valve. However, this signal should still be the best representation for the minimum expected signal intensity when a voxel's velocity estimate is reliable.

Figure 3.13 shows the RSI as a function of time through the cardiac cycle for three cases. For all cases, RSI was $< 1$ during systole, and increased during diastole. Signal enhancement due to inflow of new spins is expected with motion [50; 62; 63], the low RSI ($< 1$) during systole implies that substantial signal loss occurred within the jet.

The trend of increased signal loss in areas of high velocity flow both \textit{in-vivo} during systole and \textit{in-vitro} at high velocities is consistent with signal loss due to \textit{intravoxel dephasing}. Phase dispersal within a voxel negates the inflow signal enhancement of moving spins and leads to a reduction in the reliability of the measured phase. The sagittal image in Figure 3.10 suggests that the error may be related to underlying flow characteristics of the jet.
3.5 Conclusions

The phantom experiments successfully reproduced the underestimation of flow seen in the ZEST trial in a controlled environment.

The results demonstrated a clear relationship between flow errors and signal loss in the stenotic jet. The images were characterised by significant signal loss in the flow-compensated magnitude image, and were often accompanied by salt and pepper noise in the PC velocity image. Shortening TE reduced the signal loss in the flow-compensated magnitude image, removed salt and pepper noise from the phase image, and improved accuracy.

Subsequent work (Chapter 4) was designed to determine the underlying mechanisms relating flow estimation, intravoxel dephasing and signal loss in stenotic jets. Signal loss has been historically attributed to intravoxel dephasing and higher order motion encoding (14). There are many mechanisms proposed to influence intravoxel dephasing and signal loss. Possibilities include: partial slice excitation; spatial and temporal accelerations; in-plane resolution and motion; choice of Venc; intra-voxel velocity distributions; and the underlying turbulence characteristics of the jet. Chapter 4 reports the results of more detailed experimentation undertaken to try and determine the relative importance of these effects when imaging stenotic jets.

The ZEST sub-study of moderate to severe aortic stenosis patients found large errors in the PC estimation of SV. Signal loss was apparent throughout systole, and severe signal loss was associated with salt and pepper noise in the velocity image (Figure 3.13), which may be incorrectly interpreted as aliasing. The current standard PC sequence used clinically (TE > 2.0ms) may not be adequate to accurately characterize flow in highly turbulent jets. Chapter 5 and Chapter 6 reports the results of a small clinical study investigating the ability of the modified sequence to image stenotic jets in-vivo.

Measurements of signal intensity and (if possible) comparison with volumetric SV should be performed as checks for the reliability of PC flow studies. If signal loss is observed on the flow-compensated magnitude image in the region of the jet, a check against ventricular SV should be performed to assess the reliability of the flow data (note that this is not possible in the presence of significant mitral regurgitation).
CHAPTER 3. *IN-VITRO* EXAMINATION OF PHASE CONTRAST ERRORS

We have based signal loss measurements on the flow-compensated magnitude image, since these are routinely displayed in clinical PC imaging protocols; however, it is known that signal loss is even more severe in the velocity-encoded acquisition, and presentation of the associated magnitude image (not currently available in clinical practice) would provide greater insight on the reliability of the velocity estimate. Manufacturers should make the velocity encoded magnitude images routinely available, and highlight voxels with low RSI in both reference and encoded images, in order to warn users of probable errors in peak velocity estimates and flow. A magnitude threshold should be used to remove noisy voxels from the velocity data, similarly suggested by Nayler et al [64; 65] as early as 1986.
Examinations of factors influencing intravoxel dephasing

4.1 Introduction

Accurate detection of a magnetic resonance (MR) signal relies on the continued phase coherency of the spins, Section 2.2.1. The spreading out of the spins’ phase, intravoxel dephasing, reduces the strength of the detectable signal. Intravoxel dephasing is a side effect of the applied magnetic gradients. Gradient waveforms are designed to recover the spins phase coherency. Slice select gradients are refocussed to remove phase dispersal due to position or movement, Figure 2.10. Readout gradients are designed to ensure that the spins phase are coherent at the echo time (TE), the centre of the echo, Figure 2.17.

In phase contrast (PC), spins’ phase coherency is vital to obtain an accurate representation of the average velocity within that voxel. When the spins within a voxel are travelling at the same speed, the spins’ phase remains coherent. The recorded signal has a high signal to noise ratio (SNR) therefore the measured phase is an accurate and reliable representation of the average velocity, Figure 4.1. Flow profiles create a velocity distribution across the voxel, causing the spins to dephase relative to each other. The voxel’s SNR reduces, but, if the distribution remains symmetric the phase may still be accurate. In the flow compensated acquisition these spins should correctly refocus giving a strong signal.

Intravoxel dephasing is usually dominated by the spins’ position and velocity or flow, which can be correctly compensated through 0th and 1st moment gradient nulling. In most applications these assumptions are justified, but in aortic stenosis more complex flow patterns exist that can defeat these compensatory
CHAPTER 4. EXAMINATIONS OF FACTORS INFLUENCING INTRAVOXEL DEPHASING

Figure 4.1: Schematic diagram of the different intravoxel dephasing mechanisms. If the spins (blue vectors) are coherent they sum to give a strong signal and the measured phase is ($\phi_m$, red vector) is the same as the actual average phase ($\phi_a$, green vector). When coherency is lost the measured phase accrues an additional erroneous phase (yellow arc), at the extreme case noise (pink) begins to dominate the spins’ signal and the measured phase becomes random.

Techniques. Acceleration can cause the spins to accrue an additional erroneous phase. Large velocity distributions within a voxel can cause spin cancellation to occur and velocity fluctuations in turbulent flow\(^1\) can cause an incorrect phase accumulation. All these processes have the potential to reduce the signal to noise ratio and result in the measured phase not being a true and accurate representation of the average velocity within a voxel. In the extreme case the signal becomes

\(^{1}\)Turbulent and complex flow are often exchanged intermittently in the literature; however, significant complex flow patterns (e.g. vortices) can occur under Laminar flow conditions. These conditions may also result in intravoxel dephasing, signal loss and velocity underestimation due to the effects discussed in this chapter. In aortic stenosis jets the flow is both complex and turbulent, the ideas in this thesis are thus not concerned with separating these effects.
4.1. INTRODUCTION

dominated by noise and the measured phase becomes random, Figure 4.1.

Chapter 3 established a clear relationship between a voxel’s SNR and the accuracy of the flow and velocity estimates. Though higher order motion encoding was considered by Stahlberg and Sondergaard [44; 59; 61; 47; 60] as the most critical determinant of intravoxel dephasing, other authors place a greater emphasis on alternative mechanisms:

- partial excitation;
- in-plane resolution and motion;
- choice of maximal encoding velocity (Venc);
- intra-voxel velocity distributions;
- and the underlying turbulence characteristics of the jet.

In this chapter we perform a thorough investigation of the underlying structure of the jet and the causes of signal loss. The hypothesis for each mechanism will be introduced and experimentation performed to identify key regions and image parameters of the standard PC sequence that could be further optimised.
CHAPTER 4. EXAMINATIONS OF FACTORS INFLUENCING INTRAVOXEL DEPHASING

4.2 Flow characteristics in a jet

4.2.1 Jet structure

Aortic stenosis jets can be modelled by a bounded or confined jet in a sudden expansion, Figure 4.2 [17]. The jet can be divided into three regions.

**Irrotational Core** As fluid approaches the constriction it begins to accelerate, compensating for the decreasing flow area [16]. The flow’s kinetic energy increases and a forward pressure gradient forms across the constriction. Beyond the constriction the flow enters a high velocity irrotational central core that has either a Laminar or Turbulent profile.

**Separation region** The issuing jet starts entraining fluid from the surrounding chamber, increasing the mass flow rate and causing the flow to expand. An opposing pressure gradient develops. The fluid in the centre of the expanding wedge has a high axial momentum and inertia enabling it to issue forth against the adverse pressure gradient at the expense of velocity [66]. At the edge of the wedge a boundary layer begins to form and thicken rapidly [15]. The boundary shear and adverse pressure gradient cause the fluid to lose momentum, and results in the boundary layer coming to rest. This is known as separation or the zero crossing point [67], schematically drawn in Figure 4.2 by the line AB. Beyond the separation line the fluid’s inertia can not overcome the adverse pressure gradient causing the flow’s direction to reverse. This retrograde flow creates an annular recirculation region around the jet, supplying fluid for continued entrainment and compensating for the increased mass flow of the forward jet [68].
4.2. FLOW CHARACTERISTICS IN A JET

Reattachment, the main region  Continued expansion of the wedge shaped separation region leads to the forward flow reattaching itself to the wall and re-development of a stable forward flow profile. At the separation line large scale eddies are formed, which reduce in scale downstream of the separation line. The loss of kinetic energy does result in some recovery of potential energy or pressure [16], but the viscous and turbulence effects in the boundary layer of the separation region causes irreversible losses. The flow re-establishes at a lower static pressure.

The distance from the constriction to point B is known as the reattachment length. Under Laminar flow conditions the reattachment length is found to increase with Reynolds number, in the transitional regime it is found to decrease before slightly increasing again upon transition to turbulent flow where it remains constant (≈ $7D_o$ downstream) [67].

4.2.2 Vena Contracta

Depending on the geometry of the constriction, the central core of the jet may form a vena contracta [16], labelled A in Figure 4.2. If the fluid is led smoothly into the constriction the jet expands immediately after, Figure 4.3. The minimal cross sectional area will be located in the constriction or just downstream. In an abrupt constriction the flow continues to converge downstream. The location

Figure 4.3: When the flow is lead smoothly into the constriction, the vena contracta is equal to the cross section area of the jet; in a abrupt constriction it will be located downstream of the constriction.
of the vena contracta is dependant on the geometry of the constriction, it is
approximately one orifice diameter downstream of the constriction.
In aortic stenosis a vena contracta is commonly formed. Its location (and the
catheter’s) becomes important when invasively measuring pressure [16].

4.2.3 Boundary layer turbulence

Two fundamental characteristics of a real fluid are: i) there is no velocity discon-
tinuity; and ii) at a solid surface the velocity of the fluid relative to that surface is
zero. The boundary layer is the region near the surface where the velocity rapidly
approaches zero. Boundary layers experience greater levels of shear stresses than
in the main flow.

The formation of a boundary layer is not restricted to flow near a solid surface.
A boundary layer can form between two fluid streams that flow past each other
at different velocities [17]. Turbulent mixing occurs between these layers to
equalize their velocities. This free turbulence\(^2\) is typically found in jets. The
flow characteristics are similar to turbulent boundary layers:

- The thickness of the boundary layer increases approximately proportional
to \(z^{0.8}\), the axial distance from the intersection of the layers (\(z\)). (Laminar
  flow \(z^{0.5}\))
- The Reynolds shear stress (\(\tau_0\)) is inversely proportional to the local
  Reynolds number (\(\tau_0 \propto Re^{0.2}\)). (Laminar flow \(\tau_0 \propto Re^{0.5}\))
- the total frictional drag is approximately proportional to \(U_o^{1.8}\) and pro-
  portional to \(L^{0.8}\), the length of the coincident layers. (Laminar flow \(U_o^{1.5}\),
  \(L^{0.5}\))
- The production of turbulence in the boundary layer reduces as it thickens
  (see Eq. A.8 in Appendix A).

\(^2\)Turbulence not bounded by solid walls.
4.2.4 Turbulence in the jet

Turbulent flow is only fully developed when the small eddies and isotropic turbulence\(^3\) have reached an equilibrium [69]. Isotropic turbulence occurs close to the centre of the jet. Anisotropic turbulence would be greatest at the edge. In a free-jet or wake, turbulence is intermittent [69]. In a constrained jet, no region of intermittent turbulence develops [67].

![Figure 4.4: The turbulence's intensity, represented by the error bars, increases downstream of the constriction. It peaks just after the maximum reverse flow and then slowly decays downstream (obtained from [67]).](image)

Furuichi et al [67] measured a velocity profile in an axisymmetric sudden expansion with a ultrasonic velocity profiler. The profile shown in Figure 4.4 was taken with the transducer placed 5 mm from the edge of the expansion and at a Reynolds number of 3,591. The data was normalised against the bulk forward velocity and the zero cross over point. It shows that the turbulence's intensity, shown as error bars, increased quickly to a peak just after the maximum reverse flow, before slowly decaying as a function of axial distance. The intensity of turbulence at a given axial distance does not vary over the cross section of the jet. The decay of turbulent intensity corresponds to \(I \propto z^{-1.5} \) [66].

4.2.5 Signal loss due to turbulence

Eichenberger et al [45] considered turbulence to be the primary cause of intravoxel dephasing. Correct phase accrual relies on the velocity staying constant throughout velocity sensitive gradients. Turbulence’s random velocity fluctua-

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\(^3\)Isotropic turbulence is where the products and squares of velocity components and their derivatives are independent of direction.
tions ($u$, Eq. 1.6) may cause the spins to experience different velocities during each of the gradient lobes interfering with the spins phase accrual.

Generalized models have been developed by Gao et al [70] and Kuethe et al [71] to describe the signal attenuation due to flow and turbulence. Signal loss was found to be dependent on the intensity (Eq. 1.6) and correlation time\(^4\) ($T_c$) of the turbulent eddies [72]. Short correlation times have short-lived velocity fluctuations, the eddies experience many changes in velocity. Long correlation times or long-lived velocity fluctuations experience less changes in velocity over time.

In a bipolar gradient, the signal loss due to long-lived fluctuations was determined to be proportional to the 1\(^{st}\) moment ($M_1$) [72].

\[
S \propto S_0 e^{-\frac{\gamma^2 \langle u^2 \rangle M_1^2}{2}} \tag{4.1}
\]

In short-lived velocity fluctuations the signal loss was described as being proportional to the strength, $G$, and duration, $\tau$, of the bipolar gradient [72].

\[
S \propto S_0 e^{-\frac{\gamma^2 G \langle u^2 \rangle \tau^2 \tau}{3}} \tag{4.2}
\]

Their experiments and simulations showed that long correlation times were observed before the vena contracta and that the maximal signal loss was found just after the vena contracta where the turbulence was characterised by short correlation times. At higher flow rates the length of the jet with large correlation times decreases and energy in the jet dissipates more quickly thereby decreasing the correlation time and increasing the turbulence [72].

In a PC sequence the velocity encoding gradients (on the slice direction) and the flow compensating readout gradients are susceptible to turbulence. Gatenby et al [72] stated that signal loss may be more severe in the flow compensated gradients as these gradients are longer in duration.

The errors as a function of position, Figure 3.10, follow a similar pattern to turbulence in stenotic jets [67]. They both increase rapidly and then steadily decay as the jet dissipates downstream. After reattachment, the flow returns to that seen in a straight pipe where the intensity, scale and time dependence

\(^4\)The correlation time is a measure of the average duration of each velocity change.
4.2. FLOW CHARACTERISTICS IN A JET

of turbulence do not vary longitudinally [17]. To qualitatively investigate the error's relationship to the underlying flow characteristics in the jet (Figure 4.2), Figure 4.5 inspects the regions of signal loss in the jet from the positional experiment in Section 3.3.3.

At a TE of 3.3, signal loss initially appears as an annulus. Progression down the jet shows that the annulus expands and then encompasses the entire central region of the jet before beginning to recover once the jet has reattached to the wall. Reducing the TE to 2.0ms (not shown) removed the appearance of the annulus close (< 22mm downstream) to the plate and exhibited marginal signal loss in the centre at 42mm.

At a TE of 3.3ms, the position of images experiencing large regions of signal loss coincides with the separation region's boundary layer. The greatest regions of signal loss occur immediately after the vena contracta where the turbulence’s intensity quickly peaks and the correlation times are short. The recovery of signal reflects an easing of the turbulence's intensity and the lengthening of the correlation time. These observations are consistent with the signal attenuation models.

Imaging at 35mm downstream in the experiments, Figure 3.9, places the image slice in the position of intense turbulence with short correlation times. Higher flow rates increases the turbulence’s intensity and shortens the correlation time, increasing the signal loss. Shortening the TE decreases the duration of the bipolar gradients, reducing their susceptibility to turbulence, Eq. 4.2.
4.3 Intravoxel dephasing experiments

4.3.1 Partial excitation

**Hypothesis** There is a relative signal intensity (RSI) threshold at which partial excitation of spins is insufficient to provide an adequate estimation of flow in the stenotic jet. Halving the duration of the RF pulse will thus improve the accuracy at high flow rates.

![Image](image-url)

**Figure 4.6:** (a) The logarithmic signal drop off seen in the non-stenotic flow show is due to a lack of time for the spins to align with the external magnetic field. The larger drop off in the stenotic jet implies that an alternative mechanism is acting. Removing the effect of incomplete magnetisation (b) shows a linear drop of RSI. The linear drop off may be due to less spins experiencing the full flip angle.

**Background theory** The exponential decrease of RSI with increasing flow rate seen in the non-stenotic phantom Figure 3.8, may in part be due to incomplete magnetization of the spins and/or partial excitation. Spins as they enter need to align (fully magnetise) with the scanner’s magnetic field. The time required is proportional to T1 relaxation. Partial excitation of moving spins occurs when spins do not remain within the slice for the duration of the RF pulse. More complete slice excitation may explain part of the improved RSI seen with the shorter RF pulses of the modified PC sequence, Figure 3.9.

Figure 4.6 re-plots the RSI as a function of entrance velocity. The exponential decrease of RSI, due to incomplete magnetisation, is evident in the straight pipe
4.3. INTRAVOXEL DEPHASING EXPERIMENTS

but not in the stenotic jet. The stenotic jet’s RSI is less than the straight pipe’s RSI across the same entrance velocities. Taking the ratio of the stenotic jet and the straight pipe RSI, attempts to remove the influence of incomplete magnetisation, reveals a linear drop off with entrance velocity in the stenotic jet, which is offset according to the TE.

Method The PC sequence was modified to enable different RF pulse durations, the TE was set at the maximum pulse duration and kept fixed. The flow rate was varied between $100 - 700 \text{mL/s}$ and the axial image plane was fixed at $35 \text{mm}$ upstream and downstream of the $12 \text{mm}$ orifice plate. Other imaging parameters can be found in Table 4.1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TE (ms)</td>
<td>3.05</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>54.85</td>
</tr>
<tr>
<td>Lines / Segment</td>
<td>4</td>
</tr>
<tr>
<td>RF pulse dur. (µs)</td>
<td>1500, 1000, 500</td>
</tr>
<tr>
<td>$G_{\text{sliceselect}}$ (mT/m)</td>
<td>5.2, 7.8, 15.7</td>
</tr>
<tr>
<td>Flip angle (α) (deg)</td>
<td>15</td>
</tr>
<tr>
<td>∆z (mm)</td>
<td>6</td>
</tr>
<tr>
<td>$FOV_{\text{read}}$ (mm)</td>
<td>300</td>
</tr>
<tr>
<td>Asymmetric echo (%)</td>
<td>70</td>
</tr>
<tr>
<td>$BW_{\text{read}}$ (Hz)</td>
<td>391</td>
</tr>
<tr>
<td>∆x (mm)</td>
<td>1.17</td>
</tr>
<tr>
<td>$FOV_{\text{phase}}$ (%)</td>
<td>68.8</td>
</tr>
<tr>
<td>$G_{\text{maxflow}}$ (read/phase/slice) (mT/m)</td>
<td>13/10/10, 26/20/20</td>
</tr>
<tr>
<td>Distance from orifice (mm)</td>
<td>±35</td>
</tr>
</tbody>
</table>

Table 4.1: Image parameters for variable RF duration and $V_{\text{enc}}$ experiments.

Results Upstream of the orifice plate the PC estimate of flow agreed well with the flow meter, Figure 4.7. The RF pulse duration had no affect on the RSI, which decreased with the entrance velocity. In the stenotic jet, the flow was underestimated at higher flow rates and there was no clear difference between RF pulse durations accuracy or RSI. At low entrance velocities the downstream RSI was greater than the upstream RSI, and these converged at high entrance velocities.
Figure 4.7: Upstream (a) and downstream (b) show that accuracy is independent of partial excitation. The RSI (c) shows no difference in the RSI between the different RF pulse durations.

Discussion  The greater RSI in the stenotic jet at low flow rates indicates that initially signal enhancement from fresh spins outweighs losses from partial excitation. The lack of difference between the RF pulse durations indicates that the flow errors at longer TEs is influenced by other signal loss mechanisms (intravoxel dephasing and/or increased $T_2^*$ relaxation). The accuracy is dependent on the TE duration and not the excitation profile of the spins. The improvement of the modified PC sequence’s RSI, Figure 3.9, is most likely due to the greater flip angle (Table 3.1). Partial excitation increases the RSI drop off at high flow rates but it does not (nor the different flip angle) explain why TE impacts so significantly on accuracy.
4.3. INTRAVOXEL DEPHASING EXPERIMENTS

4.3.2 Choice of $V_{enc}$

**Hypothesis** Larger $V_{enc}$s relative to the stenotic jet’s peak velocity improve the flow accuracy.

**Background** In clinical imaging the $V_{enc}$ is normally minimized to obtain the optimal dynamic range, but this may actually increase signal loss [73]. At a given velocity, the spins accrue more phase in a lower $V_{enc}$ than with a larger $V_{enc}$ (to achieve lower $V_{enc}$s larger gradients are required, Eq. 2.39). Hypothetically, a larger $V_{enc}$ could result in less intravoxel dephasing.

![Diagram](image)

Figure 4.8: As the $V_{enc}$ is decreased the PC estimate of flow error (a) exhibits the least error at $V_{peak}/V_{enc}$ ratio of $0.6 - 0.7$. The normalised peak velocity (b) decrease as the $(V_{peak}/V_{enc} \rightarrow 1)$ and RSI (c) remains unchanged.
CHAPTER 4. EXAMINATIONS OF FACTORS INFLUENCING INTRAVOXEL DEPHASING

Method The 12mm orifice plate was imaged, 35mm downstream at two flow rates, 200mL/s and 300mL/s. The Venc, in the standard PC sequence (TE of 2.79ms), was varied up to the maximum available (999cm/s).

Results The flow was initially underestimated before being overestimated at smaller peak velocity/Venc ratios, Figure 4.8. Correct estimation occurred at a ratio of 0.6 – 0.7. The peak velocity increased with smaller peak velocity/Venc ratios. The RSI remained consistent over the dynamic range.

Discussion Increasing the Venc may reduce the RSI of low velocities and impact on the ability to quantify the jet’s retrograde flow. The noisier low velocities may explain the loss of accuracy at small peak velocity Venc ratios. No benefit towards intravoxel dephasing is apparent from this experiment. Instead, it highlights the sensitivity to reducing the dynamic range’s resolution. In practice, no prior knowledge of the stenotic jets velocity is available. The current minimisation of Venc (that avoids aliasing) is still deemed to be best practice.

4.3.3 Voxel size and partial voluming

Hypothesis If the voxel is too small, there are too few spins causing a low SNR; if the voxel is too large, there are too many spins enhancing the signal loss from intravoxel dephasing. There should be an optimum balance between the two effects.

Background Nayak et al [43] using spiral readouts, considered the effects of voxel size, in terms of slice thickness and in plane-resolution, as the most crucial mechanism for intravoxel dephasing. Intravoxel dephasing within a voxel is caused by its velocity distribution and partial voluming. Voxels on tissue boundaries may contain more than one tissue. In a magnitude image, the voxel’s resultant signal intensity is a mixture of these tissues. In PC imaging, a voxel may contain more than one tissue, have a steep velocity profile or experience bi-directional flow [73; 74; 62]. The voxel’s measured velocity could be skewed due to an asymmetric velocity distribution, or become a mixture of two flow distributions, Figure 4.1.
4.3. INTRAVOXEL DEPHASING EXPERIMENTS

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Conventional</th>
<th>Modified</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
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<td>Lines / Segment</td>
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<td>Flip angle (α) (deg)</td>
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<td></td>
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<td>55, 70, 85, 100</td>
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<td>26/20/20</td>
</tr>
<tr>
<td>Distance from orifice (mm)</td>
<td>35 down</td>
<td>35 down</td>
</tr>
</tbody>
</table>

Table 4.2: Image parameters for partial voluming experiments.

On top of the partial voluming at the vessel edge stenotic jets have steep velocity gradients, particularly in the boundary layer between forward and retrograde flow (Figure 4.2). If the assumptions are satisfied, signal loss due to the velocity distribution should be minimised in a flow-compensated magnitude image\(^5\). This would manifest itself in the phantom as an annulus of signal loss. The absence of a clear annulus pattern beyond the vena contracta, Figure 4.5, suggests that turbulence dominates signal loss.

**Method** Two experiments were conducted using the 12mm orifice plate with the image plane set at 35mm downstream. The standard PC sequence and the modified PC sequence were imaged, with a flow rate that was known to be underestimated by the respective sequences, at 300mL/s and 500mL/s respectively. The voxel volume of the standard PC sequence was varied by adjusting the slice thickness and FOV. For the modified PC sequence only the in-plane resolution was varied using the FOV and the base matrix size \(N_x\). In addition, the effect of voxel shape (by adjusting the phase under sampling) was also investigated.

\(^5\)The availability of the velocity magnitude image would be valuable here, as this signal loss mechanism should be more visible.
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Other parameters can be found in Table 4.2.

![Graphs showing results of varying voxel size in the clinical sequence with flow rate 311 mL/s.](image)

Figure 4.9: Results of varying voxel size in the clinical sequence with flow rate 311 mL/s. Increasing the voxel volume by either the FOV or slice thickness improved the accuracy of the PC estimate (a). The peak velocity was more consistent at larger voxel volumes.

**Results** At small voxel volumes the SNR was too low, noisy voxels were obtained and the result was a loss of flow accuracy and erroneous peak velocities at both flow rates, Figures 4.9 and 4.10. The standard PC sequence’s (flow rate 300 mL/s) voxels were not large enough to show a loss of accuracy even with a slice thickness of 10 mm; the modified PC sequence (flow rate 500 mL/s) showed the expected fall off with large voxel volumes.

The smallest error, 10%, occurred at a voxel volume of 20 mm$^3$. Regarding the voxel shape, the more (in-plane) isotropic$^6$ voxels had better agreement. At voxel volumes around 20 mm$^3$, the error was worse at a phase under sampling of 55%.

No clear observations can be made regarding the peak velocity. It appears more susceptible to the in-plane resolution than the slice thickness, Figures 4.9 and 4.10.

**Discussion** Figures 4.9 and 4.10 revealed that the total volume of the voxel was the most critical ($\approx 20 mm^3$).

---

$^6$An isotropic voxels means all sides are the same, a cube. The slice thickness $\Delta z$ is much greater than either $\Delta x$ or $\Delta y$ forming a rectangular prism, whose shape can be more accurately described as in-plane isotropic i.e. two sides are equal.
4.3. INTRAVOXEL DEPHASING EXPERIMENTS

Figure 4.10: Results of varying voxel size in the modified sequence at flow rate 512.7 mL/s. The PC estimate initially improves as the voxel volume is increased (a). The lowest error occurs at a voxel volume of \( \approx 20 \text{mm}^3 \) after which it got progressively worse. The peak velocity was initially centred about the \( V_{enc} \), it decreased before starting to increase again at a voxel volume of \( \approx 40 \text{mm}^3 \). The more in-plane isotropic voxels show better consistency, with voxel volumes either side of \( \approx 20 \text{mm}^3 \) exhibiting similar accuracy.

At a slice thickness of 10mm, the standard PC sequence still exhibited good agreement with the flow meter and the peak velocity was unchanged. The smallest error experienced occurred at a readout dimension of \( \Delta x = 1.5625 \), FOV of 300mm for all phase under sampling values (in the modified PC sequence). Examining the points either side of this error showed that the more isotropic voxels had better agreement.

The flow’s velocity profile varies more transverse to the jet than it does longitudinally. Thus, better in-plane resolution reduces the averaging effect of the voxel. This has a significant effect on the peak velocity estimate.

From the data, a voxel volume of 20mm\(^3\), currently applied in the standard PC sequence, gave the best accuracy. This is probably sequence dependent. If the in-plane resolution is improved or if the shape of the voxel is forced to be more (in-plane) isotropic, then increasing the slice thickness can maintain a suitable voxel volume without adversely affecting the accuracy.
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Figure 4.11: Phase contrast sequences are inherently higher order motion encoding. $\Delta m_1$ is the desired encoding and $\Delta m_2$ and $\Delta m_3$ are the unwanted higher order motion encoding. The bottom graph’s scale was increased to highlight the non-zero higher order moments in the velocity encoding acquisition.

Figure 4.12: Longitudinal velocity and average acceleration profiles in a jet. At the centre of the pipe ($y = 12$) the average acceleration (neglecting turbulence) profile could be broken into four distinct regions: an acceleration phase, a plateau and an initial and late deceleration phase. At $y = 8$ there is a brief period of acceleration period, a plateau followed by a series of deceleration zones. Near the wall, ($y = 4$), the acceleration is small.
4.3. INTRAVOXEL DEPHASING EXPERIMENTS

4.3.4 Acceleration

Hypothesis Reducing the duration of the bi-polar gradient whilst maintaining TE constant, reduces the higher order motion encoding and results in the same improvement as reducing the TE. By varying the orifice plates, the location of the image plane and the spins’ acceleration pattern, causes a spatially dependent loss of accuracy consistent with higher order motion.

Background Stahlberg and Sondergaard [59] showed that the linearity between the accrued measured phase ($\phi_m$) and the true phase accrual due to velocity ($\phi_v$) is lost if the spins are accelerating. The flow compensated and velocity encoded acquisitions are both inherently acceleration encoded, Figure 4.11. Spins potentially accrue an additional erroneous phase. Increasing the maximum available gradient in the modified PC sequence decreases the duration of the velocity encoding and compensation gradients, reducing the acceleration and other higher order motion encoding (Eq. 2.31).

Figure 4.12 shows a smoothed (5 point moving average) velocity profile and average spatial accelerations longitudinally down the jet at 4, 8, and 12 voxels from the lower edge of the phantom. The accelerations are greatest in the centre profile and close to the orifice. Downstream of the vena contracta the centre of the jet decelerates. From this graph we would expect the PC estimate of flow to be more sensitive to accelerations close to the orifice. Note however, that these estimates of acceleration ignore turbulence during the TE.

Method Two experiments were investigated. Experiment 1) investigated the effect of changing the bipolar gradient duration in the modified PC sequence by varying (a) the slew rate\(^7\) and (b) the strength of the bi-polar gradient. Both kept the TE fixed at the maximum. The image plane was set 35mm downstream of the 12mm orifice and the flow rate varied from 100 – 700mL/s.

Experiment 2) used three different orifices ($d_o = 15/12/9\text{mm}$) to examine the affect of different spatial acceleration patterns on PC’s accuracy. The image plane was either set at the vena contracta (approximately one $d_o$ downstream) or 35mm downstream of the orifice. The conventional and modified PC sequences

\(^7\)This is not an ideal experiment as changing this parameter affected all gradients, but it was used as the first attempt before the source code was made available.
CHAPTER 4. EXAMINATIONS OF FACTORS INFLUENCING INTRAVOXEL DEPHASING

were used. Flow rate was varied from $100 - 700 mL/s$ or the maximum Venc was reached.

<table>
<thead>
<tr>
<th>Variation of</th>
<th>Slew rate</th>
<th>Orifice</th>
<th>Gradient</th>
</tr>
</thead>
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<td>3.6, 2.8</td>
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<td>(mod.)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>TR (stand.) (ms)</td>
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<td>57.3, 50.9</td>
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<tr>
<td>(mod.)</td>
<td></td>
<td>45.7, 39.3</td>
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</tr>
<tr>
<td>Lines / Segment</td>
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<td>4</td>
<td>4</td>
</tr>
<tr>
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<td>500</td>
</tr>
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<td>30</td>
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</tr>
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<tr>
<td>BW$_{read}$ (Hz)</td>
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</tr>
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<td>1.25/1.56</td>
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<td>(mm)</td>
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<td>2.5/2.22</td>
<td>2.22</td>
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<td>$G_{max_{flow}}$ (read/phase/slice) (mT/m)</td>
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<td>13/10/10</td>
<td>26/20/10–25</td>
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<td>160</td>
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<td>$D_o$, 35 down</td>
<td>35 down</td>
</tr>
<tr>
<td>Orifice Diameter (mm)</td>
<td>12</td>
<td>15, 12, 9</td>
<td>12</td>
</tr>
</tbody>
</table>

Table 4.3: Image parameters for acceleration encoding experiments.

Results  Accuracy is dependent on the orifice area and the position in the jet, Figure 4.14. The 15mm orifice showed good agreement with the flow meter across all flow rates. The 12mm orifice only experienced significant underestimation at the vena contracta for flow rates > 300mL/s. The 9mm orifice experienced underestimation at both locations but it was worse at the vena contracta (> 200mL/s compared to > 300mL/s). Figure 4.13 show that shorter bipolar gradient durations (reduced acceleration encoding) had better agreement with the flow meter, but further improvement was obtained by shortening TE.
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(a) Slew rates
(b) Gradient Strength

Figure 4.13: Agreement with the flow meter was improved with shorter bi-polar gradients (using either method), but importantly minimising the overall TE adds additional improvement.

(a) $d_o = 15\text{mm}$, $1d_f$ downstream
(b) $d_o = 15\text{mm}$, $35\text{mm}$ downstream

Figure 4.14
Figure 4.14: The underestimation of flow was worse close to the orifice plate, at smaller orifices and at longer TEs.
4.3. INTRAVOXEL DEPHASING EXPERIMENTS

Discussion

Large average acceleration occurs in between the orifice and the vena contracta at the centre of the jet. At higher flow rates a certain amount of acceleration encoding is tolerable before underestimation. Further downstream, less significant decelerations caused flow underestimation to occur. This implies that while acceleration is a contributor, especially close to the orifice, it is not solely responsible for the errors.

A more clear underestimation was observed when the slew rate was varied, since varying the slew rate affects all gradients. In the PC sequence, the effect of not minimising TE is to introduce a time delay between the velocity sensitive gradients and image readout. Though improvement is observed with the stronger gradients, at the high Venc (low gradient areas) used in the experiment the actual duration of the gradients remains relatively unchanged because of the longer time required to reach the specified gradient strength. The higher order motion encoding remained similar.

In the slew rate experiment, the TE was fixed at 3.03 ms, but the minimum possible was 2.0 ms. Figure 4.13a clearly shows that if the TE is minimised to 2.0 ms better agreement is obtained with the same bipolar gradient duration.

4.3.5 Jet alignment

Hypothesis

Jet alignment is critical: rotating the image plane oblique to the jet should cause an underestimation of flow and the peak velocity should fall off over and above the cos θ relation.

Background

In the absence of intravoxel dephasing errors, the alignment of the image plane perpendicular to the forward flow in a vessel is not critical to the calculation of flow. If the direction of the flow and the image plane are misaligned by the angle θ, the flow’s velocity (V) is projected onto the encoding direction (V_m) using Pythagoras, V_m = V cos θ. The area of the vessel would also increase, by a factor of \(\frac{1}{\cos \theta}\), consequently the flow estimates are preserved when the forward flow and image plane are not exactly orthogonal.

In complex flow, where intravoxel dephasing errors are present, the cos θ relation is no longer valid. Kilner et al [75; 42; 76], while acknowledging the need to shorten TE to avoid intravoxel dephasing, considered the alignment of the image
CHAPTER 4. EXAMINATIONS OF FACTORS INFLUENCING INTRAVOXEL DEPHASING

Figure 4.15: If the jet is eccentric to the slice the spins are able to cross voxels. If there is a subsequent mixing of slow and fast moving spins this would increase the intravoxel dephasing (adapted from [75]).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<th>12mm</th>
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<td>3.6, 2.8/2.0</td>
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<tr>
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<td>1 - 10</td>
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</table>

Table 4.4: Image parameters for spin mixing experiments.
plane perpendicular to the jet to be the most critical factor. If the image plane is not perpendicular to the jet the spins may cross voxels during imaging. The mixing of fast and slow moving spins increases intravoxel dephasing. This would be especially important in jets with no core i.e. that were squirted out from a crimped valve, Figure 4.15.

**Method** Two experiments that rotated the image plane from 0 – 10 degrees about the stenotic jet, which purposely allowed spins to cross between voxels. Two flow rates of 300mL/s and 500mL/s and the 12mm orifice were used. The first experiment set the image plane 35mm downstream and used the modified PC sequence (with three different TEs 2.0/2.8/3.6ms). The second experiment set the image plane one orifice diameter ($d_o = 12mm$) downstream and used the conventional (TE 2.8/3.6ms) and modified PC sequence (TE 2.0/2.8ms) set at different TEs. Other parameters can be found in Table 4.4.

**Results** Figures 4.16 and 4.17 show that the accuracy of the flow estimate becomes very variable at larger rotations. In general the mean flow, or the mean underestimation, is maintained when the image plane is rotated about the jet. The peak velocity was more sensitive to spin mixing and misalignment.

At 300mL/s the $V\cos\theta$ relation\(^8\) is preserved for all TEs and in both experiments (except at the long TE (3.6ms) in Figure 4.16(b)).

At the higher flow rate 500mL/s, the underestimation of peak velocity was more pronounced at longer TEs and larger rotations. Figure 4.16(d) shows that at 35mm the the longer TE’s, peak velocity dropped off over and above the $V\cos\theta$ relation. Moreover, at one diameter away from the constriction where the peak velocity is greater, Figure 4.17(d), the standard PC sequence’s peak velocity headed towards the $V_{enc}$. Shortening the TE with the modified PC sequence improved the agreement with the $V\cos\theta$ relation, but in the case of the TE 2.8 variant only for small rotations.

**Discussion** The longer TEs give the spins more time to cross voxel boundaries between excitation and readout. Larger rotations increase the relative in-plane

\(^8\)The initial velocity used in the plot of the $v\cos\theta$ relation was calculated from the average velocity between the different TEs at the minimum rotation.
Figure 4.16: At 35mm downstream increasing the rotation had little effect on flow error at 500mL/s. It initially increased the error at 300mL/s. The peak velocity matched the $V\cos\theta$ relationship with increasing rotation except at the longest TE 3.6ms.

velocity of the spins. Both effects lead to more spin mixing and a loss of accuracy in the peak velocity. But, from Figure 4.2 the jet is already converging and diverging. Spin mixing must already be occurring in image planes that are perpendicular to the jet. The rotations only act to intensify the spin mixing. Nevertheless, shortening the TE reduces the time available for spin mixing and maintains a better agreement with the $V\cos\theta$ relation.
Figure 4.17: At one orifice diameter downstream all variants had reasonable agreement with the flow meter at 300 mL/s, at 500 mL/s all but the TE 3.6 ms (stand.) variant had good agreement. Similarly at 300 mL/s all variants matched the $V_{\cos\theta}$ relationship but at 500 mL/s only the TE 2.0 (mod.) variant matched. The TE 2.8 (mod.) variant initially agreed but the conventional variants overestimated and quickly went towards the $V_{\text{enc}}$. 
4.4 Discussion and conclusions

Various mechanisms have been proposed as the most critical for the accurate imaging of stenotic jets. In truth the complexity of the flow regime in stenotic jets means many mechanisms play a role. What is clear throughout the experiments is that reducing the TE consistently improves the estimate to a greater extent than many other parameters.

Partial excitation reduces the RSI of the jet. Upstream of the jet no difference in accuracy and downstream no improvement in accuracy was evident when a greater proportion of spins experienced the full flip angle. The reduction in available signal caused by partial excitation does cloud the use of RSI as a good measure of PC’s reliability. A voxel’s lack of signal enhancement ($RSI > 1$) may be due to partial excitation rather than intravoxel dephasing effects.

In a phantom experiment, prior knowledge can be used to choose the Venc, in a patient it can not. Figure 4.8 shows that the Venc can affect the accuracy and the peak velocity estimate, but increasing the Venc did not reduce intravoxel dephasing as hypothesised. It worsened the flow estimate. It is likely that this was due to a loss of an adequate dynamic range that reduced the resolution and increased the noise of voxels with low velocities. The current practice of minimising the dynamic range whilst avoiding aliasing remains best practice\(^9\).

In experiments where the modified PC sequence and the standard PC sequence were both applied with a TE of $2.8\text{ms}$, no difference in flow error can be seen, Figure 4.14. But, there was a worse agreement of peak velocity seen in Figure 4.17. The larger in-plane resolution associated with the modified PC sequence is balanced by its shorter velocity sensitive gradients and in part by its shorter readout gradient durations, which both act to mitigate errors from spin mixing. Nayak’s suggestion of in-plane resolution may be more important in the longer readout gradient durations associated with spiral imaging. Figure 4.10 shows that the best approach is to create a more isotropic voxel that maintains a suitable volume for good SNR e.g. $20\text{mm}^3$.

In the literature, the main effect associated with shortening TE is the reduction of higher order motion encoding. Large accelerations are present close to the

---

\(^9\)Once the other factors affecting intravoxel dephasing errors can be controlled, purposefully allowing velocity aliasing, which can be subsequently corrected with a suitable unwrapping algorithm may improve the dynamic range.
4.4. DISCUSSION AND CONCLUSIONS

Figure 4.13 reiterates that decreasing the duration of the bipolar gradient improves the flow estimate. Figure 4.14 showed that the modified PC sequence, with less inherent higher order motion encoding, had better agreement at higher flow rates. Both acceleration experiments, and in Figures 4.16 and 4.17, experience a worse discrepancy when a time delay between the velocity sensitive gradients and readout is introduced.

The longer time between velocity sensitive gradients and readout allows the spins to traverse a larger distance, increasing the risk that more spins cross voxel boundaries to mix with slower moving spins. The mixing of spins increases intravoxel dephasing and results in the peak velocity falling off over and above the $v \cos \theta$ relation. In extreme cases, Figure 4.17, the peak velocity began to deviate towards the Venc, i.e. were becoming dominated by noise. Minimising the TE removes the time delay, reducing the degree of spin mixing induced intravoxel dephasing.

The deceleration downstream of the vena contracta, where the signal loss covers the centre of the phantom, is less than half of that close to the orifice, Figure 4.12 yet underestimation is similar Figure 4.14. Downstream of the vena contracta turbulence is known to be worse and more intense. Decelerating flow destabilises the flow and increases the turbulent intensity and the prominence of short lived velocity fluctuations. Accelerating flow, prior to the vena contracta, stabilises turbulence. Shortening the duration of the velocity sensitive gradients reduces signal loss due to turbulence.

Turbulence does not explain the annular signal loss near the constriction where long-lived velocity fluctuations dominate. Nor can it be attributed to accelerations as these are greatest in the centre which is bright, Figure 4.5. A more likely is that spin mixing occurs. Shortening the TE thus reduces the time available for significant intravoxel dephasing, due to decreased spin mixing, to occur.

4.4.1 Recommendations for further experimentation

The experiments have been limited to constant flow. The pulsatile flow experienced in-vivo adds additional complications such as temporal acceleration and increased turbulence, and increases the possibility of significant intravoxel dephasing to occur. Furthermore the limited temporal footprint of the sequence results in the velocities being averaged over the acquisition. This may incorrectly
smooth out the velocity profile and dampen the peak velocity estimate causing the true peak to be missed. The dependency of the intravoxel dephasing errors on these effects needs to be investigated further hence the phantom needs to be extended to include pulsatile flow.

4.4.2 Recommendations for further phase contrast sequence optimisation

While reducing higher order motion encoding is an important direct effect, there are other benefits to shortening TE including mitigating the affect of turbulence's velocity fluctuations and reducing spin mixing. Any further optimisation of the PC sequence should not only focus on reducing the duration of the velocity sensitive gradients but also attempt to minimise the time between laying down the velocity encoding and reading out the image.
Aortic stenosis \textit{in-vivo} flow measurement

5.1 Introduction

As seen in the previous chapter, intravoxel dephasing has many mechanisms. Flow through a stenotic jet experiences large spatial and temporal accelerations that add or subtract an additional phase shift on top of the velocity encoding. Imaging perpendicular to the jet core has been considered vital to reduce the mixing of fast and slow moving spins [76; 42]. But, flow in a jet is diverging, and its importance in all but extremely eccentric jets is questionable. Turbulence is greater in the jet’s boundary layer that forms after the vena contracta [72; 77] and in decelerating flow, which may contribute to the increased underestimation observed beyond the aortic valve and in decelerating flow. The jet’s sharp velocity profile creates large phase distribution within a voxel; some voxels may even experience both forward and retrograde flow, which enhances intravoxel dephasing [74; 62].

In a severely stenotic jet all of these effects are enhanced.

Many image parameters have been touted as potential contributors. Reducing the voxel’s in-plane resolution reduces the number of spins available to dephase at the risk of reduced signal to noise [43] and increasing the maximal encoding velocity (Venc) reduces the velocity induced phase shift [73]. Yet, none have as many effects as reducing the echo time (TE), Chapter 4. Shortening TE to 2.0ms reduces the inherent higher order motion encoding [59; 44], decreases the time available for the detrimental mixing of fast and moving spins, and reduces the risk of turbulent velocity fluctuations disrupting the expected phase shift [45; 72; 77], the measured velocity’s reliability and accuracy \textit{in vitro}. 

\textit{Give me a lever long enough and a fulcrum on which to place it, and I shall move the world.} Archimedes
Ultimately this leads to the question, “does shortening TE have the same effect in-vivo?”

To investigate this, a small clinical trial of patients with moderate or severe aortic stenosis was undertaken. This chapter describes the clinical trial’s protocol used to acquire the in-vivo data and describes the calculation of equivalent phase contrast (PC) parameters required to systematically compare between cardiac magnetic resonance (CMR) and echocardiography. It was found that the modified sequences were more susceptible to background phase than the standard sequence. The following chapter (Chapter 6) therefore deals with background phase correction algorithms and presents the results for the trial.
5.2 Clinical Trial Protocol

15 patients with isolated moderate or severe aortic stenosis (peak aortic velocity of $\geq 3\text{m/s}$) were studied. Patients were excluded if they had left ventricular impairment (ejection fraction $< 50\%$), atrial fibrillation, more than trace mitral or aortic regurgitation or other significant valvular disease, congenital heart disease, poor echocardiographic images, inability to undergo a magnetic resonance (MR) scan, or in whom a MR scan is contraindicated.

All MR data were collected on a Siemens 1.5T Avanto scanner and echocardiography data were obtained using a Philips IE33 ultrasound system (Philips, Best, Netherlands).

5.2.1 Echocardiography

The patients underwent a comprehensive continuous wave Doppler (Doppler) and 2D echocardiography examination within 1 hour of the MR scan. Meticulous attention was paid to obtain the optimal velocity envelope and true peak trans-aortic valve velocity by sampling from multiple imaging windows (apical, right para-sternal and supra-sternal). The left ventricular outflow tract (LVOT) velocity profile was obtained by careful placement of the pulsed wave Doppler sample volume in the LVOT immediately below the aortic valve in an apical 5-chamber view. The LVOT diameter was measured by imaging the LVOT using the para-sternal long axis view. Left ventricle (LV) volumes and dimensions were obtained from para-sternal and apical views.

Analysis was performed off-line by a single experienced echocardiographer blinded to the patients’ CMR findings. Measurements were made according to American society of Echocardiography guidelines [18] and averaged from 3 to 5 cycles. The velocity time integrals (VTIs) for the LVOT ($VTI_{LVOT}$) and trans-aortic valve ($VTI_{AV}$) flow were obtained (Section 1.5.3). The peak aortic valve velocity and VTI reported from the window yielding the highest velocity signal. Mean trans-aortic valve gradients were calculated using the modified Bernoulli equation (Eq. 1.14) and the aortic valve area (AVA) was estimated using the continuity equation (Eq. 1.15).
5.2.2 Magnetic Resonance Data

**Volumetric assessment of Stroke Volume**

Volumetric assessment of the left ventricle with MR is widely considered the clinical gold standard for measuring stroke volume. The left ventricular stroke volume, obtained using the same imaging procedure described in the ZEST trial (Section 1.6.2), was used to evaluate the ability of the PC to estimate of left ventricular stroke volume (LVSV).

**Phase contrast assessment of Stroke Volume**

To determine the effect of shortening TE *in-vivo* on quantitative flow measurements, three PC sequences were implemented: the clinically available implementation of the standard PC sequence (TE 2.8ms), described in Chapter 2; the modified sequence (TE 2.0ms) introduced in Chapter 3; and a third optimised PC sequence which reduced the TE even further (TE 1.5ms).

The optimised PC sequence was achieved by maximising the Avanto’s gradient hardware ($28/22/22mT/m$) and the pixel bandwidth ($1530Hz$). The large pixel bandwidth decreased the signal to noise ratio (SNR) (Eq. 2.51), and to compensate two averages were acquired. Both the modified and optimised PC sequences’ voxels were made more transversely isotropic by increasing the phase under sampling to 70%.

The image parameters required to obtain a 22 – 26 heart beat breath hold are given in Table 5.1. The effectiveness of these three PC sequences to quantify flow was initially investigated in the stenotic phantom. The experimental procedure and analysis followed is described in Chapter 3. Specifically, the image plane was set at 35mm downstream of the 12mm orifice and the flow was varied from 100 – 700mL/s.

All three PC sequences were used to obtain (in the following order) flow measurements at the aortic valve (AV) leaflet tips (AV0cm), 1cm beyond the aortic valve leaflet tips (AV1cm) in the aortic root and 2.5cm beyond the aortic valve leaflet tips (AV2.5cm) just beyond the sino-tubular junction. The standard PC sequence was used to additionally acquire flow measurements in the LVOT and main pulmonary artery (MPA). The MPA and LVOT/aortic valve images were
### 5.2. CLINICAL TRIAL PROTOCOL

<table>
<thead>
<tr>
<th>Sequence name</th>
<th>Standard</th>
<th>Modified</th>
<th>Optimised</th>
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</thead>
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<td>4</td>
<td>7</td>
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<td>5.5</td>
</tr>
<tr>
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<td>300</td>
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<td>1530</td>
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<tr>
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<td>68.75</td>
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<td>phase under sampling (%)</td>
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<td>70</td>
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<td>2.23</td>
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<td>2</td>
</tr>
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<td>23</td>
<td>26</td>
</tr>
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<td>26/20/20</td>
<td>28/22/22</td>
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</tr>
<tr>
<td>MPA</td>
<td>150</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LVOT</td>
<td>250</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>AV0cm, AV1cm, AV2.5cm</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
</tbody>
</table>

*If aliasing occurred the V<sub>enc</sub> was increased and the acquisition repeated.*

Table 5.1: Typical breath-hold image parameters.

Planned from paired orthogonal long axis cine images through the MPA and aortic valve respectively, Figure 1.19. Short axis cine imaging of the aortic valve was obtained with an initial slice positioned at the aortic valve at end-diastole in the paired long axis cines. The slice was repeated ±6 mm to visually find the minimal valve orifice. The level with the minimum orifice was used to obtain the AV<sub>0</sub> cm flow.

25 phases were calculated and analysed by manually tracing around the vessel in each frame using ARGUS Syngo MR 2004V (Siemens Medical Systems). The PC estimate of stroke volume (PCSV) was obtained by numerically integrating the flow through the cardiac cycle as shown in Figure 5.1. The error in the SV estimate was calculated as

\[
SV_{error} = \frac{PCSV - LVSV}{LVSV} \quad (5.1)
\]
CHAPTER 5. AORTIC STENOSIS IN-VIVO FLOW MEASUREMENT

Figure 5.1: The numerical integration of flow to obtain the PC estimate of SV, is dominated by systole and provided no regurgitant flow occurs, flow should be close to zero during diastole.

Phase contrast assessment of Peak Velocity

Peak velocity was obtained using no neighbourhood averaging but with a signal magnitude threshold. Signal loss is an indicator of intravoxel dephasing and a loss of reliability in the PC estimate of velocity (Chapter 3 and [64]). Relative signal intensity (RSI) for each pixel was obtained by dividing their signal intensity with the average signal intensity across the whole vessel obtained over the last 10 frames ($S_I^S$, Section 3.4.2.) The peak velocity’s pixel must exhibit signal enhancement relative to diastolic flow (RSI $> 2$). The velocity time integral was calculated by numerically integrating, using Simpson’s rule, the area under the peak velocity versus time curve during systole. The highest peak velocity ($V_{PC, pk}$) was chosen to coincide with the highest phase contrast estimate of VTI ($VTI_{PC,max}$) between AV0cm and AV1cm.

Magnetic Resonance assessment of Aortic Valve Area

In Doppler ultrasound the AVA is susceptible to errors associated with calculating flow in the LVOT such as the accurate estimation of the LVOT diameter and the assumption that it is circular [46; 78; 50]. Because PC can measure flow volume and velocity it is theoretically possible to estimate AVA using a continuity approach [46] or more directly from the flow volume and velocity-time integral [49] obtained from the same image. Two CMR methods for estimating the AVA, both using the highest VTI at aortic valve level ($VTI_{PC,max}$), were investigated.
5.2. CLINICAL TRIAL PROTOCOL

1. VolumetricAVA used the LVSV:

\[ AVA_{vol} = \frac{LVSV}{VTI_{PC,max}} \]  (5.2)

2. FlowAVA used the PCSV at the same aortic valve level as the highest VTI:

\[ AVA_{flow} = \frac{PCSV_{max}}{VTI_{PC,max}} \]  (5.3)

5.2.3 Statistical Analysis

Statistical analysis was performed with R for windows, v2.6.2 (The R foundation for statistical computing). Bland-Altman, linear regression, and a 2-tailed paired T-test with Bonferroni correction\(^1\) (statistical significance < 0.01) were used to investigate the LVSV with echocardiography’s estimate of SV and the PCSV at each level and to compare the peak velocity, SV, VTI and AVA calculated using Doppler echocardiography and PC.

\(^1\)The two-way Anova analysis was not appropriate because significant evidence was found against the equal variance assumption i.e. the Levene test’s p-value was < 0.05.
5.3 Results

5.3.1 Validation in a phantom

Figure 5.2: Reducing the TE to 1.5ms with the optimised sequence further improves the agreement of the PC estimate of flow with the flow meter at high flow rates.

Figure 5.2 validates the ability of the modified and optimised PC sequences to further improve the PC flow estimate in the stenotic phantom at high flow rates. All PC sequences agreed well with the flow meter at low flow rates, but at higher flow rates they began to underestimate the flow. The standard PC sequence underestimated the flow at flow rates greater than 400mL/s, the modified PC sequence at flow rates greater than 600mL/s, and the optimised PC sequence continued to agree well with the flow meter at flow rates up to 700mL/s.

5.3.2 Stroke volume results

Table 5.2 shows the mean flow estimates and errors in PC estimation of flow for each PC sequence at serial locations distal to the aortic valve - AV0cm, AV1cm and AV2.5cm. The mean flow of the standard and modified PC sequences at AV0cm was similar to the mean LVSV of 87.0 ± 21.8mL; however, with the optimised PC sequence it was significantly underestimated. At AV1cm and AV2.5cm all PC sequences were underestimated but the optimised PC sequence was substantially worse, Figure 5.3. The optimised PC sequence errors’ standard deviation was approximately twice as large as the other two PC sequences.
5.3. RESULTS

(a) A V0cm

(b) A V1cm

(c) A V2.5cm

Figure 5.3: Bland-Altman analysis of SV error at and beyond the aortic valve for the three different PC sequences showed a clear underestimation of SV in the optimised PC sequence across all locations. The standard and modified PC sequences had reasonable agreement at A V0cm but underestimated the LVSV at the A V1cm and A V2.5cm.
CHAPTER 5. AORTIC STENOSIS IN-VIVO FLOW MEASUREMENT

<table>
<thead>
<tr>
<th>TE (ms)</th>
<th>Stroke volume</th>
<th>Mean±SD (mL)</th>
<th>Mean error±SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVSV</td>
<td>2.8</td>
<td>87.0 ± 21.8</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>AV0cm</td>
<td>2.8</td>
<td>93.5 ± 31.6</td>
<td>6.0% ± 23.7%</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>82.1 ± 35.0</td>
<td>−4.4% ± 24.0%</td>
<td>0.47</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>59.8 ± 51.8</td>
<td>−32.5% ± 58.1%</td>
<td>0.025</td>
</tr>
<tr>
<td>AV1cm</td>
<td>2.8</td>
<td>57.7 ± 19.9</td>
<td>−26.8% ± 14.6%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>55.5 ± 22.1</td>
<td>−28.8% ± 15.5%</td>
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</tr>
<tr>
<td></td>
<td>1.5</td>
<td>23.4 ± 46.7</td>
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<td>&lt; 0.01</td>
</tr>
<tr>
<td>AV2.5cm</td>
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<td>65.8 ± 25.6</td>
<td>−19.4% ± 16.7%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>54.6 ± 19.3</td>
<td>−29.6% ± 13.3%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>1.5</td>
<td>24.8 ± 50.0</td>
<td>−78.4% ± 51.6%</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Table 5.2: Comparison of PC flow estimates of SV with LVSV.

Figure 5.4: The background phase error manifests itself as a baseline shift in the flow (velocity) verse time curve. The baseline error accumulates through the numerical integration creating large SV errors.
5.4 Discussion and conclusions

The underestimation of the optimised PC sequence contradicts the improvement observed in the phantom, Figure 5.2.

One possible explanation for this contradiction is that the other major source of error, background phase, is worse in the modified PC sequence. Because the background phase offset is in one direction this can have a significant impact on the calculation of flow [79; 75], Figure 5.4. For example, assuming the vessel has an area of $6cm^2$ and a Venc of $500cm/s$ is applied, a 1% ($5cm/s$) residual background phase offset equates to a stroke volume error of $30ml$. Using the average LSVV ($87.0mL$) this equates to an error of $\approx 34\%$, which is similar to the error observed in the optimised PC sequence at AV0cm.

Section 2.6.3 describes how modern scanners correct for background phase. Concomitant gradients can be analytically described, and corrected using the Maxwell equations, and the effect of gradient eddy currents can be compensated using waveform pre-emphasis and active shielding.

Gradient derating is another approach for reducing background phase. Smaller gradients use shorter ramp times and therefore there is less time for eddy currents to build up, Figure 2.24. The larger gradients utilized to shorten the TE may be defeating the other eddy current compensation mechanisms, increasing the optimised PC sequence’s susceptibility to background phase, and therefore leading to the underestimations seen in Table 5.2 and Figure 5.3.

We hypothesize that, as a consequence of using higher gradients in the modified PC sequence, the background phase becomes more pronounced. Consequently, Chapter 6 aims to interrogate the background phase of each PC sequence and evaluate and apply different correction methods to remove the background phase. The remainder of the trial’s results will therefore be presented following this investigation.
6 Backgound phase correction

6.1 Introduction

Prior to the introduction of the analytical concomitant gradient correction by Bernstein et al [58], Walker et al [80] suggested that the background phase in phase contrast (PC) images was dominated by the concomitant gradients effects. It was suggested that the background phase due to concomitant gradients and eddy currents, which is spatially variable across the field of view, could be corrected by fitting a surface to the phase offset of the stationary tissue.

Modern PC sequences now correct for the induced concomitant gradients analytically. But, as recently stated by Lankhaar et al [81], the modified and optimised PC sequences that use rapidly switching gradients for fast imaging have re-introduced background phase errors into the PC image.

This chapter aims to: i) characterise the residual background phase of the different PC sequences from the clinical trial outlined in Chapter 5; ii) investigate algorithms to correct for the residual background phase and evaluate their effectiveness in-vivo; and using these corrected results to iii) systematically study, in patients with moderate or severe aortic stenosis, the effect of varying TE on the ability to quantify the stroke volume (SV), peak velocity, velocity time integral (VTI) and aortic valve area (AVA) with cardiac magnetic resonance (CMR).
6.2 Characterising the residual background phase

To investigate the background phase, each PC sequence was used to image a large NiCl₂ doped phantom with the same image parameters outlined in Table 5.1. An artificial electrocardiogram trace (R-R interval 1000 ms) was used for triggering. Various image orientations (transverse, oblique and bi-oblique) and maximal encoding velocities ($V_{enc}$) ($200/500/800$ cm/s) were investigated.

Figure 6.1: The residual background phase of the PC sequences shows the expected spatial dependence. The residual background phase was worse at different image orientations and in the optimised PC sequence.

Figure 6.1 shows that the residual background phase was essentially flat in the transverse image but began to vary spatially at different image orientations. The modified and optimised PC sequences experienced a more pronounced surface variation. Figure 6.2 plots the residual background phase from a circular region of interest (ROI) ($d = 25$ mm) located at the isocentre for each PC sequence, $V_{enc}$ and orientation. In most circumstances the residual background phase was less than 0.5%; however, there were occasions where the optimised PC sequence experienced errors greater than 1%.

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1The ideal location for imaging the vessel of interest $in-vivo$. 

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6.2. CHARACTERISING THE RESIDUAL BACKGROUND PHASE

Figure 6.2: The residual background phase of the PC sequences were largely independent of $V_{enc}$ but the optimised PC sequence was particularly susceptible to different image orientations.
CHAPTER 6. BACKGROUND PHASE CORRECTION

6.3 Proposed background phase correction methods

6.3.1 Basic subtraction methods

In most cases the residual background phase can be easily corrected by subtracting the average phase of stationary tissue adjacent to the vessel. Unfortunately, in the heart there is no such tissue and choosing tissue away from the vessel may introduce greater errors. To illustrate this, the flow error of the six regions of interest identified in the $30^\circ - 30^\circ$ bi-oblique standard PC sequence, Figure 6.3(a), are given in Figure 6.3(b). If the vessel of interest was positioned at the isocentre (ROI1) it would have an absolute flow error before correction of $4.4mL/s$. Taking the other ROIs as stationary tissue identified to correct the background phase, Figure 6.3(c) shows that it is highly likely that the error would increase. The worst results occur using ROIs 4 and 6, one of which is not so distal. Figure 6.3C clearly demonstrates the danger of using regions distal to the vessel interest, a practice that should be discouraged.

Two alternative approaches have been suggested to correct for background phase. One approach is to image a stationary phantom immediately after the patient [79]. The background phase can be estimated using the same vessel contour and the in-vivo image corrected. A second approach is to obtain an estimate of the residual background phase directly from the image itself by fitting a linear planar surface to the phase of the stationary tissue [80; 81]. Both approaches have shown promise.

6.3.2 Phantom correction methods

Chernobelsky et al [79], on a 1.5 Tesla TwinSpeed scanner (GE Healthcare, Milwaukee, Wisconsin, USA), imaged a stationary phantom directly after performing PC imaging of the proximal ascending aorta and the main pulmonary artery (MPA) in 10 normal patients with no known left to right shunt. The vessel’s ROI was overlaid on the phantom and a mean or baseline velocity was determined that would cause the flow in the phantom to be zero. The baseline velocity was reported to be reproducible from scan to scan provided the image parameters and orientation were constant. After baseline phase correction was performed the ratio of pulmonary over systemic flow reduced from 1.25 to 1.05.
6.3. PROPOSED BACKGROUND PHASE CORRECTION METHODS

Figure 6.3: The danger of using distal tissue to perform phase correction is illustrated, in only one case was the background phase error improved in all other cases it was significantly worse. Background phase correction with tissue that does not completely surround the vessel of interest should be discouraged.

The primary drawback of the phantom correction approach is that it is time consuming. Concern has also been raised over the different magnetic susceptibilities \(^{2}\) and the positioning of conducting materials (i.e. the surface coil) on the induced eddy currents.

6.3.3 Surface correction methods

On a Siemens Sonata scanner, Lankhaar et al \(^{[81]}\) investigated the ability of applying Walker et al’s \(^{[80]}\) “surface fitting to stationary tissue” to remove the residual background phase.

\(^{2}\)Adjacent tissues with different magnetic susceptibilities cause local distortions in the magnetic field. These static field inhomogeneities cause additional dephasing \((T_2^*)\) and frequency shifts of nearby spins. They mainly result in signal loss but it may also cause some image distortion \(^{[39]}\) and in PC imaging additional background phase offsets.
CHAPTER 6. BACKGROUND PHASE CORRECTION

Their algorithm is outlined in Figure 6.4. Spatial aliasing was manually removed before identifying stationary tissue as the voxels with a temporal velocity standard deviation (through the frames) below a certain threshold. The threshold was chosen such that the lowest “x” percentile were considered stationary. Stationary tissue provides a cloud of data points that a planar surface can be fitted to. This surface becomes representative of the background phase, which, when subtracted from the image, removes the background phase. Various thresholds and orders of planar surface were investigated.

The performance of the correction method was determined by comparing the spatially averaged velocity from the surface correction versus the same region in a stationary phantom imaged directly after the patient. It was found that a threshold of the lowest 25% of voxels and a linear planar surface correction gave optimal performance. In the subsequent imaging of the MPA in 13 patients it was determined that the root mean square error of the mean volume flow rate reduced from 11% to 3.1%.

When applying the temporal standard deviation mask suggested by Lankhaar et al [81] to our data large regions of heart vessels were incorrectly identified as stationary, Figure 6.6. With a linear planar surface these regions are averaged out in the fitting procedure. But, with the greater flexibility offered by higher order planar surfaces, these regions may result in an incorrect weighting of these
surfaces. The inclusion of non stationary tissue may reduce the effectiveness of higher order planar surfaces.

Because no stationary phantom data was collected, a surface approach was decided upon for further investigation. The method will be extended by introducing a new approach for identifying stationary tissue and the renewed investigation of higher order surfaces. The left ventricular stroke volume (LVSV) determined from a volumetric MR analysis will be used for comparison.
6.4 Extension of the surface background phase correction

6.4.1 Surface types

Walker et al [80] and Lankhaar et al [81] fitted planar surfaces using linear least squares minimisation, as shown in Appendix B (Section B.1). A planar surface \( P(x,y) \) of \( k \)-th order can be defined as

\[
P(x,y) = \sum_{i=0}^{k} \sum_{j=0}^{i} a_{ij} x^{i-j} y^{j}
\]

where \( a_{ij} \) are the planar surface coefficients. The degrees of freedom (DOF), the flexibility given to the surface to fit the data (illustrated in Figure 6.5), were increased with a higher order planar surface.

![Figure 6.5: The planar and finite element surfaces ability to fit to a simulated data set (5th order planar surface, DOF=21) improves as the DOF is increased.](image)

The stationary phantom was used to investigate the different order and types of surface fits. Prior to the fit the six ROIs in Figure 6.3 were removed, these ROIs were used to investigate the resultant error. The complete set of results can be found in Appendix B.

After background phase correction the background phase in each ROI was reduced regardless of the planar surface’s order, Table B.1. But on closer inspection of the error at the isocentre it was found that, at a \( 30^\circ - 30^\circ \) bi-oblique orientation, the background phase error of the optimised PC sequence was increased by
6.4. EXTENSION OF THE SURFACE BACKGROUND PHASE CORRECTION

a linear planar surface. The relative error was increased from 0.39% to significant values of 1.06%, Table B.2.

Unexpectedly, a cubic planar surface also caused the error to increase (1.79%). This poor result is related to ill-conditioning, typical termination statistics are given in Table B.3. The convergence statistics showed that a cubic (3\textsuperscript{rd} order) planar surface does not converge and is characterised by a large condition number (> 1E16). This indicates that the left hand side matrix is close to singular. Consequently, because higher order surfaces may be valuable, alternative surface representations that are not ill-conditioned were desired.

A finite element surface of k-th order can be described as

\[ F(\xi_1, \xi_2) = \sum_{i=1}^{k+1} \sum_{j=1}^{k+1} \psi(\xi_i) \psi(\xi_j) n_{ij} \]  

where \( n_{ij} \) are the finite element nodes and \( \psi \) are the linear\(^3\) or quadratic\(^4\) basis functions.

Finite element surfaces provide intermediate steps in the number of DOF fitted, Figure 6.5. The higher order finite element surfaces are better conditioned, Table B.3. The linear finite element surface also increased the error in the 30\(^\circ\)–30\(^\circ\) bi-oblique orientation. With each degree of freedom introduced, the error was reduced from 0.34% to 1.06% (DOF = 3), 0.99% (DOF = 4), 0.12% (DOF = 6), 0.07% (DOF = 9), 1.79% (DOF = 10) and 0.28% (DOF = 16)\(^5\).

Using surfaces with many DOF may result in over fitting; their increased flexibility makes them susceptible to poorly identified stationary tissue. The DOF of a quadratic finite element surface and a cubic planar surface are similar. Additionally, because the quadratic planar and quadratic finite element surfaces exhibited good performance across all results in the stationary phantom, subsequent investigations were restricted to linear and quadratic planar and finite element surfaces only.

6.4.2 Selection of Stationary tissue

The temporal standard deviation algorithm \[80; 81\] only classifies voxels into two categories, stationary and non-stationary. Moving voxels may have a similar

\(^3\)1-D linear basis functions = \( \psi_1 = 1 - \xi \) and \( \psi_2 = \xi \).
\(^4\)1-D quadratic basis functions = \( \psi_1 = 2(\xi - 1)(\xi - 0.5) \), \( \psi_2 = 4\xi(1 - \xi) \) and \( \psi_3 = 2\xi(\xi - 0.5) \).
\(^5\)The “cubic” finite element is defined with cubic-bezier basis functions
standard deviation to stationary voxels (assuming they exhibit a good signal to noise ratio (SNR)) and therefore can get incorrectly identified as stationary tissue. The inclusion of these tissues may incorrectly weight the fitted surface and is particularly important with the greater flexibility of higher order surfaces.

An alternative approach would be to investigate the frequency spectrum of a voxel’s temporal velocity variation. The proposed algorithm, outlined in Figure 6.7, is based on the average (DC) and first harmonic (H1) power images computed from the $1D - FT$ of each voxel’s signal over time [82]. Investigation of a voxel’s DC and H1 components allows tissue to be classified into one of three types, stationary, moving/flowing and noise.

- Stationary voxels’ do not vary through the cardiac cycle, these voxels would have a large DC component and a low H1 component.
- Voxels near the heart with moving tissue or flowing blood vary periodically with each heartbeat, these voxels have large DC and H1 components.
- Noisy voxels’ vary frequently, these voxels would have low DC and H1 components.

The ability to differentiate the image into three tissue types rather than two should make it less susceptible to the inclusion of moving tissue.

The DC and H1 images were obtained by converting the individual magnitude and phase difference images into a complex representation. The images are normalised and any spatial aliasing was removed before computing the $1D - FT$ on each voxel.

**The DC image:** The histogram of the DC image normally revealed two peaks, the lowest peak represents noisy voxels and the high peak represents voxels with a large DC component, either stationary or moving. The noisy voxels were removed from the image by determining the minimum of the valley between the two peaks.\textsuperscript{6} In some cases the second peak was unclear and often led to a high threshold value that removed stationary and moving tissue. To compensate the minimum of the calculated valley or the threshold value from two repetitions of

\textsuperscript{6}The trough was identified by taking the derivative of the image histogram, smoothing it and identifying the x-intercept of the line segment joining the maximum negative derivative and the next maximum positive derivative.
6.4. EXTENSION OF THE SURFACE BACKGROUND PHASE CORRECTION

Matlab’s inbuilt function “greythresh” was used to eliminate noise and create the DC mask.

**The H1 image:** Stationary tissue can be assumed to have the same H1 component as noise. After a log transformation the histogram of noise’s H1 components was Gaussian. The upper 99% confidence interval was used to determine the threshold value to eliminate stationary tissue from the H1 image. Stationary tissue can then be identified from the DC mask by subtracting the H1 mask.

![Images](a) original (b) temporal std. dev. mask (c) freq. spectrum mask

Figure 6.6: Regions of the heart’s great vessels are additionally located with the temporal standard deviation mask, in the frequency spectrum mask these same vessels are removed.

The identification of stationary tissue in a typical patient by the frequency spectrum and temporal standard deviation methods is shown in Figure 6.6. In comparison to the temporal standard deviation approach the frequency spectrum method completely removes the heart tissue and great vessels whilst maintaining a good proportion of the chest wall.

---

7 Greythresh uses Otsu’s method to classify voxels into two groups by minimising their intraclass variance.
CHAPTER 6. BACKGROUND PHASE CORRECTION

Figure 6.7: Frequency spectrum algorithm for identifying stationary tissue.
6.5. COMPARISON OF SURFACE BACKGROUND PHASE METHODS

6.5 Comparison of surface background phase methods

6.5.1 In-vivo flow correction results

The mean error and standard deviations before and after correction can be found in Section B.3. Table 6.1 summarises the statistical evidence of applying the background phase correction. The error reduced from $-0.22 \pm 0.56$, $-0.63 \pm 0.41$ and $-0.68 \pm 0.46$ to an average error across all surface orders of $0.07 \pm 0.24$, $-0.22 \pm 0.14$ and $-0.19 \pm 0.16$ for AV0cm AV 1cm and AV2.cm respectively.

Statistical Analysis

Statistical analysis was performed with R for windows, v2.6.2 (The R foundation for statistical computing). Two-way Anova with Tukey adjustments (statistical significance < 0.05) was used to consider the usefulness of applying a background phase correction to better match the LVSV for each slice orientation and TE.

Only the optimised PC sequence experienced any significant improvement after application of the correction algorithm (Table 6.1, p-values < 0.05 and Figure 6.8). No evidence of interaction was observed between the different methods used to identify stationary tissue and surface orders. No evidence of a difference was observed between surface orders or methods used to identify stationary tissue except at TE 2.8ms where there was some weak evidence (*) of a difference between stationary tissue methods.

<table>
<thead>
<tr>
<th>TE</th>
<th>Position</th>
<th>Interaction</th>
<th>no correction vs. correction</th>
<th>Stationary tissue identification</th>
<th>Surface order</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV0cm</td>
<td>0.56</td>
<td>0.05*</td>
<td>0.03*</td>
<td>&gt; 0.99</td>
<td></td>
</tr>
<tr>
<td>AV1cm</td>
<td>0.64</td>
<td>&gt; 0.55</td>
<td>0.14</td>
<td>&gt; 0.93</td>
<td></td>
</tr>
<tr>
<td>AV2.5cm</td>
<td>0.54</td>
<td>&gt; 0.81</td>
<td>0.03*</td>
<td>&gt; 0.93</td>
<td></td>
</tr>
<tr>
<td>IVOT</td>
<td>0.99</td>
<td>&gt; 0.64</td>
<td>0.09</td>
<td>&gt; 0.93</td>
<td></td>
</tr>
<tr>
<td>MPA</td>
<td>0.99</td>
<td>&gt; 0.98</td>
<td>0.51</td>
<td>&gt; 0.98</td>
<td></td>
</tr>
<tr>
<td>AV0cm</td>
<td>0.95</td>
<td>&gt; 0.85</td>
<td>0.92</td>
<td>&gt; 0.99</td>
<td></td>
</tr>
<tr>
<td>AV1cm</td>
<td>0.88</td>
<td>&gt; 0.57</td>
<td>0.46</td>
<td>&gt; 0.89</td>
<td></td>
</tr>
<tr>
<td>AV2.5cm</td>
<td>0.76</td>
<td>&gt; 0.14</td>
<td>0.25</td>
<td>&gt; 0.52</td>
<td></td>
</tr>
<tr>
<td>AV0cm</td>
<td>1.00</td>
<td>&lt; 0.05</td>
<td>&gt; 0.82</td>
<td>&gt; 0.94</td>
<td></td>
</tr>
<tr>
<td>AV1cm</td>
<td>0.99</td>
<td>&lt; 0.01</td>
<td>&gt; 0.13</td>
<td>&gt; 0.92</td>
<td></td>
</tr>
<tr>
<td>AV2.5cm</td>
<td>0.68</td>
<td>&lt; 0.01</td>
<td>0.05*</td>
<td>&gt; 0.95</td>
<td></td>
</tr>
</tbody>
</table>

Table 6.1: Summary of the statistical significance of performing background phase correction.
CHAPTER 6. BACKGROUND PHASE CORRECTION

Figure 6.8

TE 2.8ms variant

Plot of Error at AV0cm by levels of Order and Mask

Plot of Error at AV1cm by levels of Order and Mask

Plot of Error at AV2.5cm by levels of Order and Mask

Plot of Error at MPA by levels of Order and Mask

Plot of Error at LVOT by levels of Order and Mask

TE 2.0ms variant

Plot of Error at AV0cm by levels of Order and Mask

Plot of Error at AV1cm by levels of Order and Mask

Plot of Error at AV2.5cm by levels of Order and Mask

Figure 6.8
6.5. COMPARISON OF SURFACE BACKGROUND PHASE METHODS

Figure 6.8: Error before and after correction for each position and TE by levels of surface order and stationary tissue mask type. Only the optimised PC sequence shows consistent improvement after correction, but no difference between the surface order or mask is apparent. Dof - Degrees of Freedom, Std - Temporal Standard deviation Mask, Freq - Frequency spectrum Mask.

6.5.2 Implications for subsequent analysis

The larger gradients used to reduce TE exacerbate background phase error [39], Figures 6.1 and 6.2. In contrast to recent studies, that have reported improvement after phase correction [79; 81], when the surface approach was applied in-vivo significant improvement of the SV data was only observed with the optimised PC sequence. No statistical significance was apparent between the correction methods. Consequently, the data presented in this study only performed the phase correction on the optimised PC sequence where clear improvement was observed. The temporal standard deviation mask and a linear planar surface fit were used for consistency with the literature.
CHAPTER 6. BACKGROUND PHASE CORRECTION

6.6 Trial results

Of the fifteen patients studied, 11 were men and the mean age was 71 ± 10.5 years. 10 patients had calcific aortic stenosis with tri-leaflet AVs and 5 had bicuspid valves. By echo the mean aortic peak velocity was 4.2 m/s (range 3.3 m/s to 5.5 m/s), mean gradient 44.7 mmHg (range 25.6 mmHg to 75.2 mmHg) and AVA 0.85 cm² (range 0.52 cm² to 1.50 cm²). 12 patients (80%) had severe aortic stenosis.

6.6.1 Estimation of stroke volume with MRI flow data

The mean LVSV by CIM was 87.0 ± 21.8 mL. Table 6.2 and Figure 6.9 show the mean flow estimates and errors in PC estimation of flow at the different locations - MPA, LVOT, AV0cm, AV1cm and AV2.5cm. In the absence of mitral regurgitation or left-to-right shunts we expect the flow at each level to be close to the LVSV estimate. At a TE of 2.8 ms the mean PC estimate of stroke volume (PCSV) was very similar at the MPA (+1.2%), LVOT (−6.2%) and at the AV leaflet tips (AV0cm, +6.0%), but significantly lower at both AV1cm and AV2.5cm (−26.8% and −19.4% respectively). This underestimation of flow beyond the AV occurred across the range of TEs and was not improved by a TE as low as 1.5 ms.

<table>
<thead>
<tr>
<th>TE (ms)</th>
<th>Stroke volume</th>
<th>Paired T-test</th>
<th>Linear regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN±SD (mL)</td>
<td>MEAN±SD p-value</td>
<td>R² / p-value</td>
</tr>
<tr>
<td>LVSV</td>
<td>2.8</td>
<td>87.0±21.8</td>
<td>−12.8 ± 9.4%</td>
</tr>
<tr>
<td>MPA</td>
<td>2.8</td>
<td>88.3±24.3</td>
<td>−6.2 ± 10.3%</td>
</tr>
<tr>
<td>LVOT</td>
<td>2.8</td>
<td>80.2±21.8</td>
<td>−4.4 ± 24.0%</td>
</tr>
<tr>
<td>AV0cm</td>
<td>2.8</td>
<td>93.5±31.6</td>
<td>−6.0 ± 23.7%</td>
</tr>
<tr>
<td>2.0</td>
<td>82.1±35.0</td>
<td>−4.4 ± 24.0%</td>
<td>0.47 / 0.44 / &lt; 0.01</td>
</tr>
<tr>
<td>1.5a</td>
<td>88.8±27.2</td>
<td>1.4 ± 17.7%</td>
<td>0.78 / 0.51 / &lt; 0.01</td>
</tr>
<tr>
<td>AV1cm</td>
<td>2.8</td>
<td>57.7±19.9</td>
<td>−26.8 ± 14.6%</td>
</tr>
<tr>
<td>2.0</td>
<td>55.5±22.1</td>
<td>−28.8 ± 15.5%</td>
<td>0.01 / 0.49 / &lt; 0.01</td>
</tr>
<tr>
<td>1.5a</td>
<td>59.7±23.8</td>
<td>−25.2 ± 14.0%</td>
<td>0.01 / 0.62 / &lt; 0.01</td>
</tr>
<tr>
<td>AV2.5cm</td>
<td>2.8</td>
<td>65.8±25.6</td>
<td>−19.4 ± 16.7%</td>
</tr>
<tr>
<td>2.0</td>
<td>54.6±19.3</td>
<td>−29.6 ± 13.3%</td>
<td>0.01 / 0.57 / &lt; 0.01</td>
</tr>
<tr>
<td>1.5a</td>
<td>58.6±30.5</td>
<td>−26.2 ± 23.3%</td>
<td>0.01 / 0.33 / 0.03</td>
</tr>
</tbody>
</table>

a The TE 1.5 ms data has been background phase corrected using a linear planar surface with a temporal standard deviation mask, threshold 25%, to identify stationary tissue.

Table 6.2: Comparison of PC flow estimate of SV with LVSV.

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6.6. TRIAL RESULTS

(a) MPA/LVOT

(b) AV0cm

(c) AV1cm

Figure 6.9
CHAPTER 6. BACKGROUND PHASE CORRECTION

Figure 6.9: The PCSV has good agreement with the LVSV in the LVOT and in the MPA. The mean error is close to zero at AV0cm. The standard deviations show only small improvements at shorter TEs. All TEs underestimate the flow beyond the AV at AV1cm and AV2.5cm.

Although the mean PCSV at AV0cm was similar to the mean LVSV there was a much larger individual disagreement (standard deviation of the error across patients) at the valve level compared with that observed with MPA PCSV, (Table 6.2). For example, the mean error between LVSV and PCSV in the MPA was 1.2% ± 9.4% compared with 6% ± 23.7% at the AV leaflet tips. The errors’ standard deviation are generally twice as large in the aorta as the LVOT and MPA. Reducing the TE in the modified and optimised sequence gave a small improvement in the correlation\(^8\) between PCSV and LVSV and reduced the errors’ standard deviation.

Physiological variability

It is possible that physiological factors, heart rate and cardiac output, may impact on the ability to compare between the SV measurements. 12/15 patient’s heart rate increased during the scan, 2 decreased and one patient (whose scan was interrupted) heart rate initially increased and then decreased, Figure 6.10. Furthermore, holding your breath reduces the blood flow to the heart causing your heart rate and the strength of the contraction to increase in an attempt

---

\(^8\)A high \(R^2\) indicates the expected linear relationship has strong correlation and a small p-value (< 0.05) indicates that the probability that a high \(R^2\) statistic did not occur by chance.
to maintain cardiac output (CO) [7]. If we assume that CO is maintained, the changing heart rate inversely affects the stroke volume.

Correction attempts\(^9\) proved unsuccessful. These physiological effects may account for some of the individual disagreement seen in the comparison between flow and volumetric derived stroke volumes in the MPA. But, the standard deviations of the SV error in the AV is twice that in the MPA indicating the continued presence of intravoxel dephasing error.

### 6.6.2 Assessment of aortic stenosis

**The effect of magnitude thresholding**

Figures 6.12 and 6.11: No aliasing results were recorded by the observer. The peak velocities were larger and appear to better match the continuous wave Doppler (Doppler) peak velocities when no thresholding is applied for the standard and modified sequences, but the correlation between VTIs was poor with a large individual disagreement. The optimised PC sequence peak velocities slightly underestimates but also agreed well with the Doppler peak velocity, the individual agreement of the VTI remained variable.

\(^9\)Correction attempts assumed a constant CO determined from the volumetric data and estimated the stroke volume with the measured heart rate of the flow scan.
(a) TE 2.79ms without thresholding
(b) TE 2.79ms with thresholding
(c) TE 2.0ms without thresholding
(d) TE 2.0ms with thresholding
(e) TE 1.5ms without thresholding
(f) TE 1.5ms with thresholding

Figure 6.11: Without magnitude thresholding the VTI experience significant underestimation for all TEs with a large individual disagreement. Introducing the magnitude thresholding lessens the underestimation and reduces the individual disagreement. All TEs experience significant outliers and in general the AV0cm VTI agrees with Doppler better than the AV1cm.
6.6. TRIAL RESULTS

(a) TE 2.79ms without thresholding  
(b) TE 2.79ms with thresholding  
(c) TE 2.0ms without thresholding  
(d) TE 2.0ms with thresholding  
(e) TE 1.5ms without thresholding  
(f) TE 1.5ms with thresholding

Figure 6.12: The peak velocities are similar between AV0cm and AV1cm locations. Without magnitude thresholding the peak velocities are better centred about the Doppler peak velocity; however, there is a large variation. Thresholding reduces the variation, particularly at TE 2.8ms, but results in an underestimation of the peak velocity.
The magnitude threshold chosen (relative signal intensity (RSI) > 2) aimed to remove unreliable voxels. The result improves the VTI estimates for all PC sequences and the peak velocities at the standard and modified now also slightly underestimate the Doppler peak velocity. Investigation of the RSI of the voxel corresponding to the peak velocity without thresholding shows that no signal enhancement (RSI < 1) was observed in 57%/53%/11% of cases for the TEs of 2.8ms, 2.0ms and 1.5ms respectively. The larger proportion of voxels with low RSIs explains the greater difference seen with magnitude thresholding in the standard and modified PC sequences.

The magnitude thresholding is an effective method to remove erroneous voxels. Future analysis concentrates on the data with magnitude thresholding applied. The data prior to thresholding is also graphed to illustrate the danger of using voxels with low signal.

### The maximum velocity time integral and corresponding peak velocity and stroke volume data

Table 6.3 and Figure 6.13: The $VTI_{PC,pk}$ were observed at the AV0cm level in 73%, 73% and 71% for the TEs of 2.8, 2.0 and 1.5ms, respectively. In the remaining acquisitions $VTI_{PC,pk}$ was at the AV1cm level. The TE 2.8, 2.0 and 1.5ms showed 93%, 80% and 79% agreement that the peak velocity and $VTI_{PC,pk}$ occurred at the same location.

<table>
<thead>
<tr>
<th>TE</th>
<th>$V_{pk}$ (m/s)</th>
<th>Stroke volume (mL)</th>
<th>$VTI_{pk}$ (cm)</th>
<th>Mean AVA (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.8ms</td>
<td>3.87 ± 0.66 (0.83)</td>
<td>83.7 ± 33.9 (0.02)</td>
<td>89 ± 20 (0.07)</td>
<td>1.00 ± 0.26 (0.31)</td>
</tr>
<tr>
<td>2.0ms</td>
<td>3.81 ± 0.59 (0.26)</td>
<td>71.0 ± 32.0 (0.12)</td>
<td>91 ± 20 (0.05)</td>
<td>0.97 ± 0.20 (0.32)</td>
</tr>
<tr>
<td>1.5ms</td>
<td>3.89 ± 0.63 (0.44)</td>
<td>78.0 ± 29.6 (0.07)</td>
<td>93 ± 21 (0.10)</td>
<td>0.95 ± 0.22 (0.32)</td>
</tr>
</tbody>
</table>

Table 6.3: Peak velocity, VTIs, SV and mean AVA at the level of the max VTI.

CMR systematically underestimated both peak velocity and VTI compared with Doppler (Table 6.3). At a TE of 2.8ms the mean velocity was 3.87 m/s compared
6.6. TRIAL RESULTS

(a) VTI without thresholding  (b) VTI with thresholding

(c) Peak velocity without thresholding  (d) Peak velocity with thresholding

(e) PCSV without thresholding  (f) PCSV with thresholding

Figure 6.13: The maximum VTI and peak velocity shows good general agreement with Doppler. Shortening the TE to 1.5 ms improves the individual agreement of the VTI, there is one outlier. The TE 1.5 ms PCSV exhibits better agreement with the LVSV than the longer TEs. Without magnitude thresholding considerable variation is present for all estimates.
with 4.28m/s by echo, and the mean VTI was 89cm and 99cm, respectively. Except for this underestimation by CMR there was reasonably good agreement between the two methods. The mean error was \(-0.41 \pm 0.48\) m/s for the peak velocity and \(-10 \pm 14\) cm for peak VTI between the two methods. Shortening TE showed no significant improvement in the peak velocity. Figure 6.13(b) shows the optimised PC sequence VTIs have better individual agreement with Doppler; although there was one outlier.

The mean CMR and echo LVSVs were similar (87mL and 81.8mL, respectively) but with relatively poor individual agreement at the patient level. The standard deviation of the difference in SV between the methods was 19.7mL. Better correlation (Figure 6.13(e)) and better individual agreement of the SV error was observed at TE of 1.5ms (\(-4.52 \pm 21.3\) mL, \(R^2 = 0.57\)) compared with TE 2.8ms (1.83 \pm 32.6mL, \(R^2 = 0.30\)).

### Aortic Valve Area

Table 6.3 and Figure 6.14 compares the two CMR methods of estimating AVA with the echo derived AVA. The Bland-Altman analysis is relatively poor between echo and both CMR methods with a standard deviation of the error between the methods of at least 0.2cm². Compared with echo, the CMR volumetricAVA method systematically overestimated AVA. The flowAVA method showed better agreement with echo, probably because at all TEs both components of the calculation (\(PCSVAV\) and \(VTI_{PC, pk}\)) were systematically underestimated.

<table>
<thead>
<tr>
<th>TE (ms)</th>
<th>SV (\text{diff} \pm \text{SD}) (mL)</th>
<th>(VTI_{pk}) (\text{diff} \pm \text{SD}) (cm)</th>
<th>VolumetricAVA (\text{diff} \pm \text{SD}) (cm²)</th>
<th>FlowAVA (\text{diff} \pm \text{SD}) (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.8</td>
<td>1.83 \pm 32.6</td>
<td>(-10 \pm 14)</td>
<td>0.15 \pm 0.30</td>
<td>0.11 \pm 0.41</td>
</tr>
<tr>
<td>2.0</td>
<td>(-10.9 \pm 35.6)</td>
<td>(-9 \pm 20)</td>
<td>0.12 \pm 0.22</td>
<td>(-0.08 \pm 0.32)</td>
</tr>
<tr>
<td>1.5</td>
<td>(-4.52 \pm 21.3)</td>
<td>(-7 \pm 15)</td>
<td>0.11 \pm 0.22</td>
<td>0.00 \pm 0.20</td>
</tr>
<tr>
<td>Linear regression</td>
<td>(R^2/p-value)</td>
<td>(R^2/p-value)</td>
<td>(R^2/p-value)</td>
<td>(R^2/p-value)</td>
</tr>
<tr>
<td>2.8</td>
<td>0.30/0.03</td>
<td>0.53/0.01</td>
<td>0.10/0.24</td>
<td>0.11/0.23</td>
</tr>
<tr>
<td>2.0</td>
<td>0.37/0.02</td>
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<td>0.26/0.05</td>
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<td>0.49/0.01</td>
<td>0.31/0.04</td>
<td>0.57/0.01</td>
</tr>
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</table>

Table 6.4: Bland-Altman and linear regression analysis between Doppler and CMR methods for AVA estimation. \(VTI_{PC, pk}\) and AVA were compared to Doppler data and PCSV estimates were compared against LVSV.

The optimised PC sequence AVAs exhibited better individual agreement and a
stronger correlation with echo. The standard deviation of the AVA error were also similar between methods; however for the longer TE PC sequences the standard deviation of the flowAVA was larger than the volumetric AVA.

Without magnitude thresholding the resultant AVA is substantially worse. For example at a TE of 1.5ms the flow derived AVA error is overestimated at \(0.52 \pm 1.39 \text{cm}^2\) compared to \(0.00 \pm 0.20\). The inclusion of erroneous voxels resulted in poor VTI estimates.

Figure 6.14: The volumetric derived PC AVA overestimates the Doppler AVA and limited improvement is seen at shorter TEs. The flow derived AVA better matches the Doppler AVA and the variation is especially reduced with the optimised PC sequence. Without magnitude thresholding the AVA is extremely variable.
6.7 Discussion and conclusions

In this study we found important inaccuracies in the measurement of aortic flow volume by phase contrast both at, and beyond, the stenotic AV. We have also observed a relatively small but systematic underestimation of peak AV velocities and velocity-time integrals obtained by CMR compared with echo.

6.7.1 Background phase correction

The other recent phase correction studies were performed on a GE 1.5T Twin-Speed scanner [79] and a Siemens 1.5T Sonata scanner [81]. This trial was performed on a newer Siemens 1.5T Avanto scanner. The fact that the standard (or the modified) PC sequences did not require correction implies that the susceptibility of background phase may also be scanner (or even site) dependent [75].

Furthermore, despite the use of low-order surfaces potentially worsening the results in a stationary phantom (Section 6.4.1) no global difference was observed in-vivo. Potentially each case may require a different surface order fit.

Without a suitable gold standard for the background phase (and the presence of other significant errors) performing individual comparisons is inappropriate in this study. Further work into residual background phase algorithms requires the development of more specific phantom experiments or an in-vivo study on normal volunteers where other causes of error can be minimised (Section 8.3.2).

6.7.2 Stroke volume flow measurement in aortic stenosis

Decreasing TE has been shown to improve errors due to intravoxel dephasing in phantoms [59] (Section 3.2.4, Chapter 4) and applying a magnitude threshold has been proposed as a suitable method for removing erroneous peak velocities [64], Figures 6.12, 6.11, 6.13 and 6.14. The correct assessment of flow requires all voxels to be accurate. Flow measurements are more sensitive to intravoxel dephasing errors and are a better indicator of reliability than either the peak velocity or the $VTI_{PC,pk}$. Verification of SV flow estimates should be used to establish confidence in the data quality.
The comparison of the gold standard LVSV with the flows measured by PC at AV level were highly variable, and those measured beyond the stenotic AV were underestimated by between 20 to 30%. The individual agreement of the SV error reduced, at AV0cm (Table 6.2) and at the level of the max VT1 (Table 6.4), with the short TE of 1.5ms, but the errors’ standard deviation is still twice that observed in the MPA. Significant intravoxel dephasing errors are thus still present in-vivo even at a TE of 1.5ms.

6.7.3 Comparison between peak velocity and VT1

Peak trans-AV velocities and \( VTI_{PC,pk} \) underestimated that observed by Doppler echocardiography by about 10% on average. Estimation of peak velocity and \( VTI_{PC,pk} \) estimates by CMR are likely to be less susceptible to intra-voxel dephasing as accurate information in each voxel is not required. Even one voxel per phase with good signal intensity in the core of the jet could theoretically provide an accurate estimate; the aberrant low signal intensity voxels should be excluded to prevent inaccurate peak velocity estimates.

CMR PC peak velocity and \( VTI_{PC,pk} \) may always underestimate Doppler peak velocity due to spatial and temporal averaging. The image is temporally averaged over many heart beats and, through the acquisition of multiple K-space lines, within a heart beat. The voxel spatially averages the velocity measurement. More specifically, beat-to-beat variations of the stenotic jet’s orientation within the desired slice may violate PC’s assumption of identical flow patterns (Section 2.5.2). All these averaging mechanisms act to dampen extreme values such as the peak velocity. In comparison, Doppler is an instantaneous measurement whose signal intensity (therefore the planimetry of the Doppler envelope) is dependent on the number of red blood cells moving at the same velocity [10], Section 1.5.2. Further study is needed to better understand the relationship between CMR and Doppler derived velocity data.

6.7.4 Assessment of AVA by CMR compared with echo

The volumetric AVA overestimated echo AVA because the \( VTI_{PC,pk} \) was underestimated by CMR. The flowAVAs are better calibrated than echo but only because both the PCSV and VTIs are proportionately underestimated. Decreasing the
CHAPTER 6. BACKGROUND PHASE CORRECTION

TE to as low as 1.5ms does improve the individual agreement between volumetric and flow derived AVAs. The larger disagreement in the flow AVA in the standard and modified PC sequences is most probably related to the poor PCSV estimates. Presumably, because the $VTI_{pk}$’s $R^2$ values and the volumetric AVA error’s standard deviation are similar, this is related to the improved individual agreement between the PCSV at the maximum VTI.

In contrast to our study, Caruthers et al [46] and Yap et al [49] obtained a better correlation between Doppler and PC AVA. This is possibly in part because they included patients with mild aortic stenosis.

Caruthers et al [46] (TE of 3.1ms) do not report flow or LVSV comparisons. Only five patients had Doppler VTI in excess of 0.8m, all of whom were underestimated with PC. The limits of agreement in their studies are similar to those of the current study.

Yap et al [49], in patients with aortic stenosis secondary to a bicuspid AV, found a good correspondence between LVSV measured by volumetric analysis and phase contrast (TE of 2.9ms). But, their limits of agreement increased distal from the AV, consistent with intravoxel dephasing induced inaccuracies. Several patients with moderate to severe aortic stenosis showed marked variation between echo and PC methods.

It is also possible that the type of valve lesion is important. In the current study 10/15 patients had calcific aortic stenosis which may cause more turbulent flow than in a bicuspid valve.

Subtle differences in slice location may also be important. Caruthers et al [46] in a study using free breathing PC found subtle differences in slice position made no difference but it is possible that with the more accurate slice positioning with breath hold PC sequences that position is important. Yap et al [49] placed their slices at the AV leaflet at end systole which is further towards the apex than in our study where it was placed at the AV tips in end-diastole. Further investigation is needed to understand whether such small differences in slice location are important, as this would potentially limit generalisability of the technique.
6.7.5 Clinical implications

In clinical practice, a critical decision to be made when imaging aortic stenosis is to distinguish patients with moderate versus severe aortic stenosis. PC derived aortic flow measured in the stenotic jet is unreliable and though some improvement is evident they are not fully corrected by the reduced echo times possible in this study. Before CMR PC AVA are used clinically, improved techniques to measure PCSV are required.

Despite erroneous flow data it is possible to obtain peak velocities, VTIs and/or AVAs which correlate reasonably well with Doppler results. In this study, the PC method does seem to systematically underestimate peak velocity and VTI data by $\approx 10\%$ compared with Doppler. Although this is a relatively small calibration error it could lead to a clinically important mis-classification of some patients with severe aortic stenosis as having moderate aortic stenosis.

Physiological variability may increase the individual SV disagreement between volumetric and flow based methods. The volumetric measurement of SV averages over many acquisitions, averaging over repeat flow measurements may reduce physiological errors. The AV0cm and AV1cm could be considered repeat measurements. Choosing the slice location with the peak VTI may have reduced the impact of physiological variability. The repeatability of measurements in aortic stenosis patients warrants further investigation.

6.7.6 Conclusion

PCSV measured in stenotic jets is unreliable and not satisfactorily corrected by reduction in TE to 1.5ms. Before reliable estimation of AVA in more severe AS can be obtained improved techniques to measure this flow are required. Despite erroneous flow data, in this study it was possible to obtain peak velocities, VTIs and/or AVAs which correlate moderately well with Doppler results. The PC method does seem to systematically underestimate velocity and VTI data by $\approx 10\%$ compared with Doppler. Further study is needed to better understand the relationship between CMR and Doppler derived velocity data.
7

Phase contrast ultra short TE

7.1 Introduction

Previous chapters have shown that reducing echo time (TE) exhibited the greatest improvement in the reliability and accuracy of flow estimates with standard phase contrast (PC) techniques. Unfortunately, the results of the clinical trial, presented in Chapter 6, demonstrated that PC measurements are still susceptible to intravoxel dephasing errors at and beyond the aortic valve (AV), even with TEs as short as 1.5ms. The shorter TEs, and magnitude thresholding to remove erroneous voxels, did improve the agreement between PC and Doppler estimates of the velocity time integral (VTI). Yet aortic valve area (AVA) remained overestimated with the volumetric approach and exhibited large limits of agreement with the Doppler determined AVA.

The ability to shorten TE in a standard PC sequence using higher gradient performance is limited and even with the most recent hardware, residual errors are present at high flow-rates, Figure 5.2. Furthermore, the use of larger gradients results in errors from background phase due to eddy-currents, reducing some of the gains associated with improved gradient performance, Section 6.2. It would be ideal to further reduce the TE without relying on higher gradient strengths and rise times.

From Chapter 4, it was determined that further improvements in accuracy would be achieved by focussing on the duration of the bi-polar gradient as well as the overall TE. Shorter bi-polar gradients result in less higher order motion encoding and reduce signal loss due to turbulence. Reducing the overall TE mitigates the mixing of fast and slow moving spins.
CHAPTER 7. PHASE CONTRAST ULTRA SHORT TE

This chapter presents the design\(^1\) and evaluation of a PC implementation of the ultra short TE (UTE) technique, Section 1.7, with the aim of minimising TE and the bipolar gradient duration. Various concepts based on Markl et al.’s [83] novel gradient inversion approach and the UTE readout trajectory are proposed. The advantages and limitations of each approach over standard PC sequences are evaluated. The proposed sequence’s improved ability to estimate flow in a high velocity stenotic phantom is presented. Its applicability and feasibility in a normal volunteer and a patient with aortic stenosis is demonstrated.

\(^1\)Pulse sequences were developed, initially in VB13’s and then VB15’s IDEA environment, in collaboration with Dr Matthew Robson at the Oxford centre for Clinical Magnetic Resonance, John Radcliffe Hospital, Oxford UK.
7.2 Sequence development

7.2.1 Sequence concepts

In MR angiography, ultra short TE (UTE) approaches have been shown to improve image quality in regions of pulsatile flow [84]. The mechanisms for this improvement are the oversampling of the centre of K-space [53], and inherent minimisation of the first moment of the readout gradient provided by centre-out K-space trajectories [77]. With half-pulse excitation [85] the first moment of the gradients and the signal drop-out from regions of turbulent stenotic jet flow [86] are further reduced.

The half-pulse approach\(^2\) yields the shortest TEs, but requires the acquisition and combination of two excitations for each line of K-space. Introducing velocity encoding after the half-pulse acquisition prolongs the TE. The total (often breath-hold) scan time is also lengthened because, on top of the two half-pulse excitations, PC needs to collect data with different velocity sensitivities. Half-pulse acquisition was therefore rejected as a possible alternative.

PC sequences must play out both the slice excitation and velocity sensitive gradients for every TE. In stenotic jets the slice is usually oriented perpendicular to the jet and velocity is encoded in the “through slice” direction. In 2003, Markl et al [83] suggested a novel approach for creating velocity sensitivity by using gradient inversion to combine the velocity encoding with the slice selection gradients. Markl utilised the inherent velocity sensitivity of slice select gradients to shorten the repetition time (TR) to create a balanced steady-state free precession PC technique. This chapter uses the same idea to reduce the TE.

Alternatively, the slice selection gradients could be thought of as being dependent on the velocity encoding and compensation waveforms, Figure 7.1. In fact there are several possibilities:

- velocity dependent slice excitation using gradient inversion with Cartesian readout;

\(^2\)In conventional slice excitation a refocussing pulse is required to rephase the signal. The rephasing gradient can be removed by adding the data from two truncated RF pulses with slice select gradients of opposite polarity. The addition of the two acquisitions results in a signal that is in-phase. With no rephasing gradient present the data sampling can occur immediately after excitation, thus achieving extremely short TEs.
• velocity dependent slice excitation using a encoding/compensation scheme with Cartesian readout;
• conventional encoding schemes with UTE readout;
• velocity dependent slice excitation using gradient inversion with UTE readout; and
• velocity dependent slice excitation using a encoding/compensation scheme with UTE readout.

7.2.2 Velocity dependent slice excitation

A simple slice select and refocusing gradient pair is a bipolar gradient and therefore velocity sensitive, Figure 7.1. Markl et al’s [83] approach has the restriction that the maximum velocity sensitivity ($V_{enc_{max}}$) is related to the gradient area required for a given slice thickness [83]. Different $V_{encs}$ were achieved by varying the length and shape of the RF pulse and/or the slice select gradient, Figure 7.2. The largest $V_{enc_{max}}$ reported (424 cm/s) used a 600µs central lobe RF pulse with a slice thickness of 8mm. Except in clinical aortic stenosis studies the $V_{enc}$ is commonly required to be 500cm/s or more.

![Figure 7.1: The velocity dependent slice excitation concept can use either an encoding/compensation scheme (top) or Markl’s gradient inversion scheme (middle). Markl’s steady state free precession technique required, the wave form to be balanced (dotted) to ensure the magnetisation was correctly refocussed for each acquisition.](image-url)
To achieve higher \( V_{enc} \), rather than simply increasing the slice thickness, we designed the RF pulse to be a function of the slice select gradient (instead of the conventional approach where the slice select gradient is a function of the RF pulse). This allowed the \( V_{enc} \) to be more freely specified.

The slice select gradient waveform and refocussing pulse were designed to enable the desired velocity encoding (see Appendix C). The plateau \( (P_1) \) of the slice select gradient waveform dictates the available duration of the RF pulse \( (T_{rf}) \) and the gradient strength and bandwidth of the RF pulse, Eq. 2.19).

The choice of \( V_{enc} \) as a design criterion caused the total gradient duration and slice thickness to become dependent on the \( V_{enc} \). To optimise parameters, the minimum slice thickness and the total gradient duration possible at a given gradient strength, for the gradient inversion and encoding/compensated schemes, are shown in Figure 7.3. The cut-off points in Figure 7.3 indicate where no central lobe rectangular RF pulse could be played out. For both schemes the minimum slice thickness occurs prior to the minimum total gradient duration. Subsequent gains in total gradient duration are minimal, particularly for the inversion scheme. Therefore it was determined that the gradient strength applied should minimise the slice thickness for a given \( V_{enc} \).
7.2.3 UTE readout trajectory

In Cartesian based readouts, the signal must first be dephased using the pre-focussing gradients, Section 2.3.4. The signal is rephased so that at the centre of the echo, which corresponds to the centre of K-space, the spins are coherent and the signal is at a maximum. Because the UTE readouts start at the centre of K-space they do not require phase encoding gradients, read pre-focussing gradients or additional time to get back to the centre of K-space in the read direction. Data sampling occurs immediately after excitation.
Both readout gradients\(^3\) may be active during UTE readout and data sampling commonly begins directly on the gradient ramp, Figure 7.4. On the ramp the data sampling rate is half of the rate on the plateau \([52]\). The maximum gradient area required to acquire \(k_{\text{max}}\) is

\[
A_{k_{\text{max}}} = \frac{2N}{\gamma \text{FOV}} \tag{7.1}
\]

where \(N\) is the number of data points in each direction and the FOV is the same in each direction. The maximum gradient strength \(G_{\text{max}} = \frac{A_{k_{\text{max}}}}{r \cdot T_{\text{ro}}/2}\) where \(r\) is the rise time of the gradient ramp and \(T_{\text{ro}}\) is the duration of the readout gradient. The applied readout gradients, \(G_x\) and \(G_y\), can be determined using the angular sampling density \(\phi = \frac{2\pi n}{N-1}\) where \(n\) is the current, and \(N\) the maximum number of, radial K-space spokes.

\[
G_x = G_{\text{max}} \cos \phi \tag{7.2}
\]

\[
G_y = G_{\text{max}} \sin \phi \tag{7.3}
\]

Figure 7.4: UTE k-space trajectory (adapted from \([52]\)).

Radial K-space readouts have the advantage that there is no spatial aliasing\(^4\). Instead, radial K-space readouts are susceptible to streak artefacts because of the spreading out of the data sampling points at the periphery of K-space \([39]\).

\(^3\)The radial trajectory of an UTE readout means there is no specific phase/readout axis, hence they will be referred to as readout axes.

\(^4\)The MR signal is passed through a low pass filters prior to digitisation, similar to frequency encoding Section 2.3.4.
Streak artefacts are avoided when the angular distance between radial K-space spokes at the periphery ($k_{\text{max}}\Delta\phi$) satisfies the Nyquist criterion [33; 39].

$$k_{\text{max}}\Delta\phi \leq \frac{1}{\text{FOV}}$$

Therefore number of radial spokes ($N_s$) needed to completely sample over $2\pi$ is

$$N_s = \frac{2\pi}{\Delta\phi} = 2\pi k_{\text{max}} \text{FOV}$$

(7.5)

For comparison, given the same FOV, the number of K-space lines in a Cartesian readout trajectory can be determined by equating equations 2.24 and 2.21 together

$$N_y = 2k_{\text{max}} \text{FOV}$$

(7.6)

Which after equating equations 7.5 and 7.6 means that $\pi$ more K-space radial spokes compared to Cartesian K-space lines ($N_s = \pi N_y$) are required to fully cover K-space.

Nevertheless there will always be a region completely sampled. The radial streak artefacts from each object will appear outside a given radius ($r_f$).

$$r_f = \frac{\text{FOV}}{2} \left( \frac{N_s}{\pi N_y} \right)$$

(7.7)

The strength of the streak artefacts is dependent on the strength of the originating signal. If the highest intensity occurs in the centre of the FOV, the artefacts will be strongest near the periphery. This becomes useful in reducing pulsatile effects because the region (defined by $r_f^5$) about a vessel is free from artefacts and ghosting. In comparison, ghosting in Cartesian imaging causes artefacts which are strongest close to the object’s true location [53].

Prior to applying the 2D-FT, the K-space data is re-gridded on to a Cartesian grid. The dense sampling of central K-space, and the subsequent re-gridding, effectively averages the low spatial frequencies further mitigating artefacts from pulsatile flow [53; 84]. Furthermore, spatial resolution is dependent on $k_{\text{max}}$ and not on angular sampling intervals. This allows angular under sampling of K-space to reduce the scan time without sacrificing the in-plane resolution [39].

\footnote{The radius free of artefacts also depends on the motion’s frequency and resultant signal intensity.}
7.2.4 The effect of readout trajectories on TE

In the Cartesian readout trajectory an asymmetric echo (Section 2.3.5) can be used to reduce the size of the pre-phasing gradient lobe. This approach will always increase the TE relative to centric sampling schemes, Figure 2.2 and additionally causes incomplete coverage of K-space. In contrast, UTE readout trajectories do not require a pre-phasing lobe, they directly measure from the centre and entirely cover K-space. Not only does this allow the minimisation of TE but it also removes the cross terms from the concomitant gradient correction [58] required in standard PC sequences, Section 2.6.3. If combined with the gradient inversion scheme, where the gradients in the two acquisitions are equal and opposite, the self squared concomitant terms also cancel and no correction is required [58].

The encoding/compensation scheme can achieve a smaller slice thickness.\(^6\) But, the TE, even when combined with the UTE readout trajectory, is similar to the optimised PC sequence (TE 1.6\(\text{ms}\) for a 5.25\(\text{mm}\) slice thickness at a maximal encoding velocity (V\text{enc}) of 500\(\text{cm/s}\)). In comparison the gradient inversion scheme when combined with the UTE readout trajectory can dramatically reduce the TE to 0.65\(\text{ms}\) for a 8.75\(\text{mm}\) slice thickness at a V\text{enc} of 500\(\text{cm/s}\).

In Chapter 4, no adverse difference in the accuracy of flow or peak velocity for slice thickness between 8 – 10\(\text{mm}\) was seen, Figure 4.9. Hence, with its ability to minimise the duration of the encoding gradients and the overall TE, the velocity dependent slice excitation using gradient inversion with UTE readout was chosen for continued development. It uses lower gradient strengths, requires no concomitant gradient correction and also minimises TR.

7.2.5 Gradient Spoiling

In the standard PC sequence, it was sufficient to perform gradient spoiling on the slice select axis only. A similar approach was applied here. The gradient spoiler was run into the velocity dependent slice select gradient waveform. We found this approach was susceptible to very large background phase offsets, Figure 7.5(a). The background phase offset reduced as the duration of the spoiler gradient was

\(^6\)The larger gradients required to achieve the one-sided encoding means there is less restriction on the RF pulse.
CHAPTER 7. PHASE CONTRAST ULTRA SHORT TE

decreased. The application of the balanced slice select gradient profile employed by Markl et al [83], Figure 7.1, is not required in a gradient spoiled sequence, but gave better background phase characteristics (probably due to the cancellation of eddy currents from opposing ramps, Section 2.6.3) and was therefore included.

Figure 7.5: The background phase offset increased with longer slice spoiler gradients (a). It was found that balancing the gradient ramps gave the best background phase results. In contrast, the duration of the image spoilers had little effect on the background phase.

As Figure 7.5 shows, applying the gradient spoiler on the readout axes does not affect the background phase offset. Figure 7.6(b) shows that maintaining the same polarity of the spoiler gradients throughout the acquisition introduces lines through the image. This indicates inadequate spoiling and the appearance of residual magnetisation across TRs. The spoiler duration needed to be extended to \( \approx 1000\text{ms} \) to remove the lines from the image. In Figure 7.6(c) the polarity of the gradient spoilers was kept consistent with the image readout gradients. This approach allowed much shorter spoiler gradients to be applied whilst removing the residual magnetisation seen in Figure 7.6(a).

7.2.6 Proposed sequence

The proposed PC-UTE sequence is shown in Figure 7.7. The velocity dependent slice excitations are interleaved to prevent mis-registration artefacts from patient motion and flow [39]. It consists of the velocity dependent slice excitation using a central lobe rectangular RF pulse (1); the UTE centric-radial readout trajectory (2); and a gradient spoiler applied to both readout axes (3). The second velocity
7.2. SEQUENCE DEVELOPMENT

Figure 7.6: The image spoiler gradients polarity needed to be kept consistent with the readout gradients (c) otherwise residual transverse magnetisation would cause a spike in K-space that manifests itself as lines through the image.

encoded image is acquired by inverting the velocity dependent slice select gradient (4). Re-gridding was performed prior to the application of the phase difference reconstruction algorithm outlined in Figure 2.25.

Figure 7.7: The PC-UTE sequence consists of interleaved inverted balanced velocity dependent slice select gradients (i,iv), UTE readout (ii) and gradient spoiling along the readout axes (iii).
CHAPTER 7. PHASE CONTRAST ULTRA SHORT TE

7.2.7 Background phase

The background phase offset of the PC-UTE sequence was investigated in a static phantom using a prospectively gated 15 heart beat breath hold implementation with a $V_{\text{enc}}$ of 500cm/s (unless otherwise stated). A circular region of interest (ROI) ($d_I = 20\text{mm}$) was chosen in the centre of each image for the measurement of the background phase.

These results are system dependent.\(^7\) For example, at 500cm/s the background phase error is 2.2% or 11.4cm/s on Siemens 1.5T Avanto scanner and 1.1% or 5.7cm/s on a Siemens 3T Trio scanner. Nevertheless these results are still indicative of performance.

Figure 7.8 summarises the results obtained from experiments on a Siemens 3T Trio investigating the dependence on: gradient strength, whilst holding the slew rate, TE and TR constant at $160\text{mT/m/ms}$, $0.68\text{ms}$ and $2.41\text{ms}$; slew rate, whilst holding the gradient strength, TE and TR constant at $15\text{mT/m}$, $0.70\text{ms}$ and $2.57\text{ms}$; and TE, whilst holding the gradient strength, slew rate and TR constant at $15\text{mT/m}$, $160\text{mT/m/ms}$ and $3.6\text{ms}$.

The background phase offset showed marginal dependence on the gradient strength but slightly worsened with larger slew rates, the errors were $< 1.5\%$. The reduced errors seen as TE increased may reflect the longer time for the eddy currents to die away (Section 2.6.3) prior to the readout gradients being played out. The low reliance on slew rate allows a faster slew rate, $150\text{mT/m/ms}$\(^8\), to be chosen. Faster slew rates cause the gradient waveforms to have longer plateaus thereby easing the restriction of the RF pulse and resultan minimum slice thickness. The low dependence on gradient strength implies that its choice for each $V_{\text{enc}}$ will not affect the background phase and it does not have to feature in the optimisation approach.

The influence of $V_{\text{enc}}$, off-centre slice shifts, and image plane orientation on the background phase are shown in Figure 7.9 (performed on a Siemens 1.5T Avanto). Figure 7.9(a) reveals that the average phase offset over the ROI is worse at low $V_{\text{enc}}$ (larger gradient areas). The eddy currents are greater due to the larger

---

\(^7\)The development and in-vivo investigations of the PC-UTE sequence were performed on Oxford centre for Clinical Magnetic Resonance Research’s Siemens 3T Trip whilst the phantom experiments were performed on Auckland’s Siemens 1.5T Avanto. Both were running VB15 and have comparable gradient systems.

\(^8\)This slew rate can be maintained across all the 3T and 1.5T Siemens systems.
7.2. SEQUENCE DEVELOPMENT

(a) Gradient strength  
(b) Slew rate  
(c) TE

Figure 7.8: The background phase offset shows marginal dependence on the gradient strength but increases slightly with larger slew rates. Increasing the TE reduced the background phase offset.

Gradients required for shortening TE at low $V_{enc}$. Increasing the $V_{enc}$ reduces the gradient strengths required to optimise for TE, reduces the eddy currents and improves the PC-UTE results. The velocity dependent slice excitation approach is more suited to the large velocity acquisitions associated with aortic stenosis jets.

The average phase offset (Figure 7.9(b)) over the ROI and its spatial dependence increased with slice obliquity and when the image plane was offset further from isocentre (Figure 7.9(c)). The method is relatively insensitive to background phase when the image is centred at isocentre. At isocentre the background phase is constant across the stationary phantom which indicates that it is being domi-
CHAPTER 7. PHASE CONTRAST ULTRA SHORT TE

Figure 7.9: The background phase offset reduces at larger \( V_{enc} \), at more oblique orientations and at greater slice offsets.

nated by B0 spatially invariant eddy currents.

The reliance on the FOV (a), matrix size (b), readout bandwidth (c) are shown in Figure 7.10. A realistic image orientation and position determined from the scan parameters of an \textit{in-vivo} scan were used. The average phase offset over the ROI was constant with all parameters. Its standard deviation across the frames increased as the in-plane resolution increased (decreased FOV or increased matrix size) or the readout bandwidth increased. These findings are all consistent with a lower signal to noise ratio (SNR), Eq. 2.51.

Other sources of background phase need to be investigated and removed if possible. Background phase errors can be corrected in post-processing, but none
7.2. SEQUENCE DEVELOPMENT

Figure 7.10: The mean background phase error does not vary with voxel volume (FOV, matrix size) or readout bandwidth; however, the standard deviations (error bars) increases at smaller voxel volumes and larger bandwidths.

of the available correction approaches are ideal and elimination of these effects at acquisition should be the goal of further sequence development [57; 87]. The small standard deviations of the background phase offset results in Figures 7.8 and 7.9 indicate that the background phase is relatively stable, except at very large image plane offsets or if the SNR is too low where the standard deviations begin to increase. As a result, to validate the worthiness of the PC-UTE sequence in our phantom and in-vivo experiments, the current implementation restricts the image plane to isocentre and removes the remaining background phase effects with a post-processing phase correction algorithm, outlined in Section 6.4. A suitable SNR must be maintained to ensure that a good fit is obtained.
7.3 Phantom validation experiments

7.3.1 Method

All phantom experiments were performed on a Siemens 1.5T Avanto scanner and conducted as previously described in Section 3.2.3. Three PC sequences were investigated: (i) a clinical retrospectively gated 15 heart beat breath-hold standard PC sequence with flow compensation on the read and slice directions, TE 2.85ms, (ii) the modified version of the same PC sequence, TE 2.05ms, and (iii) a prospectively gated 15 heart beat breath hold implementation of the PC-UTE sequence (maximum possible number of frames varied from 15-19). The axial image plane, positioned at isocentre, was located 35mm downstream of the orifice. Typical image parameters may be found in Table 7.1.

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<th>Modified</th>
<th>PC-UTE</th>
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<td>2.05</td>
<td>1.17 - 0.44^n</td>
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<tr>
<td>TR (ms)</td>
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<td>12.35</td>
<td>65.8 - 50.2^n</td>
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<td>10</td>
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<td>RF pulse duration (µs)</td>
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</tr>
<tr>
<td>BW_{read} (Hz)</td>
<td>391</td>
<td>490</td>
<td>400</td>
</tr>
<tr>
<td>Δx (mm)</td>
<td>1.17</td>
<td>1.56</td>
<td>1.56</td>
</tr>
<tr>
<td>FOV_{phase} (%)</td>
<td>68.8</td>
<td>68.8</td>
<td>100</td>
</tr>
<tr>
<td>FOV_{phase} (mm)</td>
<td>206.25</td>
<td>206.25</td>
<td>300</td>
</tr>
<tr>
<td>Phase/angular under samp. (%)</td>
<td>50</td>
<td>70</td>
<td>78</td>
</tr>
<tr>
<td>Δy (mm)</td>
<td>2.34</td>
<td>2.22</td>
<td>1.56b</td>
</tr>
</tbody>
</table>

^a The maximum slice select gradient varied as a function of the Venc. This directly affects the minimum slice thickness and RF pulse duration. The TE/TR were subsequently minimised.

^b Angular under sampling reduces the number of radial spokes acquired. This increases the streak artefacts, but does not sacrifice spatial resolution.

Table 7.1: Image parameters for UTE validation experiments.

7.3.2 Results

A comparison between each PC sequence and the flow meter is presented in Figure 7.11. As previously demonstrated (Section 3.3.2), the standard PC se-
7.3. PHANTOM VALIDATION EXPERIMENTS

The modified PC sequence underestimated flow at higher flow rates. The error exceeded 5% at \( \approx 400 \text{mL/s} \) \((V_{\text{mean}} = 358 \text{cm/s})\). The modified PC sequence maintained accuracy up to \( \approx 600 \text{mL/s} \) \((V_{\text{mean}} = 535.4 \text{cm/s})\) before the error exceeded 5%. The PC-UTE initially underestimated flow by 25 mL/s (Error=27.4%) at 100 mL/s \((V_{\text{mean}} = 88 \text{cm/s})\) and 18 mL/s (Error=9.0%) at 200 mL/s \((V_{\text{mean}} = 175.4 \text{cm/s})\), At higher flow-rates the PC-UTE error was consistently less than 5%.

The standard deviation across frames of the standard PC sequences increased at higher flow-rates (Figures 7.11(b,c)), with the PC-UTE standard deviation remaining relatively stable (Figure 7.11(d)) at approximately a quarter of the standard PC sequence.

Figure 7.11: At high velocities the PC-UTE method is more accurate than the Cartesian method (a) and exhibits less variability (b-d) across repeated frames, however, at low flow rates it underestimated flow rate against the gold standard flow meter.

The standard deviation across frames of the standard PC sequences increased at higher flow-rates (Figures 7.11(b,c)), with the PC-UTE standard deviation remaining relatively stable (Figure 7.11(d)) at approximately a quarter of the standard PC sequence.
CHAPTER 7. PHASE CONTRAST ULTRA SHORT TE

The magnitude images provide an additional measure of reliability, Section 3.4. Low signal indicates intravoxel dephasing. The standard PC sequences exhibit severe signal loss at the higher flow-rates as shown by the dark areas in the centre of the magnitude images (Figure 7.12). In the corresponding phase images black pixels appear on the circumference and in the centre of the jet due to random phase associated with low signal from intra-voxel dephasing (as opposed to aliasing, Section 3.4). The PC-UTE phase and magnitude images show better signal and absence of random phase at all flow rates. PC-UTE maintained acceptable signal at all flow rates.

![Figure 7.12](image)

Figure 7.12: The magnitude images for the TE 2.85 and 2.05ms show significant signal loss and results in salt and pepper noise appearing at 700mL/s. In comparison the PC-UTE sequence maintained better signal loss and the phase difference image was free of salt and pepper noise within in the phantom.
7.4 In-vivo case studies

7.4.1 Method

In-vivo investigations were carried out on a Siemens 3T Trio scanner. Informed consent was obtained for all subjects and the project was approved by the local institutional ethics committee. A normal volunteer (male, 28y), and one patient (male, 55y) with known moderate to severe stenosis, were investigated using the standard PC sequence and the PC-UTE sequence as described above. The patient had no significant regurgitation (< 10mL) as determined by echocardiography.

Initial evaluation of the PC-UTE sequence was performed in the normal volunteer by imaging the descending aorta at a level likely to be free of haemodynamic flow features that could cause intravoxel dephasing. The standard PC sequence (TE 2.85ms) used a Venc of 150cm/s and the UTE-PC sequence 200cm/s. The FOV was set at 320mm for the standard PC sequence and 300mm for the PC-UTE sequence.

To compare the standard PC and the PC-UTE sequences in high velocity turbulent stenotic jets, three image planes above the valve were acquired in the patient. The first image plane was positioned perpendicular to the aorta on the tips of the AV leaflets at end systole; the second at the sino-tubular junction (STJ), and the third in the ascending aorta (ascAo). The PC-UTE was acquired with a reduced FOV (200mm compared to 320mm) to take advantage of the UTE’s freedom from spatial aliasing (voxel dimensions 1.04x1.04x8.75 = 9.5mm³ compared to 1.25x2.08x6 = 15.6mm³). The Venc was set to 500cm/s for both PC sequences and all image planes.

Prior to acquisition the bed was automatically moved to position the image plane at the isocentre of the magnet.

The same analysis procedure outlined in Section 5.2.2, Chapter 5 was applied. Background phase correction, with a linear planar surface, was performed only on the PC-UTE sequence. Stationary tissue was identified using a temporal standard deviation mask with a threshold of 25% [81].
7.4.2 Results

Velocity versus time graphs are shown for the normal volunteer and patient in Figure 7.13. In the normal volunteer the PC-UTE sequence shows good agreement with the standard PC sequence in the descending aorta (Figure 7.13a). In the aortic stenosis patient, good agreement between the mean velocity profiles was seen at the STJ, the UTE’s mean velocity was less and more during systole at the AV and ascAo respectively but remained centred on zero during diastole.

![Figure 7.13: Good agreement in the mean velocity was obtained in the normal volunteer. In an aortic stenosis patient the PC-UTE maintained good agreement in the aortic valve (b) and the sino-tubular junction (c) and maintained a larger mean velocity during systole in the ascending aorta (d).](image-url)
7.4. IN-VIVO CASE STUDIES

The SV of the standard PC sequence decreased as the slice moved distal from the aortic valve. The standard PC sequence SV estimates ranged by 58.5 mL. The PC-UTE sequence’s SV was less at the AV but remained similar in the STJ and ascAo. The UTE’s SV only ranged over 20.4 mL.

<table>
<thead>
<tr>
<th>Position</th>
<th>AV</th>
<th>STJ</th>
<th>AscAo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke volume (mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>114.5</td>
<td>92.5</td>
<td>56.0</td>
</tr>
<tr>
<td>UTE</td>
<td>62.4</td>
<td>82.8</td>
<td>80.2</td>
</tr>
<tr>
<td>Peak velocity (m/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Standard</td>
<td>292.0</td>
<td>334.2</td>
<td>141.8</td>
</tr>
<tr>
<td>UTE</td>
<td>247.4</td>
<td>295.4</td>
<td>174.3</td>
</tr>
</tbody>
</table>

Table 7.2: Stroke volumes and peak velocities of the AS patient.

Investigation of the systolic magnitude images (Figure 7.14) revealed that signal loss occurred in the standard PC sequence. At the aortic valve the signal loss surrounded the enhanced signal of the jet; at the sino-tubular junction it corresponded to the jet region; and in the ascending aorta, it occurred in the centre of the vessel. In comparison the PC-UTE exhibited a more uniform signal to noise ratio across the whole vessel at each of the three imaging levels.
CHAPTER 7. PHASE CONTRAST ULTRA SHORT TE

Figure 7.14: The standard PC sequence shows areas of signal loss at all three valve levels, however the PC-UTE sequence maintains a better signal intensity at all levels.
7.5 Discussion and Conclusions

In this chapter we have designed a PC implementation of an UTE sequence that combines velocity encoding and slice selection to reduce TE to 25% of an equivalent standard PC sequence. The shorter TE minimizes the effects of intravoxel dephasing and improves the reliability and accuracy of the time over which the velocity estimate is measured reducing signal loss (figures 7.12 and 7.14) and improves the reliability and accuracy of the PC measurement as shown by the good agreement between the PC-UTE sequence and the flow meter at high flow rates (Figure 7.11). These imply that the PC-UTE sequence will be more robust to intravoxel dephasing effects in patients.

7.5.1 Characteristics of the PC-UTE method

In the design of the PC-UTE sequence we have imposed the limitation of playing out the RF pulse during the plateau of the gradient in order to provide good quality slice profiles, but this has the effect of slightly increasing the minimum TE. Given this design restriction we believe that the approach we have used yields the shortest possible TE for any given gradient slew-rate. This novel approach to acquisition has been shown to yield substantial decreases in TE, consequently the PC-UTE sequence developed here has some features that differ from standard PC sequences.

Simultaneous excitation and encoding effect on slice thickness

The combination of the slice-selection and velocity encoding gradients allows the TE to be reduced from $2.85\text{ms}$ to $0.65\text{ms}$ at a $V_{\text{enc}}$ of $500\text{cm/s}$, but restricts the sequence to through-plane velocity encoding.

Furthermore, the optimisation approach utilised causes the minimum slice thickness to depend on the slice selection gradient strength and hence the desired $V_{\text{enc}}$. The resultant larger slice thickness ($8.75\text{mm}$ at a $V_{\text{enc}}$ of $500\text{cm/s}$ compared to the common clinically applied $6-8\text{mm}$), is compensated to some extent by the shorter RF pulse. For a jet velocity of $300\text{cm/s}$, ($V_{\text{enc}}=500\text{cm/s}$, Table 7.3) and a standard PC sequence with an RF pulse of $1000\mu\text{s}$ the spins travel $3.00\text{mm}$
during the pulse compared to 1.26mm for the 420µs pulse in the PC-UTE sequence.

Inversion of slice selection gradients

Inversion of the slice selection gradients to acquire two images for calculation of the phase difference image rather than a standard flow encoded and flow compensated acquisition results in increased sensitivity to scanner imperfections. \( B_0 \) inhomogeneities (\( \Delta B_0 \)) manifest themselves as an offset which moves the slice profiles in opposite directions. If there is both a \( B_0 \) and a through slice gradient (due to poor shimming) then the slice offset can combine with the gradient to create a phase difference or velocity error. Markl et al [83] reported that for the two acquisitions, slice position errors (\( \Delta z \)) increase with the weaker slice select gradients (\( G_s \)) used for higher \( V_{enc} \) \( (\Delta z = 2\Delta B_0/G_s) \). These errors give rise to misaligned slice profiles and incorrect cancellation of the inherent background phase using the phase difference reconstruction.

The \( B_0 \) inhomogeneities are larger distal from the isocentre and hence a larger mismatch between the slice profiles’ alignment is the most probable explanation for the worse background phase offsets at off-centre shifts, Figure 7.9. The inverted slice selection gradients in off-centre slices require the frequency to be offset with opposite polarity for slice selection. In the future, it is necessary to account for this in the PC-UTE sequence, however, this may be problematic with some hardware implementations.

K-space read-out trajectory

The immediate sampling of the centre of K-space reduces signal loss due to intravoxel dephasing and is an important advantage of the PC-UTE sequence. The dense sampling of central K-space causes the low spatial frequencies to have a better signal to noise ratio than the higher spatial frequencies. The subsequent re-gridding effectively averages the image and makes the technique more robust to artefacts from patient motion and pulsatile flow at the expense of increased blurring at tissue borders. Additionally, the cross-term concomitant phase errors (overlapping of XY and Z gradients) are eliminated because no flow-compensation gradients are required for centric K-space trajectories. Self-
7.5. DISCUSSION AND CONCLUSIONS

Squared concomitant phase errors are also eliminated with the use of the inverted velocity dependent slice select gradients [58].

The centric radial readout trajectory has the disadvantage of being inefficient in its coverage of the edges of K-space. To obtain full coverage of a $n \times n$ voxel image, we require $\pi n$ centric-radial lines while a standard PC image only requires $n$ lines. This disadvantage is partially overcome by the shorter TR, and the opportunity to undersample K-space radially, but generally has the effect of reducing the temporal resolution of the PC measurements.

For example, a standard PC sequence with a $V_{enc}$ of 500 cm/s has a TE/TR of 2.85/13.27 ms, and the PC-UTE 0.65/5.8 ms. To achieve a 15 heart beat breath-hold, with 60% phase undersampling, the standard PC sequence must acquire 4 lines per heart beat with a temporal resolution of 53.1 ms. To achieve the same breath-hold a 78% angular undersampling PC-UTE technique must acquire 10 centric-radial spokes per heart beat with a temporal resolution of 58 ms. The latter has the advantage that k-space is completely sampled and image reconstruction does not rely on a-priori assumptions and post-processing required with the standard PC asymmetric echo readout.

Improving the temporal resolution

With a retrospective implementation, the shorter TR means that K-space data is obtained over many small windows using numerous radial spokes thereby offering more time instances for interpolation of reconstructed K-space matrices. The greater number of views per segment used also allows a larger number of intermediate images to be re-created using the view sharing approach discussed in Figure 2.5.2. Both of this approaches improve the temporal resolution.

Furthermore, variants of the UTE centric-radial readout such as twisting radial line, TwiRL [84], or segmented spiral acquisition approaches [53] may be able to improve the sampling efficiency of K-space whilst yielding the benefits of centric sampling. These approaches sample the periphery of K-space better, reducing the amount of views (radial spokes) that need to be acquired each segment. This would directly improve the true temporal resolution or temporal footprint of the PC-UTE sequence, Section 2.5.1.
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7.5.2 Improvements for intravoxel dephasing

The PC-UTE sequence has a number of features that improves its robustness to intravoxel dephasing effects including: a) higher order motion effects and turbulence are effectively mitigated by reducing the duration of the velocity sensitive gradients; b) the effect of misalignment of the jet on spin mixing is less important because of the overall reduction in TE and readout gradient durations; and c) voxel size and partial volume effects can be moderated by freely being able to specify the FOV with no spatial aliasing.

Higher order motion encoding and turbulence

The principal advantage of the inverse velocity dependent slice select gradients is that it reduces the number and duration of the gradient lobes played out within the TE. The result is less inherent higher-order motion encoding (Table 7.3) and less time for turbulent velocity fluctuations to degrade the voxel's signal [72]. These reduce the intravoxel-dephasing within a voxel, reduce signal loss (Figures 7.12 and 7.14) and improve the velocity estimate as shown in Figures 7.11 and 7.13.

<table>
<thead>
<tr>
<th>Venc (cm/s)</th>
<th>Min. ΔZ (mm)</th>
<th>Min.TE (ms)</th>
<th>RF (µs)</th>
<th>Acc. encoding (mT/m.ms³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
<td>6</td>
<td>2.85</td>
<td>1000</td>
<td>10.3</td>
</tr>
<tr>
<td>400</td>
<td>5.4</td>
<td>0.82</td>
<td>540</td>
<td>9.1</td>
</tr>
<tr>
<td>500</td>
<td>7.5</td>
<td>0.71</td>
<td>500</td>
<td>7.8</td>
</tr>
<tr>
<td>600</td>
<td>8.8</td>
<td>0.65</td>
<td>420</td>
<td>6.7</td>
</tr>
<tr>
<td>750</td>
<td>10.0</td>
<td>0.59</td>
<td>380</td>
<td>5.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.36</td>
<td>300</td>
<td>3.6</td>
</tr>
</tbody>
</table>

Table 7.3: Sequence comparison of the minimum slice thickness, minimum TE, RF pulse duration and acceleration encoding. Note gradient performance is restricted to the standard PC sequences limits, $G_{max} = 10 mT/m$ and $SR_{max} = 90 mT/m/ms$.

Spin mixing

Kilner et al [76; 42] emphasises aligning the image plane perpendicular to the jet. However, a jet consists of converging flow upstream of the vena contracta and diverging flow downstream, Section 4.3.5. Voxel and jet alignment is therefore an ambiguous concept. When an image is acquired, spins from different
locations with different velocities may be present in the voxel due to the time between velocity encoding and readout [42] and during the readout gradients [43]. This mixing of spins act to increase intravoxel dephasing effects and is potentially worse if the image plane is misaligned with the predominately forward flow velocities of the jet. The decreased TE and shorter half echo centric-radial readout trajectories of the PC-UTE technique act to minimise the time between and during encoding and readout, thereby reducing detrimental spin mixing, Section 4.4.2.

Partial voluming

There is evidence that the sensitivity to intravoxel dephasing may not be equal for the through-plane and in-plane dimensions [88]. In our experiment, the voxel volume was conserved between PC sequences, but the PC-UTE had a better in-plane resolution. This may have reduced its susceptibility to the larger velocity variations seen across the jet. In Section 4.3.3 overall voxel volume which maintains an adequate number of spins to give a good SNR was deemed to be more critical for accurate flow estimation. The ability to reduce the FOV without spatial aliasing is an additional advantage of the PC-UTE sequence as it can enhance the in-plane resolution and potentially reduce the spatial averaging of the voxel across the jet, thereby yielding better peak velocities, Section 6.7.3.

7.5.3 Summary and Future work

A through-plane PC-UTE sequence, incorporating the velocity encoding into the slice selection gradients, has been designed and implemented. The TE is approximately 25% of the equivalent standard PC sequence. This effectively eliminates the effects of higher-order motion and intravoxel dephasing, which improves the reliability and accuracy of the velocity estimate. The PC-UTE sensitivity has been validated quantitatively on the high velocity stenotic phantom ($V_{\text{mean}}$ up to $\approx 10 m/s$), and clinical feasibility has been demonstrated in a normal volunteer and a patient with a stenotic valve.

The current PC-UTE sequence implemented is susceptible to background phase errors, particularly due to the mis-alignment of slice profiles from $B_0$ inhomogeneities slice shifts. Further improvements would be gained by making the
PC-UTE sequence retrospectively gated. Promising techniques that adjust the PC-UTE sequence's RF pulse, the subsequent slice selective gradients and the K-space trajectory of readout gradients in post-processing have recently been proposed by Lu et al.[57].

In summary, PC-UTE sequences or their variants have the potential to provide faster high resolution PC images that are more robust to intravoxel dephasing present in high velocity turbulent jets. A clinical study should be performed to validate this method. The merits of using the proposed PC-UTE sequence needs to be further validated against Doppler ultrasound and standard PC sequences in a larger cohort of normal volunteers and patients.
8

Conclusion

8.1 Thesis summary

In some cases, the routine clinical assessment of aortic stenosis with continuous wave Doppler (Doppler) ultrasound requires clarification. Currently, the only alternatives to estimate aortic valve area (AVA) are invasive. This thesis was interested in investigating phase contrast (PC) cardiac magnetic resonance (CMR) methods as a possible alternative. But, in the ZEST trial (Section 1.6.2), it was found that the PC estimate of stroke volume (PCSV) underestimated the left ventricular stroke volume (LVSV).

The thesis consisted of a thorough examination into the errors associated with measuring flow and velocity in aortic stenosis jets and investigated different methods to improve the in-vivo measurements. This chapter summarises our principal findings and outlines areas of future research.

8.2 Principal findings

A phantom was designed and constructed to replicate the underestimation seen in the ZEST trial, Chapter 3. Subsequent phantom experiments identified that the echo time (TE), an image parameter, was too long. The errors were caused from signal loss due to intravoxel dephasing in the forward flow jet voxels. Extreme signal loss eventuated in salt and pepper noise, which, with a mean velocity of zero, resulted in the underestimation. Shortening the TE from 4.8ms to 2.0ms (by utilising the larger gradients available with current hardware) reduced the signal loss and resulted in a more reliable and accurate phase contrast measure-
Sequences with shorter TEs along with a magnitude threshold to remove erroneous voxels are required to adequately estimate flow, peak velocities and VTIs in-vivo.

More extensive experimentation, Chapter 4, into other image parameters revealed that reducing the overall TE and the duration of the velocity sensitive gradients consistently exhibited the most improvement. Further optimisation of the PC sequence would benefit from reducing the duration of the bi-polar gradients to minimise the higher order motion encoding and signal loss due to turbulence, whilst reducing the overall TE would prevent the mixing of fast and slow moving spins.

The results of the clinical trial in Chapter 6, showed that maximising the gradients to shorten TE did not satisfactorily improve the PCSV with the modified and optimised PC sequences. The larger gradients, required to reduce the TE, increased the PC sequences susceptibility to background phase. But, correction with the surface fit proposed in the literature only showed significant statistical evidence for improvement in the TE 1.5ms variant. The PCSV still underestimated the LVSV beyond the aortic valve and showed larger variability at the aortic valve compared to the main pulmonary artery (MPA) and left ventricular outflow tract (LVOT).

Despite erroneous flow data, the inclusion of a magnitude threshold in Chapter 6 meant it was possible to obtain peak velocities, VTIs and/or AVAs which correlated moderately well with Doppler results. The PC method seemed to systematically underestimate Doppler velocity and VTI data by \(\approx 10\%\). Apart from intravoxel dephasing, CMR's inherent spatial averaging across the image and temporal averaging over and through the heart beat contributes to the underestimation.

Furthermore, taking the data from the level with the maximum VTI was similar to performing repeat measurements and may have reduced physiological variation between measurements. It is recommended that future studies incorporate repeat measurements to better investigate the affects of physiological variability.

Errors remain dominated by intravoxel dephasing effects. PCSV, which is more sensitive, is better suited than peak velocity to verify the reliability of the PC data. Before reliable estimation of AVA in more severe aortic stenosis can be obtained using methods dependent on PCSV, improved techniques to measure
8.2. PRINCIPAL FINDINGS

this flow are required.

Chapter 7 proposed and validated an alternative PC sequence based on the ultra short TE (UTE) centric radial readout trajectory and velocity dependent slice selection gradients. The velocity dependent slice selection gradients minimised the duration of the velocity sensitive gradients and in combination with a centric readout scheme minimised the overall TE as suggested in Chapter 4. The new PC-UTE showed excellent linearity with the flow meter in the stenotic phantom at flow rates in excess of $1000\text{mL/s}$ and good signal loss characteristics in an in-vivo case study. The PC-UTE sequence requires further validation but it (or a future variant) is an encouraging potential alternative for more reliable estimates of velocity and flow with CMR.

8.2.1 Conclusions

The thesis main contributions can be summarised as follows:

1. Errors due to intravoxel dephasing are still present in the measurement of moderate-severe aortic stenosis jets with PC.

2. Current TE's available with conventional PC sequences are too long to reliably measure flow and velocity accurately.

3. It is recommended that both magnitude images (reference and encoded) be made available to the user, so that the reliability of the PC data can be better assessed and an appropriate magnitude threshold applied.

4. Comparisons of SV estimates are critical to verify the reliability of the PC data.

5. Reducing the duration of the velocity sensitive gradients as well as the overall TE best mitigate intravoxel dephasing effects.

6. New methods such as the PC-UTE (or a future variant) that use the minimisation of TE and velocity sensitive gradients as the driving design criteria are required for obtaining a robust technique to reliably and accurately measures peak velocities in AS jets.
8.3 Future research

8.3.1 Changes to the Phantom

To date the current phantom has been deemed an adequate representation of the problem. Spatial accelerations have been used to interrogate the affects of higher order motion. Turbulence and the affects of jet structure are permanently present and the influences of most image parameters could be satisfactorily investigated. Unfortunately, the in-vivo investigation showed that simply reducing TE did not remove all intravoxel dephasing errors and highlighted the difficulty in comparing between ultrasound and MRI in an uncontrolled environment.

A number of changes need to be made to the phantom to further interrogate the differences.

- Incomplete magnetisation of spins: The logarithmic decay seen in the non-stenotic phantom was due to inadequate time for the spins to align with the magnetic field. This meant that signal loss in the stenotic phantom was in part due to incomplete magnetisation as well as from intravoxel dephasing. To ensure complete magnetisation either the water should be doped to reduce $T_1$, the phantom needs to be repeatedly passed through the scanner and/or a reservoir needs to be included upstream to allow adequate time for the spins to align prior to the imaging plane.

- Doppler compatibility: Comparisons between Doppler and MR were restricted to in-vivo measurements. Phantom experiments would be useful for a better understanding of the differences between the two modalities. A curve, elbow, or T-junction downstream of the orifice plate needs to be added to make the jet visible to a Doppler beam, similar to what was recently proposed by Baltes et al [89].

- Sizes and shape of the orifice: Teirstein et al [90] found that irregular shaped orifices did not interfere with the ability of Doppler ultrasound to accurately estimate pressure gradients. To our knowledge a similar experiment has not been reported in MR. The size shape and resultant jet has been hypothesised to increase the intravoxel dephasing therefore limiting the applicability of MR in the diagnosis of aortic stenosis jets [75] Figure 4.15. Creating new orifice plates that better match physiological
shapes (slits, the “Y” shaped Mercedes symbol) and the use of artificial valves warrant further investigation.

- Pulsatility: Temporal variability is required to investigate the temporal averaging affect of a PC sequence versus the comparatively instantaneous Doppler measurement. Temporal accelerations, the breakdown of the jet’s structure during diastole and imaging parameters that effect the TR, such as the number of lines per K-space (segments) could thus be investigated, Section 4.4.1. Furthermore, the ability to dynamically vary the pulses would allow a more physiological consistent experiment.

These modifications would create a versatile phantom that better represents the in-vivo problem. The phantom would be in a better position to evaluate MRI’s ability with conventional and new PC sequences including the proposed PC-UTE, spiral and Fourier-velocity sequences\(^1\) [91; 92; 89] to quantify flow and velocity. Moreover, with a gold standard measure of velocity it may be possible to investigate the usefulness of unwrapping algorithms and other modelling techniques to enhance MR’s measurement capability.

### 8.3.2 Background phase

The larger gradients used to minimise TE exacerbated PC’s second source of measurement error, residual background phase. Though limitations in the selection of stationary tissue and the surface order used in the surface fit correction proposed in the literature were shown, the lack of a gold standard and the contribution from other sources of error, measurement and physiological, prevented a more in-depth evaluation in-vivo. The best approach for background phase correction has yet to be determined. The imaging of a phantom [79] after each case is time consuming at a busy clinical scanner and surface fits [81] may be susceptible to stationary tissue identification and the order of the fit. It is possible due to the scanner [75], PC sequence and orientation used that each acquisition may benefit from a different surface order fit. Further validation of the methods proposed in Section 6.2 are required.

One approach would be to repeat the in-vivo measurements on a stationary phantom as already suggested by Chernobelsky et al [79] and Lankhaar et al [81].

\(^1\)Fourier velocity sequences measure the velocity spectra by stepping through various velocity encoding gradients, analogous to the phase encoding gradients.
CHAPTER 8. CONCLUSION

This approach assumes that phase shifts due to the different magnetic susceptibilities of tissues are small and the dependency of the induced eddy currents in conducting materials (such as the receiver coil\textsuperscript{2}) on position is negligible.

Another possibility would be to create a phantom that represents the rib cage (the tissue predominately picked up by the stationary tissue identification methods) to surround the phantom. The non-stenotic phantom could be positioned at either a fixed elevation, at a known angle to the centre-line or combination of the two and the orientation of the image plane adjusted accordingly. The flow meter thus provides the gold standard flow rate to optimise the correction algorithms.

Alternatively, as suggested in Section 7.5.3, techniques \cite{57} that either prospectively adjust the PC sequence’s RF pulses or retrospectively corrects the K-space trajectories by measuring the actual gradient played out may prevent and reduce the residual background phase to acceptable levels.

8.3.3 PC-UTE

The PC-UTE phantom results are promising. A larger cohort of patients is required to validate its usefulness \textit{in-vivo}.

Numerous techniques are available to improve the efficiency of covering K-space. TwiRL or segmented spiral acquisitions have the potential to reduce the number of radial-K-space spokes required per heart beat reducing the temporal footprint of the PC-UTE sequence. The residual background phase would benefit from making the PC-UTE sequence retrospective\textsuperscript{3}. Furthermore, the RF pulse and K-space trajectory adjustments should make it less susceptible to misaligned slice profiles and other eddy current related background phase errors.

Currently only one of the possible concepts was implemented and investigated. Though this implementation yielded the shortest possible TE the other variants would help understand where the error is most critical, excitation encoding verses readout. One may even prove adequate with less susceptibilities to background phase. In particular, the use of a velocity dependent slice excitation with a

\textsuperscript{2}The receivers surface coil orientation and position on the patient/phantom could affect the residual background phase.

\textsuperscript{3}A retrospective PC-UTE sequence has now been implemented and will be used in a clinical trial of 20 patients at Auckland that aims to validate the potential of PC-UTE sequences to better diagnose aortic stenosis jets.
reference/encoding scheme may reduce the susceptibility to \( B_0 \) inhomogeneities by removing the gradient inversion. It would also decrease the minimum slice thickness required for a given maximal encoding velocity (V\text{enc}). The TE could be better minimised by relaxing the maximum gradient restriction on the second and thirds lobe of the reference encoding gradient, Figure 7.1.

8.3.4 Modelling in phase contrast MR

MR is inherently averaging. The image is built up and averaged over many heartbeats. In breath-hold imaging, the acquisition of multiple K-space lines per heart beat means that MR also averages within a heart beat. Lastly, the voxel is a spatial average. The averaging of a signal strengthens the mean values but dampens extremes such as the peak velocity. In comparison Doppler instantaneously measures velocity of individual red blood cells. Measurement noise is manually segmented out and generally only a few heartbeats are analysed and averaged.

Modelling may be useful to compensate for MR's inherent averaging. For example, Box et al [93] fits a 3-D paraboloid to estimate the actual velocity profile in the internal carotid artery. The velocity profile is used to calculate the peak velocity and the systolic wall shear stress. A similar model-based post processing algorithm could be used to calculate the peak velocity in aortic stenosis jets. A fitted profile can reduce the spatial averaging within an image. Going one step further and coupling the measurement data to a computational fluid dynamics model could enhance the temporal data. Computational fluid mechanics may even be able to provide PC with new diagnostic and perhaps prognostic capabilities.
Whenever anyone says, 'theoretically,' they really mean, 'not really.'

Dave Parnas

The fluid mechanics of a Jet

Valve dysfunctions result in a turbulent jet. In aortic regurgitation a jet is formed between the high pressure of the aorta into the low pressure left ventricle (LV) during diastole. The LV can be considered a large cavity therefore an aortic regurgitation jet can be modelled as a free jet [16]. In aortic stenosis the LV has higher pressure than that of the aorta and the jet occurs between the LV’s large cavity into the relatively small cavity of the aorta. The aortic stenosis jet is modelled by a confined jet [16].

This appendix outlines the primary concepts of fluid mechanics relating to jets and turbulence.

A.1 Principle equations of fluid motion

A.1.1 Conservation of mass

For an incompressible fluid the fluid density, $\rho$, remains constant. The conservation of mass, the basis of the continuity equation [17; 15; 66; 18; 94], states that the mass entering a fluid volume must equal the mass leaving the fluid volume

$$\frac{\partial U_\beta(x, t)}{\partial x_\beta} = 0 \quad \text{(A.1)}$$

where $U_\beta(x, t)^1$ is the instantaneous velocity, at a given time, $t$ and position $x$.

---

$^1$\(\alpha, \beta\) take the values of 1, 2, and $3$ and indicate the use of the summation convention where repeated indices are summed.
A.1.2 Conservation of momentum

In the LV and the aorta the diameter of the vessel is much greater than the average diameter of a red blood cell. Blood in the large vessels can be modelled using a Newtonian fluid. The Conservation of momentum for a Newtonian fluid is given by the equation [17; 15; 66; 18; 94]:

$$\frac{\partial U_\alpha}{\partial t} + U_\beta \frac{\partial U_\beta}{\partial x_\beta} = -\frac{1}{\rho} \frac{\partial P}{\partial x_\alpha} + \nu \left( \frac{\partial U_\alpha}{\partial x_\beta} + \frac{\partial U_\beta}{\partial x_\alpha} \right)$$ (A.2)

where \( P \) is the instantaneous pressure and \( \nu \) the kinematic viscosity.

A.1.3 Naiver-Stokes Equation

Combining equation A.1 with equation A.2 gives the fundamental equation of motion in fluid mechanics, the Naiver-Stokes equation2 [17; 15; 66; 18; 94]

$$\frac{\partial U_\alpha}{\partial t} + \frac{\partial U_\alpha^2 U_\beta}{\partial x_\beta} = -\frac{1}{\rho} \frac{\partial P}{\partial x_\alpha} + \nu \nabla^2 U_\alpha$$ (A.3)

A.1.4 Reynolds equation

From Section 1.4.2 we stated that instantaneous velocity can be thought of as a time averaged velocity \( \bar{U} \) and a random fluctuation \( u \) and showed that the instantaneous velocity’s root mean square (\( u_{rms} \)) can be used to denote a measure of turbulence. Similarly, a corresponding formation can be made for pressure. Substituting in these values into equation A.3 and time averaging we find:

$$\frac{\partial \bar{U}_\alpha}{\partial t} + \frac{\partial \bar{U}_\alpha^2 \bar{U}_\beta}{\partial x_\beta} + \frac{\partial (u_\alpha u_\beta)}{\partial x_\alpha} = -\frac{1}{\rho} \frac{\partial \bar{P}}{\partial x_\alpha} + \nu \nabla^2 \bar{U}_\alpha$$ (A.4)

This is simply the Naiver-Stokes equation written in the form of time averaged velocity and pressure with the inclusion of the term involving \( u_\alpha u_\beta \). This term is referred to as the Reynolds stress and represents the transport of momentum due to the random fluctuations [18]. It was noted by Reynolds that the random velocity fluctuations reflects the viscous stresses due to random motion. An important hypothesis for turbulence is that \( u_\alpha u_\beta \) can be expressed as linear

\[2\nabla^2 = \partial^2 / \partial x_\alpha \partial x_\beta.\]
A.1. PRINCIPLE EQUATIONS OF FLUID MOTION

relationship of the mean rate of strain and an effective co-efficient of viscosity. The Reynolds equation reduces to three independent variables, $\bar{U}_\alpha$, $\bar{P}$ and $u_\alpha u_\beta$.

An equation for motion for the uctuating velocity can be found from subtracting the Reynolds equation A.4 from the Naiver-Stokes equation A.3:

$$\frac{\partial u_\alpha}{\partial t} + \frac{\partial \bar{U}_\alpha}{\partial x_\beta} u_\beta + \frac{\partial \bar{U}_\beta}{\partial x_\alpha} u_\alpha - (u_\alpha u_\beta - \bar{u}_\alpha \bar{u}_\beta) = -\frac{1}{\rho} \frac{\partial p}{\partial x_\alpha} + \nu \nabla^2 u_\alpha$$  \hspace{1cm} (A.5)

A.1.5 Energy balance equation for fluctuations

Energy balance is a simple method for considering the physics of turbulence [18]. The total kinetic energy, $E_T$, of a fluid volume, $V$, bounded by a surface, $S$ can be expressed in terms of the instantaneous velocity, $U_\alpha(x,t)$ as

$$2E_T = \sum \int_V \rho U_\alpha^2 dV$$  \hspace{1cm} (A.6)

From the Naiver-Stokes equation A.3 we can derive an expression for $E_T$:

$$\frac{dE_T}{dt} = \int_V \rho U_\alpha f_\alpha dV + \int_V \rho \epsilon dV$$  \hspace{1cm} (A.7)

where $f_\alpha(x,t)$ is an externally applied force per unit mass and $\epsilon$ is the energy dissipation per unit time and per unit mass ($\epsilon = \nu \sum \alpha \sum \beta \left\{ \frac{\partial U_\alpha}{\partial x_\beta} + \frac{\partial U_\beta}{\partial x_\alpha} \right\}^2$).

Equation A.7 states that the rate of change of energy is equal to the rate at which forces do work on the fluid less the rate at which viscous effects convert kinetic energy into heat.

The derivation of a formula for the total rate of change of turbulent energy can be found from the Reynolds stress tensor [18] and is summarised as

$$\frac{\partial \bar{u}_\alpha}{\partial t} + \bar{U}_\beta \frac{\partial \bar{u}_\alpha^2}{\partial x_\beta} = -\frac{\partial}{\partial x_\beta} \left\{ \frac{u_\alpha^2 u_\beta}{\rho} + \frac{2}{\rho} u_\beta p \right\} - 2u_\alpha u_\beta \frac{\partial \bar{U}_\alpha}{\partial x_\beta} + \frac{\partial^2}{\partial x_\beta^2} \bar{u}_\alpha^2 - 2\nu \frac{\partial \bar{u}_\alpha}{\partial x_\beta}^2$$  \hspace{1cm} (A.8)

The total rate of change of turbulent energy with time is given by the net effect of the terms on the right hand side [18]. Terms A and C do not contribute to the global energy balance. Their physical interpretation is the diffusion of turbulent energy through space by non-linear and viscous actions respectively.
APPENDIX A. THE FLUID MECHANICS OF A JET

Term B is known as the production term it is interpreted as the transfer of energy from the mean field to the fluctuating velocity, term D represents the irreversible dissipation of kinetic energy into heat.

A.2 The boundary Layer

Two fundamental characteristics of a real fluid are that

1. There is no velocity discontinuity
2. At a solid surface the velocity of the fluid relative to that surface is zero.

As a consequence there is a region close to the surface where the velocity rapidly approaches zero. This region is called the boundary layer. The boundary layer experiences greater shear stresses than the main flow. The boundary layer’s large velocity gradient increases the importance of viscosity effects.

Flow across a smooth plate is a simple method to investigate a boundary layer [17], Figure A.1. A boundary layer forms when the viscous action near the surface causes the flow to slow down. As more flow is slowed down the boundary layer thickens. The edge of the boundary layer can be defined as the streamline at which the velocity is equal to $0.99U_o$. Initially the boundary layer consists of laminar flow and is thickening at a rate proportional to $x^{0.5}$ when the pressure is uniform. As more fluid is slowed down the flow in the boundary layer enters a transition region and thickens rapidly, until it completes the transition

Figure A.1: Boundary layer across a smooth plate, the scale in $y$ is enlarged relative to $x$ (adapted from [17]).
to turbulent flow. The thickness of the boundary layer in the turbulent region thickens at a rate proportional to $x^{0.8}$ [17].

In the turbulent regime, because the velocity gradient becomes more uniform, there has to exist an additional sub-laminar region close to the wall to bring the velocity to zero. The point at which the boundary layer moves from laminar to turbulent depends on the roughness of the surface, the turbulence in the main flow but predominately depends on the relative Reynolds number of the boundary layer. In practice the laminar boundary layer is often so short that it is neglected.

### A.3 Jet structure’s variability

#### A.3.1 Jet Flapping

![Jet Flapping Diagram]

Figure A.2: Jet Flapping is where the principal direction of the forward velocities flap across the jet’s centre line.

In Figure 4.2, the point B represents the time averaged reattachment of the jet. In actuality the jet is moving about within the pipe. Figure A.3 shows the variation of the zero-crossing point equivalent to the reattachment point as a function of time. This process is known as flapping. Flapping occurs through the transverse distribution of pressure. High pressure builds up in areas containing the principal direction of jet velocities, low pressure in areas of recirculation. The jet acts to moves from high to low pressure and appears to flap about the jet’s centre line [68], Figure A.2 reflecting the variation seen in the reattachment point.

From Figure A.3 it can be seen that no periodicity can be seen, but this does not remove the suggestion that vortex shedding\(^3\) could be occurring [67].

---

\(^{3}\)Vortex shedding is, via changing pressure distribution, the transverse alternation of low pressure vortices that are created in recirculation zones and move downstream with the flow.
APPENDIX A. THE FLUID MECHANICS OF A JET

The variance of the reattachment point is largest in Laminar flow, peaking at approximately a Reynolds number of 700. In the transitional regime (Reynolds=1000) variation begins to increase and peaks at a Reynolds of 2000 marking the transition to turbulence. In turbulent flow the variation is constant at approximately 2.5 times the step height and follows a Gaussian distribution centred around 5 step heights [67].

![Graph showing variation in reattachment lengths with time](image)

Figure A.3: Variation in reattachment lengths is shown by the variable zero-crossing point as a function of time (obtained from [67]).

A.3.2 Jet Precession

Jet Precession occurs when the expansion ratio is significantly large that a fundamental jet oscillation is created. The oscillation causes the jet’s principal direction to rotate about an axis other that it’s own [95], the central axis of the expansion, Figure A.4. Superimposed on the fundamental frequency, higher frequency oscillations corresponding to jet flapping provides added complexity.
to the jet motion [68]. The amplitude of the jet flapping is largest close to the expansion. Downstream, jet flapping becomes smaller in scale and jet precession begins to dominate [95].

Jet precession can be understood by thinking of the jet as a solid object. When the jet flaps across the centre line it hits the wall at an oblique angle creating a tangential momentum component. The flapping jet appears to reflect off the wall [68]. The coupling of the two motions creates a sustained precession.

The occurrence of precession is dependant on jet flapping. The precessional frequency of the jet increases relative to the flapping frequency as the expansion ratio increases. Explained by assuming that when the jet flap is displaced the same amount from the centre line, a larger reflection angle will occur in a pipe of greater downstream diameter, leading to a greater precessional frequency.

### A.3.3 Strouhal Number

The Strouhal Number is important because it represent the real time scale of the jet precession and flapping, it is used to establish a similarity between different geometries and Reynolds numbers [68]. It is usually associated with the aeolian tones created by vortex shedding from wires vibrating in the wind [15]. In jet mechanics the Strouhal number can take the form

\[
St = \frac{2}{\sqrt{\pi}} E^2 \frac{fd}{U_i}
\]  

where \( E \) is the expansion ratio, \( d \) is the upstream diameter, \( U_i \) is the bulk velocity at the inlet and \( f \) is the the flapping or precessing frequency [68]. A larger expansion ratio increases the frequency of the flapping or precession. It was found that in an expansion ratio of 3.5 – 6.0 both regular precession and flapping
occurred. The precession Strouhal number increased linearly with expansion ratio whilst the flapping Strouhal number was constant. As the expansion ratio increases the precession begins to dominate.

In the experiments the expansion ratio is always greater than 3.7. The time scale of jet precession and flapping can be estimated using the Strouhal number relationships identified in [68]. Over the orifice diameters 15 – 9mm the flapping frequency reduces from \( \approx 1.24 \) – \( \approx 0.44 \) Hz and the precession frequency increases from \( \approx 0.38 \) – \( \approx 0.46 \) Hz. Because a breath-hold scan is much longer than these time scales the jet movement may be averaged out to give correct flow measurements. This averaging effect may dampen extreme values such as the peak velocity.

Bellhouse and Bellhouse, in the investigation of the mechanism for valve closure, defined the Strouhal number for humans [96] to be

\[
St = \frac{d}{2\tau V_{pk}}
\]  

where \( d \) is the aortic diameter, \( \tau \) is the duration of systole and \( V_{pk} \) is the peak aortic velocity. In this application the Strouhal number is related to the frequency of the unsteady flow rather than the flapping of the jet. It is used to support the notion that sinus vortices, which close the aortic valve, are formed or destroyed by viscous diffusion [96]. For this to be true it was found that \( Re \geq 100 \) and \( St \leq 0.1 \). In normal humans at rest the peak \( Re = 3455 \) and \( St = 0.0422 \). During exercise the Reynold number is found to increase, up to 8500 and the Strouhal number to decrease to 0.023. The findings supported their hypothesis of sinus vortices being the mechanism behind valve closure.

In moderate to severe aortic stenosis patients whose expansion ratio is greater than 3.5 the duration of systole is shorter than either jet flapping or precession. But, the direction of the jet may not be consistent between each heart beat due to the sinus vortices. Again measuring over multiple heart beats may reduce this effect on the flow at the expense of extreme values.
Anybody who has been seriously engaged in scientific work of any kind realizes that over the entrance to the gates of the temple of science are written the words 'Ye must have faith.'

Max Planck

B. Background phase algorithm development

This appendix outlines the surface fitting procedure and the performance results on the stationary phantom and in vivo.

B.1 Surface fitting

Each voxel’s background phase ($b$) is projected onto the surface using its known position ($x, y$) in the image. The points can be described as a linear system of equations $\|Ax - b\|^2$. For example a 2nd order plane can be described as

$$
\begin{bmatrix}
1 & x & y & x^2 & xy & y^2 \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots
\end{bmatrix}
\begin{bmatrix}
a_{00} \\
a_{10} \\
a_{01} \\
a_{20} \\
a_{11} \\
a_{02}
\end{bmatrix}
= 
\begin{bmatrix}
b_1 \\
\vdots \\
\vdots \\
\vdots \\
\vdots \\
b_n
\end{bmatrix}
$$

(B.1)

and a 1st order finite element

$$
\begin{bmatrix}
\psi_1(\xi_1)\psi_1(\xi_2) & \psi_1(\xi_1)\psi_2(\xi_2) & \psi_2(\xi_1)\psi_1(\xi_2) & \psi_2(\xi_1)\psi_2(\xi_2) \\
\vdots & \vdots & \vdots & \vdots \\
\vdots & \vdots & \vdots & \vdots
\end{bmatrix}
\begin{bmatrix}
n_{11} \\
n_{12} \\
n_{21} \\
n_{22}
\end{bmatrix}
= 
\begin{bmatrix}
b_1 \\
\vdots \\
\vdots \\
\vdots
\end{bmatrix}
$$

(B.2)

To minimise the sums of the errors using a linear least squares approach we differentiate with respect to the unknown values $x$ and set equal to zero. The resulting normal equations can be written as, $A^TAx = A^Tb$. Solving these equations, using Matlab’s inbuilt conjugate gradient solver, gives the coefficients of the fitted surface.
APPENDIX B. BACKGROUND PHASE ALGORITHM DEVELOPMENT

Table B.1: Effect of fitted surface on the relative error across the surface.

<table>
<thead>
<tr>
<th>Orientation</th>
<th>Axial</th>
<th>30° axial-coronal rotation</th>
<th>60° axial-coronal rotation</th>
<th>Coronal</th>
<th>25-30° Bi-Oblique</th>
<th>25-45° Bi-oblique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venc</td>
<td>200</td>
<td>500</td>
<td>800</td>
<td>200</td>
<td>500</td>
<td>800</td>
</tr>
<tr>
<td>TE 2.0ms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bi-linear Plane</td>
<td>0.08</td>
<td>0.44</td>
<td>0.22</td>
<td>0.07</td>
<td>0.13</td>
<td>0.14</td>
</tr>
<tr>
<td>Bi-quadratic Plane</td>
<td>0.08</td>
<td>0.34</td>
<td>0.14</td>
<td>0.07</td>
<td>0.08</td>
<td>0.17</td>
</tr>
<tr>
<td>Bi-cubic Plane</td>
<td>0.09</td>
<td>0.43</td>
<td>0.22</td>
<td>0.08</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>Bi-linear FE</td>
<td>0.08</td>
<td>0.41</td>
<td>0.19</td>
<td>0.07</td>
<td>0.11</td>
<td>0.16</td>
</tr>
<tr>
<td>Bi-quadratic FE</td>
<td>0.07</td>
<td>0.53</td>
<td>0.22</td>
<td>0.05</td>
<td>0.09</td>
<td>0.22</td>
</tr>
<tr>
<td>Bi-cubic/linear FE</td>
<td>0.07</td>
<td>0.12</td>
<td>0.25</td>
<td>0.19</td>
<td>0.50</td>
<td>0.19</td>
</tr>
<tr>
<td>Bi-quadratic/linear FE</td>
<td>0.14</td>
<td>0.14</td>
<td>0.24</td>
<td>0.10</td>
<td>0.38</td>
<td>0.16</td>
</tr>
<tr>
<td>Bi-cubic/linear FE</td>
<td>0.13</td>
<td>0.13</td>
<td>0.24</td>
<td>0.16</td>
<td>0.30</td>
<td>0.19</td>
</tr>
<tr>
<td>Bi-linear/linear FE</td>
<td>0.10</td>
<td>0.20</td>
<td>0.24</td>
<td>0.09</td>
<td>0.34</td>
<td>0.17</td>
</tr>
<tr>
<td>Bi-quadratic/linear/linear FE</td>
<td>0.13</td>
<td>0.09</td>
<td>0.18</td>
<td>0.05</td>
<td>0.08</td>
<td>0.06</td>
</tr>
<tr>
<td>Bi-quadratic/linear/linear/linear FE</td>
<td>0.16</td>
<td>0.10</td>
<td>0.09</td>
<td>0.05</td>
<td>0.07</td>
<td>0.06</td>
</tr>
<tr>
<td>Bi-cubic/linear/linear/linear FE</td>
<td>0.13</td>
<td>0.09</td>
<td>0.09</td>
<td>0.06</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>Bi-linear/linear/linear/linear FE</td>
<td>0.16</td>
<td>0.07</td>
<td>0.16</td>
<td>0.05</td>
<td>0.07</td>
<td>0.06</td>
</tr>
<tr>
<td>Bi-quadratic/linear/linear/linear/linear FE</td>
<td>0.10</td>
<td>0.11</td>
<td>0.11</td>
<td>0.04</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

B.2 Background phase in a stationary phantom

The following tables relate to Chapter 6, Section 6.4.1 on page 154.

Relative improvement of the background phase after correction

After background phase correction the background phase in each ROI was reduced regardless of the order or type, Table B.1. At a coronal orientation with the TE 2.0ms and the TE 1.5ms variants, the relative improvement\(^1\) of low-order surface fits show they were not effective 0.9 and 1.58 respectively. On closer inspection of the error at the isocenter, Table B.2, the TE 2.0ms (0.14% before and 0.17% after correction) and the TE 1.5ms variants (0.05% before and 0.28% after correction) both had relatively low errors. But, the TE 1.5ms shows that low order surface fits and a 3\(^{rd}\) order plane fit increases the error (1\(^{st}\) order planar surface 1.06%, 1\(^{st}\) order finite element surface 0.99%, 3\(^{rd}\) order planar surface 1.79%) significantly in a 30\(^{o}\) - 30\(^{o}\) bi-oblique orientation despite good relative improvement across the ROIs (0.13).

\(^{1}\)Relative improvement is the average of each region's absolute error normalised by that ROI's absolute error before correction i.e. values less than 1 show improvement, values greater than 1 show the fit worsened the result.
B.3. STROKE VOLUME RESULTS BEFORE AND AFTER CORRECTION

### Table B.2: Effect of fitted surface on the relative error at the isocentre.

<table>
<thead>
<tr>
<th>Protocol</th>
<th>TE 2.0ms variant</th>
<th>30-degree</th>
<th>60-degree</th>
<th>Coronal</th>
<th>25-30-Bioblique</th>
<th>25-65-Bioblique</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.05%</td>
<td>0.05%</td>
<td>0.05%</td>
<td>0.05%</td>
<td>0.05%</td>
<td>0.05%</td>
</tr>
<tr>
<td>Axial</td>
<td>0.09%</td>
<td>0.09%</td>
<td>0.09%</td>
<td>0.09%</td>
<td>0.09%</td>
<td>0.09%</td>
</tr>
<tr>
<td>60-degree</td>
<td>0.12%</td>
<td>0.12%</td>
<td>0.12%</td>
<td>0.12%</td>
<td>0.12%</td>
<td>0.12%</td>
</tr>
<tr>
<td>Coronal</td>
<td>0.17%</td>
<td>0.17%</td>
<td>0.17%</td>
<td>0.17%</td>
<td>0.17%</td>
<td>0.17%</td>
</tr>
<tr>
<td>25-30-Bioblique</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
<tr>
<td>25-65-Bioblique</td>
<td>0.25%</td>
<td>0.18%</td>
<td>0.18%</td>
<td>0.18%</td>
<td>0.18%</td>
<td>0.18%</td>
</tr>
</tbody>
</table>

**Ill-conditioning**

Analysis of the convergence statistics for a 30°-30° bi-oblique orientation show that higher-order planes are ill-conditioned and often do not converge, Table B.3.

### B.3 Stroke volume results before and after correction

Table B.4 shows the resulting error (compared with the volumetric stroke volume (SV) data) before and after correction, see Chapter 6, Section 6.5.1. Only the TE 1.5ms variant shows consistent reduction in variance at each location.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Iterations</th>
<th>Termination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilinear Plane</td>
<td>413000</td>
<td>6</td>
</tr>
<tr>
<td>Biquadratic Plane</td>
<td>1.47E+11</td>
<td>47</td>
</tr>
<tr>
<td>Bicubic Plane</td>
<td>5.38E+16</td>
<td>169</td>
</tr>
<tr>
<td>Bilinear FE</td>
<td>26.7</td>
<td>6</td>
</tr>
<tr>
<td>Biquadratic FE</td>
<td>1210</td>
<td>18</td>
</tr>
<tr>
<td>Bicubic-bezier FE</td>
<td>48200</td>
<td>73</td>
</tr>
<tr>
<td>Bilinear Plane</td>
<td>232000</td>
<td>5</td>
</tr>
<tr>
<td>Biquadratic Plane</td>
<td>46100000000</td>
<td>36</td>
</tr>
<tr>
<td>Bicubic Plane</td>
<td>9.48E+15</td>
<td>566</td>
</tr>
<tr>
<td>Bilinear FE</td>
<td>26.5</td>
<td>5</td>
</tr>
<tr>
<td>Biquadratic FE</td>
<td>1190</td>
<td>17</td>
</tr>
<tr>
<td>Bicubic-bezier FE</td>
<td>46800</td>
<td>60</td>
</tr>
<tr>
<td>Bilinear Plane</td>
<td>233000</td>
<td>5</td>
</tr>
<tr>
<td>Biquadratic Plane</td>
<td>47100000000</td>
<td>41</td>
</tr>
<tr>
<td>Bicubic Plane</td>
<td>9.84E+15</td>
<td>78</td>
</tr>
<tr>
<td>Bilinear FE</td>
<td>26.6</td>
<td>6</td>
</tr>
<tr>
<td>Biquadratic FE</td>
<td>1210</td>
<td>17</td>
</tr>
<tr>
<td>Bicubic-bezier FE</td>
<td>48600</td>
<td>52</td>
</tr>
</tbody>
</table>

Table B.3: Convergence statistics of the fitted surfaces performed on the stationary phantom at a $30^\circ - 30^\circ$ bi-oblique orientation.
### B.3. STROKE VOLUME RESULTS BEFORE AND AFTER CORRECTION

<table>
<thead>
<tr>
<th>TE</th>
<th>Mask Order</th>
<th>LVOT Position</th>
<th>MPA</th>
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<tr>
<td>no correction</td>
<td>-0.07 ± 0.12</td>
<td>0.02 ± 0.13</td>
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<tr>
<td>STD 3</td>
<td>-0.09 ± 0.12</td>
<td>-0.03 ± 0.13</td>
<td></td>
</tr>
<tr>
<td>STD 4</td>
<td>-0.09 ± 0.12</td>
<td>-0.03 ± 0.13</td>
<td></td>
</tr>
<tr>
<td>STD 9</td>
<td>-0.04 ± 0.13</td>
<td>0.01 ± 0.14</td>
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</tr>
<tr>
<td>2.8ms STD 10</td>
<td>-0.01 ± 0.14</td>
<td>0.03 ± 0.15</td>
<td></td>
</tr>
<tr>
<td>FT 3</td>
<td>-0.10 ± 0.13</td>
<td>-0.06 ± 0.12</td>
<td></td>
</tr>
<tr>
<td>FT 4</td>
<td>-0.10 ± 0.13</td>
<td>-0.06 ± 0.12</td>
<td></td>
</tr>
<tr>
<td>FT 9</td>
<td>-0.10 ± 0.15</td>
<td>-0.07 ± 0.14</td>
<td></td>
</tr>
<tr>
<td>FT 10</td>
<td>-0.10 ± 0.15</td>
<td>-0.08 ± 0.14</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>AV0cm</th>
<th>AV1cm</th>
<th>AV2.5cm</th>
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<tr>
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<td>STD 4</td>
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<td>-0.13 ± 0.23</td>
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<tr>
<td>FT 3</td>
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<td>FT 9</td>
<td>0.08 ± 0.29</td>
<td>-0.36 ± 0.20</td>
<td>-0.26 ± 0.21</td>
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<td>FT 10</td>
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<td>-0.36 ± 0.18</td>
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<td>-0.11 ± 0.24</td>
</tr>
<tr>
<td>FT 3</td>
<td>0.03 ± 0.29</td>
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<td>-0.26 ± 0.18</td>
</tr>
<tr>
<td>FT 4</td>
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<tr>
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<td>-0.26 ± 0.30</td>
</tr>
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<td>-0.18 ± 0.25</td>
</tr>
<tr>
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</tr>
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<td>-0.20 ± 0.15</td>
</tr>
<tr>
<td>STD 4</td>
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<td>-0.19 ± 0.17</td>
</tr>
<tr>
<td>STD 9</td>
<td>0.12 ± 0.26</td>
<td>-0.14 ± 0.14</td>
<td>-0.08 ± 0.18</td>
</tr>
<tr>
<td>1.5ms STD 10</td>
<td>0.12 ± 0.26</td>
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<td>FT 3</td>
<td>0.01 ± 0.24</td>
<td>-0.29 ± 0.17</td>
<td>-0.25 ± 0.18</td>
</tr>
<tr>
<td>FT 4</td>
<td>0.03 ± 0.23</td>
<td>-0.27 ± 0.14</td>
<td>-0.25 ± 0.16</td>
</tr>
<tr>
<td>FT 9</td>
<td>0.08 ± 0.20</td>
<td>-0.25 ± 0.12</td>
<td>-0.25 ± 0.13</td>
</tr>
<tr>
<td>FT 10</td>
<td>0.08 ± 0.19</td>
<td>-0.25 ± 0.15</td>
<td>-0.24 ± 0.15</td>
</tr>
</tbody>
</table>

Table B.4: Error before and after correction.
What is a scientist after all? It is a curious man looking through a keyhole, the keyhole of nature, trying to know what’s going on.

Jacques Yves Cousteau

Velocity dependent slice excitation

This appendix details the calculation of a the velocity dependent slice select gradient waveform, Figure C.1 for a given maximum gradient ($G$), and maximal encoding velocity ($V_{enc}$).

![Diagram of Velocity dependent slice select waveform](image)

Figure C.1: Velocity dependent slice select waveform.

The $0^{th}$ order moment or the gradient areas of each lobe must equate to zero to remove phase accrual due to position

\begin{align*}
\Delta M_0 &= \int G(t) \, dt = 0 \quad \text{(C.1)} \\
0 &= -G \left( P_1 + \frac{r}{2} \right) + G \left( P_2 + r \right) \quad \text{(C.2)} \\
&\quad + G \left( r - \frac{r}{2} \right) \quad \text{(C.3)}
\end{align*}
which can be rearranged to relate the plateau time of both lobes as

\[ P_1 = P_2 + \frac{r}{2} \]  

(C.4)

The 1st order moment, \( \Delta M_1 \), of the gradient waveform can be calculated as follows:

\[ \Delta M_1 = \int G(t) t \, dt \]  

(C.5)

\[
\frac{\pi}{\gamma Venc} = G \int_0^{P_1} -t \, dt + G \int_{P_1}^{T_1+r} \left( \frac{1}{r} (t - P_1) - 1 \right) t \, dt \\
+ G \int_{T_1+r}^{T_1+T_2} t \, dt + G \int_{T_1+T_2}^{T_1+T_2-r} \frac{1}{r} (t - (T_1 + T_2)) t \, dt
\]  

(C.6)

Combining Eq. 2.39 and substituting in Eq. C.4 yields the quadratic equation for \( P_2 \):

\[ P_2^2 + 3r P_2 + \frac{47}{24} r^2 - \frac{\pi}{\gamma Venc G} = 0 \]  

(C.7)

which can be solved using the quadratic formula.

A valid solution is only obtained if \( P_1 \geq \frac{t_f}{2} \) i.e the plateau of the slice select lobe is long enough to play out a central lobe rectangular RF pulse.
References


REFERENCES


REFERENCES


REFERENCES


[56] D. C. Ghiglia and L. A. Romero. Robust two-dimensional weighted and unweighted


REFERENCES


REFERENCES


## Nomenclature

### Background phase algorithm parameters
- $\psi_n$: finite element basis function
- $a_{ij}$: planar surface coefficients
- $F(\xi_1, \xi_2)$: values of a finite element surface
- $n_{ij}$: finite element nodes
- $P(x, y)$: values of a planar surface

### Catheterisation and thermodilution parameters
- $K$: Gorlin constant
- $K_p$: computation constant
- $T_b$: initial blood temperature
- $T_b(t)$: time-varying blood temperature recording
- $T_i$: temperature of the injected saline
- $V_i$: volume of the injected saline
- $SEP$: systolic ejection period

### Echocardiography parameters
- $\lambda$: wavelength of sound in a medium
- $\Phi$: the sweep angle
- $\phi$: angle of projection
- $\theta$: angle of incidence between the beam and the direction of the object
- $a$: diameter of the transducer
- $c$: speed of sound in a medium
- $f$: frequency of sound
- $T$: transition distance
- $v_{obj}$: velocity of the object or scatterer
- **Duty factor**: percentage of time spent in transmit mode
- **Pulse Duration**: time between successive pulse
- **Pulse length**: length of the transmit pulse

### Fluid mechanics parameters
- $\epsilon$: energy dissipation per unit time and per unit mass
- $\mu$: viscosity of a fluid
- $\nu$: kinematic viscosity
- $\omega$: circular frequency of the heart’s cardiac cycle
- $\rho$: density of a fluid
- $A$: cross sectional area of the vessel
- $B$: magnetic field of flow meter

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NOMENCLATURE

\( C_d \) the ratio of ideal discharge
\( d \) diameter of the vessel \( m \)
\( d_i \) internal diameter of pipe/orifice \( \text{mm} \)
\( E \) expansion co-efficient
\( E_T \) total kinetic energy \( J \)
\( f_a(x, t) \) externally applied force per unit mass \( m^2/s \)
\( I \) turbulence intensity \( \% \)
\( L \) entrance length \( m \)
\( L_e \) electrode spacing in flow meter \( m \)
\( P \) instantaneous pressure \( Pa \)
\( Q \) flow \( mL/s \)
\( S \) surface \( m^2 \)
\( T_m \) measurement time interval required to smooth out turbulence \( s \)
\( T_c \) correlation time of velocity fluctuations \( s \)
\( U \) average velocity of a fluid \( m/s \)
\( u \) turbulence's fluctuating velocity component \( m/s \)
\( U_f \) velocity in the flow meter \( m/s \)
\( u_{rms} \) root mean square of the fluctuating velocities \( m/s \)
\( V \) fluid volume \( m^3 \)
\( V \) induced voltage in the flow meter \( V \)
\( St \) strouhal number
\( U \) instantaneous velocity \( m/s \)

**General parameters**

\( V_{phantom} \) mean velocity in the phantom \( \text{cm/s} \)
\( \sigma_N \) a normalised standard deviation of the velocity measurement in a voxel
\( \sigma_S \) average standard deviation of the velocity measurement in stationary tissue
\( \sigma_{voxel} \) standard deviation of the velocity measurement in a voxel
\( A_{voxel} \) area of a voxel \( \text{cm}^2 \)
\( N_{voxel,i} \) number of voxels in the contour
\( RSI_P \) relative signal intensity over the phantom
\( RSI_{voxel} \) relative signal intensity of a voxel
\( SI_P \) signal intensity over the phantom
\( SI_S \) signal intensity of stationary tissue
\( SI_{voxel} \) signal intensity of a voxel
\( U_{E,O} \) expected mean velocity at the orifice \( \text{cm/s} \)
\( U_{E,P} \) expected mean velocity in the pipe \( \text{cm/s} \)
\( V_{voxel,i} \) measured velocity in a voxel \( \text{cm/s} \)

**Magnetic resonance parameters**

\( \alpha \) the flip angle
NOMENCLATURE

\[ \Delta m_n \] the difference of the nth moment between PC acquisitions \[ mT.s^n/m \]
\[ \Delta \phi \] phase difference between acquisitions \[ rad \]
\[ \Delta \phi_{corr}(x,y,z) \] the corrected phase \[ rad \]
\[ \Delta \phi_c(x,y,z) \] the concomitant phase error \[ rad \]
\[ \Delta_{RF} \] bandwidth of RF pulse \[ Hz \]
\[ \Delta_x \] readout encoding step size \[ mm \]
\[ \Delta_y \] phase encoding step size \[ mm \]
\[ \Delta_z \] slice thickness \[ m \]
\[ \gamma \] the gyromagnetic ratio \[ rad/(s.T) \]
\[ \hat{\rho} \] the effective spin density of a homogeneous volume element \[ (\Delta x, \Delta y, \Delta z) \] \[ spins/m^3 \]
\[ \kappa_B \] Boltzmann’s constant
\[ \nu_0 \] transition frequency \[ Hz \]
\[ \omega_0 \] the larmor frequency \[ rad/s \]
\[ \omega_{rf} \] transmit frequency of the RF pulse \[ rad/s \]
\[ \phi(t) \] phase accumulation \[ rad \]
\[ \rho_0 \] the density of spins per unit volume \[ spin/m^3 \]
\[ \sigma_m^2 \] the variance of the noise fluctuations of the measured signal
\[ \tau \] duration of a bipolar gradient \[ ms \]
\[ G(t) \] the applied gradients, \( G_x(t), G_y(t) \) and \( G_z(t) \) \[ mT/m \]
\[ A_y \] maximum gradient area of the phase encoding lobe \[ mT.s/m \]
\[ B \] magnetic field \[ T \]
\[ B(x,G(t),t) \] the magnetic field is as a function of position, the applied gradients and time \( T \)
\[ B_0 \] an external magnetic field \[ T \]
\[ B_1 \] an applied magnetic field i.e. an RF-pulse \[ \mu T \]
\[ B_{eff} \] the effective magnetic field \[ \mu T \]
\[ BW_{ro} \] bandwidth of the readout gradient \[ Hz \]
\[ e_{Bo}(G(t)) \] \( B_0 \) eddy currents due to the applied gradients \[ mT/m \]
\[ E_1 \] energy level of the current spin state \[ J \]
\[ e_{l}(G(t)) \] linear eddy currents due to the applied gradients \[ mT/m \]
\[ e_{other}(x,t) \] eddy current resulting from other sources \[ mT/m \]
\[ emf_s \] the sample’s electrical and magnetic field \[ V \]
\[ FOV_x \] field of view in the readout direction \[ mm \]
\[ FOV_y \] field of view in the phase encoding direction \[ mm \]
\[ G_{x,ro} \] strength of the readout gradient \[ mT/m \]
\[ G_x(t) \] readout gradient axis \[ mT/m \]
\[ G_y(t) \] phase encoding gradient axis \[ mT/m \]
\[ G_z(t) \] slice select gradient axis \[ mT/m \]
\[ h \] Planck’s constant \[ Js \]
\[ I \] a nuclie’s spin quantum number
\[ k_x \] readout frequency \[ m^{-1} \]
NOMENCLATURE

$k_{y,\text{max}}$  maximum spatial frequency in the phase encoding direction  \( m^{-1} \)
$k_y$  phase encoding frequency  \( m^{-1} \)
$M$  the net magnetisation vector  \( \mu T \)
$M_I$  spin state defined by the nuclei’s spin quantum number  \( \mu T \)
$m_n$  the nth gradient moment i.e. $m_0$, $m_1$, $m_n$  \( mT.s/m, mT.s^2/m, mT.s^n/m \)
$M_o$  the net magnetisation vector at equilibrium  \( \mu T \)
$M_{xy}$  transverse component of the net magnetisation vector in the rotating frame of reference  \( \mu T \)
$M_z$  longitudinal component of the net magnetisation vector in the rotating frame of reference  \( \mu T \)
$N_{\text{acq}}$  number of acquisitions
$N_{\text{down}}$  Number of spins opposing the external magnetic field
$N_{\text{up}}$  Number of spins aligned with the external magnetic field
$N_x$  number of sample points in the readout direction
$N_y$  number of sample points (lines) in the phase encoding direction
$R$  resistance  \( \Omega \)
$S(k_x, k_y, k_z)$  K-space representation of the induced signal of the FID
$S_i(t)$  the voxel signal, the demodulated voxel signal can be represented as a real ($S_R(t)$) and imaginary ($S_I(t)$) or complex signal ($S_Z(t)$)
$s_m(k)$  measured signal
$T_1$  $T_1$ relaxation time constant  \( ms \)
$T_2$  $T_2$ relaxation time constant  \( ms \)
$T_2^*$  $T_2^*$ relaxation time constant  \( ms \)
$T_{fp}$  the temporal footprint of a sequence  \( ms \)
$T_k$  Temperature  \( K^o \)
$T_{res}$  the temporal resolution frame rate of a sequence  \( ms \)
$t_{rf}$  the duration of the RF pulse  \( \mu s \)
$T_{ro}$  duration of the readout gradient  \( ms \)
$T_{\text{scan}}$  the overall scan time of a sequence  \( ms \)
$v$  the spins’ velocity within a voxel  \( cm/s \)
$x’y’z$  laboratory frame of reference
$x_n, y_n$  voxel (pixel) co-ordinates
$xyz$  rotating frame of reference
$Z_o$  complex representation of a voxel (pixel)
$SNR$  signal to noise ratio
$V_{\text{enc}}$  aliasing or maximal encoded velocity  \( cm/s \)
$vps$  the number of view per segment
$\phi_c (x, y, z)$  the phase shift due to the concomitant magnetic field  \( rad \)

Physiological parameters

$\Delta P$  pressure difference (gradient) across the valve  \( mmHg \)
NOMENCLATURE

\( \tau \) duration of systole \( \text{ms} \)

\( CSA_{LVOT} \) cross-sectional area of the left ventricular outflow tract \( \text{cm}^2 \)

\( d_{LVOT} \) diameter of the left ventricular outflow tract assessed by 2D-echo \( \text{m} \)

\( V_{PC,pk} \) peak velocity determined by PC which coincides with the same level as \( VTI_{PC,max} \) \( \text{m/s} \)

\( V_{pk} \) peak velocity in the stenotic jet \( \text{m/s} \)

\( VTI_{Jet} \) velocity time integral of the jet assessed by Doppler \( \text{m} \)

\( VTI_{LVOT} \) velocity time integral of the left ventricular outflow tract assessed by Doppler \( \text{m} \)

\( VTI_{PC,max} \) the maximum VTI between the AV0cm and AV1cm levels as determined by PC cm

\( AVA_{Doppler} \) aortic valve area assessed by CW-Doppler \( \text{cm}^2 \)

\( AVA_{flow} \) aortic valve area determined from a flow derived PC assessment of SV and \( VTI_{PC,max} \) \( \text{cm}^2 \)

\( AVA_{vol} \) aortic valve area determined from a volumetric MR assessment of SV and \( VTI_{PC,max} \) \( \text{cm}^2 \)

\( AVA \) aortic valve area \( \text{cm}^2 \)

\( CO \) cardiac output \( \text{L/min} \)

\( HR \) heart rate \( \text{beats/min} \)

\( LVEDV \) left ventricular end diastolic volume \( \text{mL} \)

\( LVESV \) left ventricular end systolic volume \( \text{mL} \)

\( LVSV \) a volumetric MR assessment of stroke volume using CIM \( \text{mL} \)

\( PCSV_{max} \) flow derived PC assessment of stroke volume corresponds to the same level as the \( VTI_{PC,max} \) \( \text{mL} \)

\( PCSV \) flow derived PC assessment of stroke volume \( \text{mL} \)

**Parameters used to design the UTE pulse sequence**

\( \Delta \phi \) angular spacing between radial spokes \( \text{rad} \)

\( \phi \) radial spoke angle \( \text{rad} \)

\( A_{k_{max}} \) maximum gradient area required to acquire \( k_{max} \) \( \text{mT.s/m} \)

\( FOV \) field of view in in each direction \( \text{mm} \)

\( G \) gradient strength of the velocity dependent slice select lobe \( \text{mT/m} \)

\( G_{max} \) maximum gradient corresponding to the maximum gradient area \( \text{mT/m} \)

\( k_{max} \) maximum spatial frequency to acquire \( \text{m}^{-1} \)

\( N \) number of data points to sample in each direction

\( N_s \) number of radial radial spokes

\( P_1 \) duration of the 1st velocity dependent slice select lobe’s plateau

\( P_2 \) duration of the 2nd velocity dependent slice select lobe’s plateau

\( r \) rise time of the gradient ramp \( \text{ms} \)

\( r_f \) radius of the region free of radial streak artefact \( \text{mm} \)

\( T_1 \) duration of the 1st velocity dependent slice select lobe

\( T_2 \) duration of the 2nd velocity dependent slice select lobe