Analysis of Morphological and Blood Flow Characteristics of the Human Thoracic Aorta

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Abstract

The human aorta is often affected by many cardiovascular diseases, including atherosclerosis, aneurysm and dissection. There is considerable evidence suggesting that these diseases are associated with the morphology and haemodynamic functions of the aorta, but not all these parameters can be measured directly in vivo. In particular, the helical flow characteristics and haemodynamic wall parameters can only be evaluated from quantitative information on a flow field resolved both in space and time. This study provides a comprehensive analysis of geometric and haemodynamic characteristics of the human aorta through subject-specific simulations of blood flow based on medical images.

Computational fluid dynamics (CFD) models of the thoracic aorta were developed based on in vivo anatomical and flow data acquired using magnetic resonance imaging (MRI). In order to capture potential transitional and turbulent flow in the aorta, the correlation based shear stress transport-transitional (SST-Trans) turbulence model was employed. Detailed flow analyses were performed on multiple cases of normal thoracic aortas with a tricuspid aortic valve (TAV) and abnormal aorta with a bicuspid aortic valve (BAV).

Results obtained from this study gave quantitative insights into the flow distributions and wall shear stress (WSS) patterns in normal and abnormal aortas. Morphological features and flow patterns of the TAV and BAV aortas were compared. In addition to standard flow parameters, specific indices were evaluated to allow for direct comparisons between the two groups; these included flow reversal ratio (FRR), helicity flow index (HFI) and shear range index (SRI). The results showed that all examined aortas tapered from the proximal ascending segment to the distal descending segment, with the BAV aorta showing a more distinct tapering. Although flow patterns were qualitatively similar in the TAV and BAV aortas, there were substantial quantitative variations. Highly disturbed flow was observed in all examined aortas during part of the cycle, mostly in the systolic deceleration phase. Predicted WSS was higher in the TAV aorta than in the BAV aorta, with the highest WSS occurring in regions around the major arch branches. Comparisons between the predicted and measured velocities showed a good agreement, demonstrating that MR image-based CFD modelling methodology can be used to obtain reliable haemodynamic parameters that are important in clinical assessment and management of aortic diseases.
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With pleasure and genuine appreciation, I would like to thank my supervisor, Professor Yun Xu, for her immense experience, guidance, helpful but weighted comments that spurred me on. I thank you especially for the opportunity to take on this study and fulfill my interest and wish to research, to develop and to contribute something. I thank my husband ‘Layi, and my sons ‘Tenne, ‘Bade and ‘Tokunbo for their love and unwavering support. You have been amazing and I am proud of your understanding and unqualified belief, patience and trust. Many thanks also to Doctor Zhuo Cheng, Doctor Ryo Torii, Professor Mohiaddin and Professor Nigel Wood for their invaluable experience, advice and engaging comments. I got reminded and learnt many new fun maths tricks with interesting research anecdotes. Professor Nina Thornhill, thank you for the challenge. I am indebted to the Radiologists and team at the Royal Brompton Hospital London for their collaboration and time. My appreciation and thanks to my friends, notably again to Zhuo (Doctor Cheng) and Afet for their support, for being there to share my achievements, disappointments, sometimes confounding thoughts and laughters with me. I thank Susi Underwood for her openness, constant support, refreshing anecdotes and helpful reminders. The Chemical Engineering Admin, ICT and Security teams have been most invaluable and appreciate especially to Graham, Terrence, Nam and Severine. Anusha and team, my run teammates (Al Dyson TT), thank you for the one London Duathlon I ever raced. Hope to do more of it. A big appreciation to all my sprite young friends notably all of 414, MO3 and M17A offices 2011- 2016 and all others who in one way or another were there for and with me during my research and study at Imperial College. You are all so knowledgeable and awesome. Best wishes to you always. Finally, a very big appreciation and thanks to my entire family and friends (all over the world) for your excellent support. You all have been marvelous.

Life is amazing, boisterous, and chaotic and still can remain calm and yet again amazing, but if only we try... hence do try, strive more to achieve more.

In memory of my Mum, Dad and siblings who left so early!
Declaration

I hereby declare that this thesis is my own work and investigation carried out at Imperial College London and all references made to other work have been acknowledged and referenced in the text.

Oluwatoyin Fadeke Fatona

October, 2016
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Abbreviations

AAo: Ascending aorta
AS: Aortic Stenosis
BF: Backward Flow
CCA: Common carotid artery
CFD: Computational fluid dynamics
CT: Computer tomography
CVD: Cardiovascular diseases
DICOM: Digital imaging and communication in medicine standard
EBT: Electron Beam Computed Tomography
ECG: Electrocardiogram, echocardiography
ETL: Echo Train Length
FF: Forward Flow
FFT: Fast Fourier transform
FLASH: Fast low angle shot
FOV: Field-of-view
FSE: Fast spin echo
FSI: Fluid structure interaction
FVM: Finite volume method
GE: Gradient echo
HASTE: Half-Fourier single-shot turbo spin echo
LES: Large eddy simulation
LVOT: Left ventricular outflow track
MRA: Magnetic resonance angiography
MRI: Magnetic resonance imaging
MDCT Multi: Detector Computed Tomography
OSI: Oscillatory shear index
PC: Phase contrast
PET: Positron emission tomography
PSs: Pulse sequences
RANS: Reynolds-averaged Navier-Stokes
Re\v: Strain-rate (or vorticity) Reynolds number
RF: Radio frequency
RMS: Root mean square
Re\s: Turbulent Reynolds number
Re_{\text{cr}}: Critical Reynolds number
SE: Spin echo
SST: Shear stress transport
SST-Trans: SST transitional
TAA: Thoracic aortic aneurysm
TAWSS: Time-averaged wall shear stress
TE: Echo time
TOF: Time-of-flight
TR: Repetition time
TrueFISP: True fast imaging with steady state precision
TSE: Turbo spin echo
UDS: Upwind interpolation
Venc: Velocity encoding
WSS: Wall shear stress
Greek and Roman Symbols

a₁ Model constant
α Closure coefficient
α Womersley parameter
β₀ magnetic field strength
β SST closure constant
β* closure coefficient
δ Stokes layer thickness
ε Dissipation per unit mass
γ Intermittency
τ Shear stress
Ω Absolute value of vorticity
θ Theta
ρ Density
π 3.142
σₖ Closure coefficient
σ* Closure coefficient
σₐ Closure coefficient
σₐ₂ Closure coefficient
κ Turbulence kinetic energy
μ Dynamic viscosity
ν Kinematic viscosity
ω specific dissipation rate
Chapter 1

1 Introduction

1.1 The Human Aorta

The aorta is the largest artery in a human body that takes oxygenated blood from the left ventricle of the heart through the aortic valve and delivers it to the rest of the body. There is evidence of dynamic interplay between the anatomy and aortic blood flow with the occurrence of disturbed flow phenomena and turbulence. Though the morphological and haemodynamic features influence the performance of the aorta to a large extent, the exact mechanism of interplay and influence is still not well understood.

The human aorta illustrated in Figure 1.1 is normally about 30.48 cm long and located within the thoracic and abdominal regions. It consists of two anatomic sections: the thoracic aorta and abdominal aorta. The thoracic aorta depicted is the region of interest (ROI) in this study and it is further divided into three sections: the ascending thoracic aorta, the aortic arch and the descending thoracic aorta.

In this study magnetic resonance imaging (MRI) and computational fluid dynamics (CFD) were used to acquire anatomical and flow data, to model, investigate and analyse the morphology and flow patterns of subject-specific thoracic aorta with tricuspid aortic valves and bicuspid aortic valves towards a better understanding of the aorta. The computational model of the thoracic aorta and the three major arch branches (i.e. the brachiocephalic, left common carotid and left subclavian arteries) was based on three-dimensional (3-D), transient, incompressible Navier-Stokes equations and the robust shear stress transport-transitional (SST-trans) model.
Figure 1.1: The human aorta is depicted showing the main thoracic and abdominal aorta sections and major branches (www.iradonline.org1).

It is expected that results from this study will provide quantitative insights into the flow patterns, wall shear stresses and other flow-derived parameters in the thoracic aorta, such as helicity density, flow reversal ratio and haemodynamic wall indices. This will facilitate direct comparison of the characteristics of the thoracic aorta among subjects and between different groups. Importantly, it is hoped that the knowledge acquired will contribute towards future improvement of clinical management of the aorta.

1.2 Motivation for Research

With about 2% of the world population affected every year, cardiovascular diseases like atherosclerosis, aneurysm and dissection are still endemic and undermining the socio-economy growth through morbidities and mortalities. Clinically, there is a great need for in vivo measurement of physiological and pathophysiological parameters that can give a clearer understanding of the human aorta. There is a clinical demand for parameters and information that can assist in the management and care of patients with aortic diseases. The need to understand the aorta better and the need for more objective and measurable parameters of the thoracic aorta, coupled with the need to contribute towards alleviating or reducing the pain and loss due to cardiovascular diseases, provided the motivation and drive for this research. The aorta with its major function to transport and distribute blood to the body is very important to health. Obviously, any changes in the aortic components, e.g. valve cusps and wall tissue composition, geometric dimensions, along with changes in flow velocity
and patterns would influence the function of the aorta. The ability to qualitatively and quantitatively describe blood flow behavior and patterns throughout the cardiac cycle by a combination of MRI and CFD provides a great opportunity to gain a better understanding of the complex aortic flow.

Many previous studies have suggested that abnormal flow patterns could be indicative of pathophysiological processes, e.g. Hope et al., (2011) provided evidence of abnormal and eccentric flow in the ascending aorta of bicuspid aortic valve (BAV) patients along with elevated and asymmetric wall shear stress (WSS) which may increase the risk of aortic aneurysm. Barker et al., (2010) examined both normal and BAV patients and found significantly different systolic WSS values in the ascending aorta. Using a WSS-based index value, the BAV patients were found to express a heterogenic dilatation pattern. Though helical and secondary flows have been demonstrated to be consistent features in healthy aortas, e.g. Kilner et al., (1993), it has been suggested that these flow features could have significance in both circulatory dynamics and the development of atheroma in the arch. Abnormal haemodynamic stresses together with recirculating and disturbed flow have been found to influence the rupture of atherosclerotic plaque and aortic aneurysm (Slager et al., 2005, Tan et al, 2009).

Considerable research effort and resources are being deployed into studies of the aortic blood flow and development of surgical devices or minimally invasive procedures for endovascular repair of the aorta; e.g. Singh et al., (2015) investigated flow profiles and haemodynamics in the aorta before and after personalized external aortic root support (PEARS) implantation, and Cheng et al., (2015) assessed the morphology and haemodynamic of the biovalsalva composite valve-conduit graft. However, aortic aneurysm remains the 13th leading cause of death in Western countries and there is an estimated incidence of 12.7 cases per 100,000 for thoracic aortic aneurysm (TAA). Thoracic aortic aneurysm and dissection (TAAD) is a constant clinical concern, and understanding the complex aortic flow in TAAD remains a significant challenge. The changing anatomy of the aorta and the unsteady nature of blood flow with 3D velocity patterns, pressure, wall shear stress and other biomechanical features require further investigation. Any enhancement to the knowledge of how normal and abnormal aortas function will play a role in improving cardiovascular health. Patient-specific aortic flow modelling combining MRI and CFD allows evaluation of important haemodynamic and functional parameters that cannot be obtained by in vivo measurement alone, and applying this combinatorial technique to physiological and pathophysiological thoracic aortas makes an interesting and challenging research topic.

1.3 Study Objectives and Research Strategy

The aim of this study is the development of MRI based patient-specific CFD models of the thoracic
aorta for quantitative analyses of morphological and haemodynamic parameters that can be used to assess and compare the haemodynamic functions of the aorta for individual patient and between patients. It is hoped that such a modelling tool will aid in clinical diagnosis, treatment and management of thoracic aortic diseases.

The overall aim is accomplished through the following specific objectives:

1. Acquire anatomic and flow information of the aortas in TAV and BAV subjects by means of MRI. Use image analysis tools to extract 3D geometric and flow information, in order to construct patient-specific geometry and boundary conditions for CFD simulations.

2. Develop subject/patient-specific models of the aorta based on the geometric and flow features extracted, and simulate, analyse and characterise aortic flow. Determine the flow patterns, wall shear stresses and other flow descriptors in these aorta models.

3. Examine and determine the differences in aortic morphology between TAV and BAV. Compare and distinguish morphological and flow features in the ascending aorta of a normal subject with TAV from that of a patient with BAV.

It is hoped that results obtained from this study will help to elucidate the role of haemodynamic factors in the development of aortic abnormalities in BAV patients and to determine the link between morphological factors and flow characteristics in the aorta.

1.4 Plan of the Thesis

This thesis consists of six chapters, essentially conceived as two parts. The first part consists of Chapters 1, 2 and 3 which together introduce the study and give the background information, reasons and motivation, along with the literature, and methodology underpinning the research. Chapter 2 gives a wide and detailed literature survey that covers both the medical and engineering knowledge and aspects. Chapter 3 describes the methodology and covers the materials and methods employed. The second part comprises Chapters 4, 5 and 6 which present the study cases, results, analysis and findings with discussions. Chapter 4 is the multi-case study of subject-specific thoracic aorta with TAV, whilst Chapter 5 presents the patient-specific study of thoracic aorta with BAV. Chapter 5 also contains a comparative analysis of the two valve types (BAV and TAV) studied. Chapter 6 is the concluding chapter where the study findings are summarised and limitations discussed together with suggestions for future work.
Chapter 2

2 Literature Review

This chapter presents the literature survey of work carried out towards improved understanding of the human aorta with a particular focus on the modelling and characterization of the thoracic aorta through phase contrast magnetic resonance imaging (PC MRI) and computational fluid dynamics (CFD) techniques. Relevant background materials from clinical, medical imaging and engineering aspects are covered. Importantly, the state-of-the-art MRI and CFD techniques are described for their applications in the examination of 3-D aortic geometry, haemodynamics and flow parameters. Section 2.1 gives the medical background and perspective on the morphology, haemodynamics and interrelated functions of the aorta. The circulatory system, the structural make-up of the aorta, aortic valve types and diseases of the aorta are described. Medical imaging of the aorta is described in Section 2.2 whilst experimental studies of the aorta are described in Section 2.3. Computational modelling of aortic flow is described in Section 2.4. A summary is given in Section 2.5.

2.1 Medical Background

Clinical examinations, experiments and investigative medical research have shown that the human aorta morphology, haemodynamics and transport signals are interrelated. The periodic pumping of blood from the heart into the aorta initiates both geometric and haemodynamic changes, which together influence and characterise the aortic system functions. The local geometric and haemodynamic factors, such as the shape of the aorta and wall shear stresses are connected and influence one another. It is being recognised that the aetiology and progression of many cardiovascular diseases including atherosclerosis, aneurysm and dissection are linked to the morphology and haemodynamics of the aorta. There is an increasing use of CFD models to improve our understanding of the physiological and pathophysiological characteristics of the human aorta. The performance of the aorta along with the flow patterns and stress parameters are needed for improved management of the aorta, particularly in the design of aortic prosthetics and other cardiovascular devices.

2.1.1 The Human Circulatory System

The human circulatory system consists of the pulmonary and systemic circulations (with the latter circulation forming the major portion of the system). The human heart is illustrated in Figure 2.1(a);
and the blood circulatory system, is depicted in figure 2.1(b).

![Diagram of the human heart and circulatory system](https://en.wikipedia.org/wiki/Circulatory_system)

**Figure 2.1:** (a) The human heart and (b) The human circulatory system (from https://en.wikipedia.org/wiki/Circulatory_system).

**Pulmonary circulation**

Venous blood enters the right atrium from the superior and inferior vena cava and flows through the tricuspid valve into the right ventricle. The right ventricle is primarily made of muscles and filled with blood when the muscle is relaxed. This relaxation period is the diastole. This period is followed by the contraction period known as systole, the period where some of the ventricular blood is pumped into the pulmonary trunk at low pressure. The pulmonary artery divides into the right and left pulmonary arteries that supply each lung. At the lungs, gases are exchanged by diffusion. Oxygen is inhaled and carbon dioxide is exhaled. With the exchanges done, oxygenated blood returns to the body through the pulmonary veins passing into the left atrium and into the left ventricle.

**The Systemic Circulation**

The left ventricle during systole, contracts to eject the blood (at a much higher pressure than in the pulmonary circulation) into the aorta. The blood flows through the aorta and its many branches and it is distributed according to the functional requirement and/or immediate metabolic need. Importantly, the cardiovascular system can be described and characterised in terms of its haemodynamic parameters, particularly by pressure, volume, cardiac output, vessel resistance and compliance. The mechanical work done by the cardiac muscle is dependent on two variables, the blood volume and pressure. Cardiac muscle contraction causes a rise in pressure in the atria and ventricles, whilst cardiac muscle relaxation induces a decrease in pressure. The differences in pressure cause the opening and the closing of the mitral valve (MV) and the aortic valve (AoV) on the left side of the heart (depicted in Figure 2.1 (a)) during a cardiac cycle. In the systemic circulation, blood flows continuously from the pulmonary veins to the left atrium. Approximately 80% of the blood contained
in the atrium passes to the left ventricle before the atrium’s contraction and the remaining 20% after. The atrium is considered a primer pump that allows for high ventricular pumping efficiency. Immediately following the beginning of the ventricle’s contraction (systole), the pressure inside the ventricle increases sharply, powering mitral valve closing (MVC). This phase is called isovolumetric contraction, during which the blood volume does not change. Approximately 0.03 s later, the ventricle exerts sufficient pressure to open the aortic valve (AoVo), initiating blood ejection. The opening of the AoV occurs when the intraventricular pressure reaches 80 mmHg. This is the ejection phase (Figure 2.2). During the ventricular systole, the atrium accumulates large blood quantities because the MV is closed. After the contraction, the ventricle relaxes (diastole) suddenly, causing the intraventricular pressure to decrease rapidly to diastolic values. This event is called isovolumic relaxation (Figure 2.2).
Figure 2.2: Typical pressure and blood flow of a cardiac cycle in a healthy man – Pressure = Press, Left Ventricular Volume = LVVol, Left Ventricular Pressure = LVP, Left Arterial Pressure = LAP, Arterial Pressure = AP, Left Ventricular End Diastole Volume = LVEDV, Ventricular End Systole Volume = LVESV. (Klabunde, 2009).

After the intraventricular pressure decreases and blood accumulates in the atrium, the pressure increases, forcing MV opening (MVo) and thus starting a new pumping cycle with the filling phase, when the blood passes to the left ventricle (Hall, 2011).
Blood Pressure
The range of arterial and systemic circulation pressure depicted in Figure 2.2 is usually 120/80 mmHg in a resting normal adult. The higher value of 120 mmHg is at systole whilst 80 mmHg is the diastolic pressure. Blood pressure is not static and undergoes some natural variation according to the individual age and size. There is also variation from one heartbeat to another. Figure 2.3 (right panel) shows blood pressure in the ascending aorta over a cardiac cycle with the peak systolic pressure above 120 mmHg.

Figure 2.3: Flow rate and blood pressure in the ascending aorta over a cardiac cycle (adapted from Davies et al., 2010).

The Cardiac Output measures the blood flow rate and it is the total blood volume ejected per minute by the left ventricle to the aorta. Cardiac output equals the stroke volume, which is the amount of blood ejected in one contraction multiplied by the heart rate, which is the number of contractions per minute. The blood flow rate is determined mainly by the vessel pressure gradient and the resistance to flow. The vessel resistance increases with contraction of the vessel and decreases with dilation of the vessel. In a resting normal adult, blood flow volume is in the region of 4 to 6 litres per minute but this amount does vary and can be slightly more or less according to the individual make up. The instantaneous flow rate measured in the ascending aorta, represented in Figure 2.2 is the peak of this flow rate in systole, for a healthy adult, which can reach approximately 500 mL/s according to result/study by Blanco et al., (2015). Generally, the distribution and amount of blood to the different organs vary. The amount to the brain is given as 13% (Widmaier et al., 2008). The amount of blood split to the three main aorta arch branches, the brachiocephalic, the left common carotid artery and the left subclavian artery is assumed to be between 15-30%. The actual volumetric flow to the aortic arch branches is contextual issue.

Considering that both pressure and blood flow are pulsatile with the spatio-temporal and function varying characteristics, it may be suggested that many aspects of circulation are best understood by
using average values, and studying various characteristic time points in the cardiac cycle.

2.1.2 The Aorta

The human aorta consists of the thoracic and abdominal aorta with a complex three-dimensional geometry that curves, branches and tapers to about 50% of its original size at the abdominal section. The aorta depicted in Figure 2.4, has a non-uniform configuration and it can be divided into two distinct sections – the thoracic aorta and the abdominal aorta. The thoracic aorta (TAo), which is the region of interest (ROI) in this study, consists of three main parts namely: the ascending aorta, the aortic arch (the region where the aorta curves about 180°), and the descending thoracic aorta.

![Figure 2.4](https://goo.gl/images/GL4s3l): (a) illustration of a typical human aorta – showing the thoracic aorta (above the diaphragm) and abdominal aorta. (b) illustration of the thoracic aorta (Google Images - https://goo.gl/images/vcG6WH).

The ascending aorta extends from the aortic valve to the origin of the innominate artery, with its proximal part referred to as the aortic root. The aortic root is complex in both its configuration and constituents and can vary as depicted in Figure 2.5. The aortic arch begins at the innominate (or brachiocephalic) artery and ends at the ligamentum arteriosum, with its most distal aspect, the aortic isthmus being quite often slightly narrowed. The aortic arch in comparison to the other thoracic aorta regions is generally non-planar and its centerline does not lie in a plane. The aortic arch curve is a morphological feature common to all individuals but can be essentially different in the shape and position from one individual to the other. The curvature and planarity aspect can be appreciated from
the study and illustrations by Kilner et al., (1993). Aortic curvature is an important geometric parameter as it can affect the magnitude and direction of displacement forces acting on aortic endografts (Figueroa et al., 2009).

**Figure 2.5:** The ‘Aortic Annulus’ or aortic valve is a complex structure with many components. The aortic valve and supporting ventricular structures are depicted - the green ring 1 is the sino-tubular junction, green ring 2 is the virtual basal ring and red ring 3 is the anatomic ventriculo-aortic junction. (Del Valle-Fernandez et al., 2010).

The descending thoracic aorta begins at the ligamentum, and its proximal portion may appear slightly dilated and it has been termed the aortic spindle (Litmanovich et al, 2009). Three great arterial branches that arise sequentially from the aortic arch namely: the innominate artery (the first and typically the largest branch and is usually seen more caudally than the other branches). It gives rise to the right subclavian and right common carotid arteries; the right vertebral artery subsequently originates from the right subclavian artery. “The left common carotid artery arises at a more cephalad level and has the smallest diameter of the three major arterial branches”. The left subclavian artery is the third branch and it arises from the posterior superior portion of the aortic arch. This normal branching pattern is seen in about 70% of individuals. The most common variation is combined origin of the innominate and left common carotid arteries, which is seen in 20-30% of individuals. In about 5% of cases the left vertebral artery arises as a separate branch directly from the aorta, between the left common carotid artery and the left subclavian artery. The descending thoracic aorta ends just above the diaphragm, and from here the abdominal portion of the aorta begins. The thoracic aorta (TAo) is a focus of major interest (ROI) in recent and older studies - including those of Klipstein et al., (1987) and Bogren et al., (1999), and recent studies. The abdominal aorta, reviewed by Litmanovich et al., (2009), extends from the diaphragm to the level of the fourth lumbar vertebra and further develops into bifurcation and more single and paired arteries. Importantly, it is the variations and differences in the aorta, e.g. the aortic valve type (Choudhury et al., 2009), the wall structure, the
arch angle, the bi-furcating angles, the changing diameters, and other different branch features and shapes with their associated flow patterns that can in a combination of ways lead to pathologic consequences.

The changing diameters of the aorta are of particular clinical interest and often determined for assessment. Using MRI modality and regarding normal limits of the aortic dimensions (at the pulmonary level), diameter of ascending aorta can reach up to $30 \pm 4$ (mm) and $24 \pm 4$ (mm) in the descending thoracic aorta in young adults (Wolak et al., 2008).

The aorta wall (Figure 2.6) is composed of three structurally different layers of tissue. These layers starting from the endothelium lined lumen side are the tunica intima, the tunica media and tunica adventitia. The average thickness of the ascending aorta wall average has been determined as 2.8 (mm) with no significant association with age or gender by Turkbey et al., (2014).

Figure 2.6: Idealized structure of a healthy aortic wall - depicting the three basic structural tissues: the intima (I), media (M) and adventitia (A). (Gasser et al., 2006).

Generally, these layers are made up of elastin, collagen, smooth muscle and endothelial cells that together give the aorta its elastic and tensile properties; and contribute to the vasodilating and vasoconstricting effects. Varying degrees of structural changes occur in all layers of the aortic wall during aortic functions and processes. The basic structure is depicted in Figure 2.6. Tunica Intima is the innermost layer of the aorta and it provides a barrier between the blood plasma and underlying
connective tissue. The primary function of endothelium is to retain the plasma and formed elements of blood within the circulation by forming a semipermeable membrane between the blood and tissues, thus, allowing nutrients to be transported rapidly. It also secretes the vascular regulation and anti-hemostatic agents and a clotting factor, thereby preventing thrombosis. Endothelium is associated with the inflammatory defence against pathogens. Disordered endothelial function could lead to the development of arterial atheroma (Levick, 2003). The Tunica Media made up of concentric sheets of smooth muscle tissue and high-density elastic fibres is usually the thickest layer. It has an externally bounding elastic membrane. The elastic fibres make the wall extremely resilient, allowing the tolerance of the pressure changes within cardiac cycle and smoothing the surging pressure and flow waves (Windkessel function). Tunica Adventitia is a sheath of connective tissue consisting of collagen fibres and scattered bands of elastic fibres.

The thickness ratio of intima/media/adventitia in aorta is found to be 1/6/3 in normal aorta (Gao et al., 2006). In their review, Tsamis et al., (2013) elaborated on the connective fibres and structure of the human aorta in aging and disease. The normal aorta has a high degree of elasticity that aids it to propel blood from the left ventricle to the systemic vasculature and a microstructure and architecture that supports this function. The microstructure is made up of elastin and collagen, micro fibres that respectively give the elastic properties and strength to the aortic wall. According to several studies, it is the change in the quantity, composition and architectural structure of these fibres that lead to mechanical and functional changes associated with one or the other of the known aortic diseases. Importantly, it has been found that in large arteries like the aorta, the loss in quality and quantity of elastin and alteration to its architecture with progressing age lead to a loss in wall compliance; and this in turn leads to both a decrease in the distal blood flow and an increase in aortic pulse pressure. Further, a large pulse pressure (PP) is said to suggest a stiffened aorta, the increased (wide) PP has been shown to be a very strong predictor of cardiovascular mortality, especially of coronary mortality, (Benetos et al., 2000). In a recent study, Tsamis et al., (2013) demonstrated that the delamination strength of ascending thoracic aortic aneurysms (ATAA) was lower than that of non-aneurysmal ascending thoracic aorta (ATA) control. Further, the reduced strength was more pronounced among bicuspid (BAV) vs. tricuspid aortic valve (TAV) patients, suggesting a different risk of aortic dissection for BAV patients.

**Tricuspid Aortic Valve (TAV)**

The normal aorta has a three-leaflet valve, the tricuspid aortic valve (TAV) shown in Figure 2.7. This valve has three cusps known as the right coronary, left coronary (named in correspondence with the Valsalva sinuses that give rise to the two main coronary arteries) and non-coronary. These cusps are very similar in size and provide unrestricted systolic opening. The aortic cusps have a semilunar attachment to the aortic root and a free margin where they have an increased thickness and a central
nodule (of Arantius). The insertions of adjacent cusps meet at the level of the sinotubular junction, forming the commissures. The other known malformed variants of the valve are the unicuspid, bicuspid, and the quadricuspid.

**Abnormal Bicuspid Aortic Valve (BAV)**

The BAV, depicted in Figure 2.7, is the most common congenital heart defect affecting 1-2% of the population. In the BAV anomaly, the cusps are fused during valvulogenesis with the resulting morphological changes characterized by a mismatch between the total length of the free edge and the circumference of the aortic root, as well as thickening and calcification of the leaflets, often leading to abnormal function in the valves (Katayama et al., 2016).

![Tricuspid Aortic Valve (TAV) and Bicuspid Aortic Valve (BAV)](image)

*Figure 2.7: Images of tricuspid and bicuspid aortic valves (Adapted from A.D.A.M., Inc.)*


There are a variety of BAV types that can be congenital or acquired. However, they are more often congenital than acquired. The acquired BAV occurs when there is a fibrous fusion between the left and right cusps of pre-existing TAV. Sievers and Schmidtke, (2007) have classified BAV into three major types as bicuspid with no raphe, with one raphe and with two raphes, whilst Schafer et al., (2008) identified and categorised the leaflet morphology of the BAV into three types namely: Type 1- fusion of the right and left coronary cusps (R-L BAV), Type 2- fusion of the right and non-coronary cusps (R-N BAV) and Type 3- fusion of the non-coronary and left coronary cusps (N-L BAV). In generally terms, BAV is a deformed aortic valve with two functional cusps or leaflets, which are often unequal in size. BAV is generally diagnosed late in adulthood when the deterioration of the abnormal leaflet becomes clinically evident. BAV patients are associated with aortic root and ascending aorta...
aneurysm with increased risk of developing aortic dissection and serious complications amongst other diseases. Many of the studies carried out so far have been on the left-right coronary cusps fusion type and it has been reported that this morphological type is more common in men. Significantly, BAV is known to be a disease of both the valve and aorta and because of this added extent of area affected, clinical and surgical decision-making is more complicated and many patients that need to undergo aortic valve replacement will also need aortic root surgery. However, with or without surgery, patients with BAV require continued surveillance. In emphasis, Siu et al., (2010) have stated that though recent studies have improved our understanding of the genetics, the pathobiology, and the clinical course of the BAV disease, there are questions still unanswered.

With age, and usually in adulthood, the abnormal stress across the valve leads to calcification. Individuals with BAV are more likely to develop calcific aortic stenosis (AS) than those with normal TAV and it has been suggested that geometric variations in BAV classification maybe a contributing factor to the high incidence of stenosis in patients with BAV. Arteriosclerosis, Aneurysm and dissection are the three most concomitant diseases of the thoracic aorta with significant differences in shear stress measured in the aorta with TAV and that with a BAV. These differences are attributed to anatomic valve form and haemodynamic differences. In a study of patients with TAV and BAV valve types with aneurysm, it has been found that blood pressure and wall shear stress are key haemodynamic predictors of aneurysm dilatation and it has been suggested that dissimilarities in presentation are most likely associated to aortic valve type anatomy, (Pasta et al., 2013). Dilation of the aorta is a common and frequent complication in patients with BAV and a recent study by Ruzmetov et al., (2015) aimed to determine the relationship between the subtype of leaflet fusion, right and noncoronary leaflet (R/N) fusion versus right and left leaflet (R/L) fusion, and the patterns of aortic dilation and valve dysfunction in young patients (range 0 to 40 years) with BAV. They found that patients with R/N fusion were more likely to have ascending aorta dilation, whereas patients with R/L fusion were more likely to have dilation of the aortic root. In addition, patients with R/N fusion presented at a younger age and were more likely to have aortic stenosis. Their study has brought up a few conjectures about BAV morphology and associated aortic diseases, such as the influence of BAV subtype on the shape of aneurysm. Their study has also generated debates and suggestions on genetic interplay, morphology and haemodynamics of the BAV, with requests for more informative data. Highlighting on the issues raised about disease management, clinical practice and procedures, Ruzmetov et al., (2015) have suggested that there may be a correlation between the valve subtype; a correlation that may come in time to influence operations. However, this suggestion is based on the fact that they have some data available which they look to present in the near future.

Quadricuspid aortic valve (QAV): it is noteworthy and useful to know that apart from the abnormal BAV, there is the less known quadricuspid aortic valve (QAV). The QAV is a rare type with an
estimated prevalence of 0.013% to 0.043%. Its diagnosis, clinical course, and management are less well defined relative to other aortic valve abnormalities (Jagannath et al., 2011). Most often, QAV is an isolated finding coexisting with random concomitant lesions. As expected, the position of the coronary artery ostia relative to the sinus of Valsalva in QAV differ compared to TAV.

2.1.3 Thoracic Aorta Diseases

Atherosclerosis is a common disease that affects large and medium-sized arteries. It is caused by the deposition of lipids and fats along the sub-endothelial vessel wall. Further deposition and accumulation of modified lipoproteins in the arterial wall compound the disease. The progression and development of atherosclerosis is linked to many factors, particularly nitric oxide (NO) which plays an important role in regulating wall homeostasis (Cooke, 1996). NO is a vasodilator agent secreted in the endothelium, the endothelium being a regulator of vascular tone. Though arterial NO production is stimulated by shear stress, leading to flow induced dilatation in large arteries which help increase the blood flow to muscles during exercise; recent studies have highlighted that physical size and conditioning are presenting with more alterations of haemodynamic variables, with more difficulty in interpretation (e.g. Duncker et al, 2008). Reduction of NO production and availability is thought to contribute to atheroma formation. Generally, atherosclerosis is a condition in which the vessel wall thickens due to progressive build-up of plaque and it is usually localized in the curvature and branching regions of the artery such as the aortic arch and major arteries. The major vessels that are affected by atherosclerosis are the coronary arteries, which supply oxygenated blood to the heart, and the carotid arteries, which provide oxygenated blood to the head and brain. It has been generally observed that atherosclerosis develops preferentially in branches and in curved regions of the arterial tree where blood flow is disturbed, and wall shear stress is low and oscillates in direction (Cooke and Dzau, 1997). In a recent study on shear stress signalling and its regulation of endothelial signalling, Zhou et al., (2014) concluded that it is the coordination of multiple signalling networks and not, individual separate pathways that link the mechanical signals to specific genetic circuitries, and which effectively orchestrate the mechanoresponsive networks and consequently evoke comprehensive genetic and functional responses.

Thoracic Aortic Aneurysm (TAA) manifests as a bulging in a weakened area of the thoracic aorta. The most common location of TAA is the ascending thoracic aorta. There are many other types of aortic aneurysm and TAA is the second most common type after abdominal aortic aneurysm (AAA), which occurs in the infrarenal abdominal aorta.

Thoracic Aortic Dissection (AoD) is defined as the progressive separation of the layers of the thoracic aortic wall. Usually, an intimal tear typically originates above the sino tubular junction (STJ)
and this tear breaking through the endothelium then allows blood to flow through the wall, consequently and progressively separating the media tissue along the axial direction of the aorta.

**Thoracic Aortic Stenosis** or coarctation of the aorta is a congenital valvular pathology where the aorta is narrowed causing impaired blood flow to downstream vessels and organs. Along with narrowing, stenosis has been found to bring about other pathologic features including cardiac hypertrophy and other degenerative changes in proximal aorta according to findings by Nicholas et al., (2011). There is increased blood pressure in the upper part of the body due to the small volume receiving the full stroke volume. Aortic coarctation (CoA) can be a causative agent of heart failure. 80% of patients with aortic coarctation (CoA) are known to have a bicuspid aortic valve. Importantly, aortic valve (AoV) disturbances are known to affect flow distribution and recent investigations by Wendell et al., (2013) have exemplified that it is necessary to include aortic valve morphology in CFD simulations towards identifying areas of deleterious haemodynamics in the thoracic aorta flow.

### 2.1.3.1 Geometric Influences

The thoracic aorta geometry is different amongst individuals and the characteristic features of dimension, branching, bending, twisting and non-planarity have a substantial influence on flow patterns and wall shear stress. Combining subject-specific data with computational fluid dynamics (CFD) is a very useful approach to researching blood flow ranges and variations in both normal and diseased arteries. Many CFD studies of the aorta and particularly of the thoracic aorta, always engage geometry as a crucial variable. A recent study by Bensalah et al., (2014) indicated that geometry is the strongest determinant of backward flow (BF). The aorta is non-planar, tortuous with diameters that vary both spatially and temporally. Bulk helical flow, has been found to be a consistent feature of intra-aortic flow in the healthy and normal aorta, (Kilner et al., 1993), and further, the characteristics of helical flow are generally attributed to the 3-Dimensional asymmetric aortic shape and valve type. It may be possible to correlate the aortic geometry to helical bulk flow quantities. It is probable that the curvature and tortuosity of the thoracic aorta can be directly related to the magnitudes and directions of helical structures and vortices in aortic flow, and indirectly to aortic diseases. A study of the femoral artery, by Wood et al., (2006) found a strong relationship between increased tortuosity and disturbed haemodynamic patterns. Cheng et al., (2010) studied aortic dissection, depicted in Figure 2.8, and found that the aortic geometry in type B aortic dissection can be extremely complex with variety of influences from patient to patient. It was found that topological characteristics, such as the extent of dissection, the curvature of dissected aorta, the location and size of the primary tear, and the narrowing scale of the true lumen, are highly patient-specific. Further, these morphological factors, which determine the flow pattern and haemodynamic conditions in dissected aorta, are believed to play an important role in the long-term development of aortic dissection.
Geometrical Analysis involves quantification of a number of geometric features including diameters, tortuosity, non-planarity and arch angle. Generally, for a better understanding of flow distribution and turbulence occurrence in the aortic arch, it is being emphasised that geometrical information is highly important in CFD analysis, (Tokuda et al., 2008). Essentially, geometric features are key parameters for haemodynamic evaluation and therefore need to be defined and measured in a consistent and reproducible manner.

Tortuosity, is used to convey information about the curvature at individual points on the centreline of a vessel segment, however, it generally does not have a common and acceptable definition, (Wood et al., 2006). Generally, tortuosity can be defined as the variation in blood vessel curvature. Curvature is an intrinsic feature of blood vessels. Increased curvature may be due to disease or aging of the vessel. Abnormal tortuosity is an important clinical indicator of various conditions. In spite of its importance, the evaluation of tortuosity is usually limited to crude subjective assessment. There are a number of possible measures of tortuosity that have been proposed but there is no consensus yet on which is the most appropriated. Martin et al., (2011) expounded on a number of methods to measure tortuosity of the aorta including a definition based on the distance factor, which has many limitations; and alternative methods which include the net total curvature of the aorta computed as a line integral of local curvatures, the number of inflection points, angle change along vessel segments, and the standard deviation of successive coordinates along the vessel midline. Importantly, Martin et al., (2011) suggested that a useful measurement method of tortuosity should have a number of features reflecting the clinician’s subjective assessment of the amount of tortuosity, including ability to detect variations and extent of the vessel. They explained that changes in curvature might affect aortic haemodynamics and therefore have clinical consequences. They highlighted the limitations of definition of tortuosity and its characterization and proposed a method that measures changes in
curvature using a fast Fourier transform (FFT) which is said to be a useful tool for the characterization of tortuosity that affords a compact, graphical means of evaluating vessel tortuosity. Wood et al., (2006), evaluating curvature and tortuosity of the superficial femoral artery as a possible risk factor for peripheral disease; employed the distance factor (DF) and two other measures of curvature and tortuosity. In their conclusion they reported a strong relationship between increased tortuosity and disturbed haemodynamic patterns.

Further, in quantifying the non-planarity of the aorta, it has been suggested and reiterated in a view by King et al., (2002) that due to the great variety of geometries, a single measure of non-planarity can never fully characterize the aorta. The non-planarity of the aorta is an important factor that influences arterial flows and consequently influences the pathogenesis of various disorders as elucidated by Caro et al., (1996). It is important to find a means to quantify aortic non-planarity in order to correlate the dynamic curvature data and variations with flow patterns and wall shear stress.

Arch Angle. In consideration of the non-planarity and configuration of the aortic arch, when taking measurements of the arch angle it is important to identify and define the measuring plane. Yoshii et al., (1988) introduced two characteristic angles: one is the angle between the ascending aorta and the ascending arch leg, and the other between the ascending and descending arch legs. These angles are quantitative measures of the distortion of the arch. Agnoletti et al., (2008) found that sharper angulation of the aortic arch is associated with early pulse wave reflection.

2.1.3.2 Haemodynamic Influences

Blood flow is dynamic and constantly changing both spatially and temporally as blood is pumped from the heart and pulsating throughout the cardiac cycle. Features of blood flow are affected by vessel geometry, blood density and viscosity. In the cardiovascular system, haemodynamic parameters including blood velocity and pressure are constantly changing. These parameters affect local conditions and play a role in the aetiology of many diseases. Wall shear stress (WSS), a force due to blood flow that acts tangentially on luminal wall is known to contribute to progression of many diseases, including atherosclerosis, aneurysm and dissection amongst others. WSS is a biomechanical function of the velocity gradient of blood on the endothelial surface. Contrary to theory, WSS is not constant along the arterial tree and Reneman and Hoeks, (2008) used this important understanding in their study on in vivo WSS and consequences for the design of arterial system, and categorically concluded that it should be learned and understood that “in any particular artery, mean shear stress will be higher, the smaller the animal is”. Kazakidi et al., (2009) found further evidence for age- and species-related differences in WSS patterns, by examining endothelial morphology around branches. Moreover, endothelial cells and their nuclei are known to align with the predominant flow direction and elongate with increasing shear. WSS acts on endothelial cells that line the vessel wall, and has
been particularly correlated to atherosclerosis. Ando et al., (1987) experimentally showed that low WSS caused migration and proliferation of endothelial cells and, Cho et al., (2000) highlighted on common signalling pathways that induce migration and suppress apoptosis. Significantly, the endothelium is highly sensitive to flow characteristics and to the accompanying hemodynamic forces particularly shear stresses. Within large arteries, atherosclerotic lesions develop at predictable sites of complicated flow where separation, transient flow reversals, flow and average low shear forces are common characteristics. Davies (2008) remarked that in vivo studies need to meet the challenge to dissect the endothelial mechanotransduction mechanism that contributes to the susceptibility of inflammation and atherosclerosis. This remark suggests a call and need for a better understanding of the synergism between haemodynamic factors (e.g. wall shear stress) and endothelium transcription. Further, the distribution of WSS is closely related to plaque vulnerability. Importantly, arterial wall remodelling is regulated by WSS, e.g. arteries enlarge in response to high WSS.

2.2 Medical Imaging

Medical imaging allows for ex and in vivo measurement of detailed structures of the body (anatomy, bones and tissue etc.) for physiological analysis in health and disease. It incorporates radiology and many technologies including X-ray radiography, medical ultrasound and magnetic resonance imaging (MRI) amongst others. There are many imaging modalities used specifically to measure anatomy, blood flow and instantaneous blood velocity. The more known types and accepted modalities are - hot film velocimeter and laser Doppler anemometry for (ex vivo) point velocity measurement; computer tomography (CT) used to obtain excellent anatomic images, ultrasound (also known as sonography or ultrasonography) is used to image body organs and tissues and to detect blood flow. CT has been found to be an excellent imaging modality for diagnosing aortic dissection. It is a widespread and commonly available modality in use at hospitals. Echocardiography (ECG) – a simple test used to check the rhythm and electrical activity of the heart; whilst positron emission tomography (PET) is an imaging system used to observe metabolic processes in the body, to assess tissue and organ function and to detect early signs of disease; and MRI is usually employed to obtain both anatomic and blood flow data of the human aorta. The subject of imaging modalities is thoroughly reviewed and described in the text, Webb’s physics of medical imaging (Fowler, 2012), whilst MRI is comprehensively explained and described in relevant textbooks (e.g. Bushong, 2003). Phase-contrast MRI is an efficient and non-invasive technique for measuring blood flow in vivo, and has been commonly used in recent studies to examine flow in the human aorta (Frydrychowicz et al., 2008, Markl et al., 2011, Lorenz et al., 2014) The intrinsic sensitivity of MRI to flow, motion and diffusion offers the possibility to acquire spatially registered information simultaneously with the morphological data within a single experiment. The characterization of the dynamic components of blood flow and
cardiovascular function provide insight into normal and abnormal conditions, with considerable progress being made in recent years by many recent studies. Cheng et al., (2015) in a recent study objectively assessed and characterized the haemodynamics and blood profiles in patients with implanted BioValsalva composite valve conduit. MRI has very high diagnostic accuracy and has become popular and widely accepted by clinicians as a valuable tool for diagnosis and management of cardio-vascular diseases; and it is being used routinely for measurement of disease severity and the assessment of patient response to medical therapy and surgical intervention (Stankovic et al., 2014).

4D flow imaging with MRI (i.e. time resolved phase-contrast MRI using velocity encoding along all three flow directions and 3D anatomic coverage) as a technique has been further developed over the last few decades to provide not only morphological information on cardiovascular anatomy, but also functional information on cardiac perfusion, myocardial viability, and blood flow. This functional information may allow a more instantaneous and thorough assessment of cardiovascular diseases with treatment decisions made.

2.2.1 Magnetic Resonance Imaging (MRI) of the Aorta

MRI, a non-invasive means of creating images of soft tissues in vivo by detecting differences in atomic spin due to magnetic field, has become an important tool for the clinical evaluation of patients with cardiovascular disease. Since its introduction in the late 1980s, 2-dimensional phase-contrast (2D PC MRI) has become a routine part of standard-of-care cardiac MRI for the assessment of regional blood flow in the heart and great vessels because it “provides better access to all segments of the aortic and pulmonary system” (Gabbour et al., 2015). More recently, time-resolved PC-MRI with velocity encoding along all three flow directions and 3D anatomic coverage (also termed 4D flow MRI), has been developed and applied for the evaluation of cardiovascular haemodynamics in multiple regions of the human body. 4D flow MRI allows for the comprehensive evaluation of complex blood flow patterns by 3D blood flow visualization and flexible retrospective quantification of flow parameters. This spatio-temporal retrospective analysis can be used to quantify blood flow in selective regions of interest.

2.2.1.1 Basic Features and Terminology in MRI

The MRI signal provides information about the spatial frequency content of the image rather than directly about the spatial positioning of the information in the image, (Bushong, 2003). In MRI, there are many techniques and combination of options that are applied to get the best anatomic and haemodynamic reading and understanding of the region of interest (ROI). Towards a clearer understanding of MRI sequences obtained from routine clinical data acquisition and used in research, a few of the important MRI system features and parameters are first enumerated and described below.
**Tesla, (T)** is the unit of measurement of the magnetic strength of an MRI system, i.e. the measure of magnetic flux density. The MRI systems commonly employed in medicine and clinical research are usually 1.5 or 3T. The Siemens 3T Magnetom MRI is a recent system with improved imaging capabilities. In the MRI system operation and processing, the primary magnetic field is called $\beta_0$, which refers to static permanent magnetic field, e.g. 1.5T or 3T in megahertz. At 1.5T, $\beta_0$ is equal to 63.9 MHz (i.e. 1.5 T x 42). The hydrogen atoms in the body align to $\beta_0$ in a parallel or anti parallel manner.

**Precession** - the protons spin along the longitudinal axis of the magnetic field. This axis is orientated along the long axis of the body (patient). The spinning of the protons is known as precession and the rate or frequency of spin is called the Lamour frequency. The frequency changes in proportion to the magnetic field strength.

**Magnetic field gradients** are an essential and inherent part of an MR scanner. Along with the main magnetic field, $\beta_0$, the MRI is enhanced with three sets of secondary magnets or gradient coils which give MRI the capacity to image directionally in the x, y and z axes. The gradient coils (named x, y and z according to the direction along which they act) alter the strength of the primary magnet. The gradient coils generate magnetic fields directed along the z axis but varying linearly in x, y and z directions, consequent to the change in the magnetic strength, the precession frequencies between slices change. Importantly, the change in magnetic field strength due to the gradient coils allow for the spatial encoding for MRI images in the sagittal (x), coronal (y) and axial (z) axis or image localization. The way in which the gradients are used depends upon the application (Fowler, 2012).

**Gradient echo** (GE) is a sequence produced by reversing the direction of a magnetic field gradient or by applying balanced pulses of magnetic field gradient before and after a refocusing radio frequency (RF) pulse so as to cancel out the position dependent phase shifts that have accumulated due to the gradient. An important and useful parameter in GE sequencing is the Flip Angle, defined as the angle through which the spin axis of protons is flipped. GE was introduced to get shorter imaging times by introducing flip angles much smaller than 90°.

**Velocity Encoding** (Venc) - In radiology and for MRI velocity information capture, VENC (Venc) stands for velocity encoding, a parameter that has to be specified before performing a PC MRI or MRA study. Venc, (often encoded in cm/s), needs to be chosen to encompass the highest velocities likely to be found within the vessel of interest. It is typical to apply a Venc of 150 cm/s for aortic measurements, (Markl et al., 2011). In selecting a Venc, it is necessary for the user to define an upper limit. By definition, Venc is the maximum velocity (positive or negative) that can be detected without
error. When actual velocities (vessel) are higher than Venc, aliasing occurs. Defining a lower Venc reduces noise and possible degradation effect of images caused by noise. However, PC MRI velocity noise is directly proportional to Venc and inversely proportional to signal-to-noise ratio (SNR) in the corresponding magnitude images and it therefore necessary to get the Venc value right. Generally, most MR sequences demonstrate more or less significant sensitivity to flow, which can lead to artifacts in many applications. A theoretical analysis and study about velocity encoding and imaging (Markl, 2005) showed that the intrinsic sensitivity of MRI to motion can be used to image vessels and also to quantify blood flow and tissue motion. This is based on the fact that local spin magnetization is a vector quantity; in addition to magnitude phase images can be extracted from the measured MR signal. Magnitude and phase images can be derived from the length and transverse magnetization. In combination with appropriate encoding gradients, phase images are motion sensitive and can be used to directly measure the local velocities of moving spins on pixel-to-pixel basis, Markl et al., (2012).

Venc is an important and required user defined PC MRI parameter. It represents the maximum flow velocity that can be acquired. Generally, and as explained by Lotz et al., (2002), the more the encoding velocity matches the real velocity of the region of interest, the more precise the measurement becomes. Importantly, when the underlying velocity exceeds the acquisition Venc setting, velocity aliasing can occur which is typically visible as a sudden change from high to low velocity within a region of flow. If aliasing artifacts are present, accurate flow visualization and quantification may be compromised unless antialiasing correction can be successfully performed (Lotz et al., 2002). Alternatively, the Venc can be increased and the acquisition is repeated to avoid aliasing. However, velocity noise is directly related to the Venc. Therefore, whilst selecting a high value for this parameter may alleviate the issue of velocity aliasing, the high value will also increase the level of velocity noise in flow velocity images. As a result, the Venc should ideally be selected as high as needed to avoid aliasing but as low as possible to reduce velocity noise. As a general rule, in order to capture the best image quality, the chosen Venc should represent the physiological velocity of the vessel of interest and be adapted to the measurement of interest and present hemodynamic conditions. Typical settings for Venc are: 150-200 cm/s in the thoracic aorta, 250-400 cm/s the aorta with aortic stenosis or coartation, 100-150 cm/s for intra-cardiac flow, 50-80 cm/s in large vessels of the venous system. If a large imaging volume with various vessels is examined there may be no optimal Venc setting and the value has to be chosen in accordance to the clinical question, Stankovic et al., (2014). Usually, a dedicated set of imaging parameters and sequences are employed for the MRI acquisition for flow study of the aorta, e.g. as employed by Stalder et al., (2008) where all volunteer scans were performed with identical Venc of 150 cm/s, i.e. Venc_x,y,z = 150 cm/s.

Markl et al., 2011, used flow sensitive 4D MRI to study the reproducibility of flow and wall shear
stress in the aorta. Both the scan and rescan reproducibility, as well as observer variability of flow sensitive (4D) MRI in the aorta for the assessment of blood flow and global and segmental WSS were investigated.

**Image Matrix**

Due to storage constraints, the image is sampled in space and in time within the image matrix - the layout of the rows and columns that contain the numbers that represent intensity in cells. Each digital MR image consists of a matrix of imaginary cells with each having various brightness levels (the grey scale). The brightness of a cell is determined by the computer generated number on the cell whilst the size of the imaging matrix is determined by the characteristics of the imaging system and the capacity of the computer. Spatial resolution is limited by pixel size. It can be improved by using a larger image matrix.

**2.2.1.2 Recent Advances and Applications**

MRI has grown as a diagnostic tool since it was first developed. There has been enormous progress made in the development of a variety of new techniques that ensure highly reproducible measurements. The acquisition time has been improved on and shortened considerable by imaging approaches (e.g. sparse sampling techniques, multiband echo planar imaging, and multidimensional parallel imaging) that enable the acquisition of multiple slices at a very fast rate (Markl et al., 2015). Image reconstruction algorithms are also being investigated, developed and improved on for migration to different model platforms (Gillam et al., 2016). The availability of a variety of techniques has brought about new applications. The areas and aspects of the aorta and functions that can be examined have increased and the advancement of MRI is helping to increase our understanding of the thoracic aorta. Along with the improved measurement techniques there are major improvements to the modality strength. New improved MRI machines with stronger double field strength of 3T are superseding the 1.5T machines, and many hospitals and radiological functions are migrating to the use of 3T for routine clinical purposes. There are field strengths up to 10 Tesla now available for some specialised areas of research. There is an emergence of new pulse sequences towards the optimisation of imaging for investigating thoracic aorta diseases and the application of these pulse sequences is improving the accuracy of research findings. However, the confidence and experience of the clinician and researcher and observer performing and interpreting the techniques are crucial for diagnostic accuracy.

**Phase-contrast (PC) MRI** can be used to measure and quantify pulsatile blood flow in the human vascular system. PC MRI methods encode macroscopic motion into the phase of the MR signal. The basic principle of MRI technique was introduced by Carr and Purcell, (1954), who reported the first observation of coherent motion on the MR-signal, and by Hahn (1960), who applied flow-sensitive
MRI to detect seawater motion. Essentially, traditionally, and until recently MRI of flow using phase contrast method is accomplished using techniques that resolve single-directional flow in two spatial dimensions (2D) of an individual slice. 3D spatial encoding combined with three-directional velocity-encoded phase contrast MRI (or 4D flow MRI) is now developed and has drawn increased attention and use in studies. The use of 4D MRI may be necessary and key in the investigation of blood flow in certain pathologies like thoracic aorta disease, e.g. thoracic aortic dissection.

A few key examples of the investigatory studies using 4D MRI are described. Kilner et al., (1993) examined the distribution of secondary flows in the human aorta of healthy subjects and were amongst the first to observe and investigate helical flow in the aortic arch, which was found to be predominantly right-handed. Further, differences were found between subjects in the way that helical flow continued from the arch regions over into helical flows in the descending aorta. Four-dimensional (4D) MR velocity mapping (from time-resolved cardiac gated three-directional velocity data) has been developed to study normal flow patterns in the thoracic aorta, (Bogren and Buonocore, 1999). More recently, Markl et al., (2012), Cheng et al., (2015) amongst many researches have shown that 4D flow MRI offers the ability to measure and to visualize the temporal evolution of complex blood flow patterns within an acquired 3D volume. MRI advancements and methodological improvements permit the acquisition of 4D flow MRI data encompassing individual vascular structures and entire vascular territories such as the heart, the adjacent aorta, the carotid arteries, abdominal, or peripheral vessels within reasonable scan times. In a recent review (Markl et al., 2016) new and currently used 4D flow MRI methods including the cartesian and radial data acquisition and approaches for accelerated data acquisition, cardiac gating, and respiration control were introduced. This article gave an overview of the potential of the 4D imaging technique for different parts of the body from head to peripheral arteries.

Examples of studies that have taken advantage of both 2D and 4D PC MRI include Lorenz et al (2014), who used 4D flow MRI to investigate aortic valve disease and to demonstrate altered haemodynamics due to changes in aortic geometry. Essentially, Lorenz et al used 4D flow MRI to test the feasibility of quantitative helicity analysis using equidistantly distributed 2D planes along the entire aorta. Their study provides a quantitative analysis and detailed evaluation of the spatial and temporal distribution of helical flow (main direction and intensity of helicity) within the aorta of healthy subjects and BAV patients. The study illustrated that the quantification of helical flow is feasible. The study showed a good inter-individual agreement and repeatability of the method in healthy subjects and considerable increased helical flow in BAV patients. The method has the potential to serve as a reference distribution for comparisons of helical flow between healthy subjects and patients or between different patient groups. However, Lorenz et al., advised that this study does not allow a determination of the causal factor, i.e., whether an increase of helicity creates changes in
the aortic morphology/valve or vice versa but rather that, the investigation of helicity and its quantification, together with other 3D flow characteristics is for more understanding and to predict the development of aortic diseases involving modifications of the vessel wall or the AoV.

There are many improvements and advancements to MRI and PC MRI in the last decade. Major improvements have been in the types of machines and imaging protocols and sequences towards a standard that will give similar and interpretable results across board with minimised errors. Advanced technical developments, like parallel imaging techniques, e.g. k-t GRAPPA, have improved overall scan times to about 8-12 minutes for 4D flow MRI of the aorta and 10-20 minutes for whole heart coverage. This short and reasonable acquisition times have made the use and application of 4D flow MRI in a clinical setting more feasible. 4D flow MRI is able to provide an improved assessment of arterial haemodynamics, which can aid in the diagnosis and therapeutic management of cardiovascular diseases. Gabour et al., (2014) in a comparative analysis of 4D flow MRI blood quantification of the aorta compared to 2D PC MRI found excellent correlation and agreement between 2D P-C MRI and 4-D flow for net flow and excellent correlation with good agreement for regurgitant fraction, which is the amount of blood regurgitated into a cardiac chamber divided by the stroke volume. However, the study found that peak velocities were significantly underestimated (P = 0.32) by 2D PC MRI when compared to Doppler echocardiography (echo), the reference standard for blood velocity analysis, whilst 4 D flow analysis resulted in higher (aortic: P=0.001) or similar peak velocities relative to echo. With these results, Gabbour et al., (2015) concluded that 4D flow has the potential to become a clinical alternative to 2D PC MRI. Further, on advances and pulse sequence techniques for PC MRI data acquisitions, Untenberger et al., (2015) have proposed a method that introduces asymmetric gradient echoes for highly undersampled radial FLASH MRI. The set of asymmetric gradient echo sequences have been suggested to offer significant technical advances for real time phase-contrast flow MRI, where the incorporation of velocity compensation in slice and read directions without compromising temporal resolution sets the basis for quantitatively accurate studies. Using the method, the resulting temporal gain, is said to offer full velocity compensation for real-time phase-contrast flow MRI, which minimizes false-positive contributions from complex flow and further enhances the temporal resolution compared with acquisitions with symmetric echoes. This proposed method needs further validation and extensive application. Towards more advancement, an article, (Editorial), Magnetic Resonance in Medicine at 30, considering the future of MRI in the coming 30 years has suggested refocusing on highly relevant areas and topics such as k-space trajectories, molecular agents and rapid imaging that helped shape the fields of MRI and spectroscopy in the last 30 years.
2.3 Experimental Studies of the Thoracic Aorta

Experimental phantom and in vivo studies of the human aorta have been carried out over many decades to examine blood flow in the human aorta and these studies have shown that flow in the human aorta is complex, with possible occurrence of turbulent flow. Turbulent flow is characteristically different from laminar flow as it is generally chaotic and distorted with time varying features. It may occur when the Reynolds number, \( \text{Re} \) - defined as the ratio of inertial to viscous forces, is greater than 4000. Turbulence is a state of motion characterized with random and chaotic three-dimensional vorticity. Where turbulence occurs, it usually dominates other likely flow regimes and phenomena, and results in increased drag, energy dissipation, and mixing. Turbulent blood flow is a natural occurrence in the human aorta. It has attracted much interest in the last five decades, because of its likely contribution to endothelial transcriptions, flow transport and altered haemodynamics. Though turbulent blood flow occurs naturally in the aorta, the exact contribution of turbulence to a variety of pathophysiology effects is not clear.

Experimental studies can be carried out using different imaging modalities or measurement techniques, e.g. hot film probe, CT, MRI as well as laser or optical methods, such as particle imaging velocimetry (PIV). These methods have been employed either separately or in combination to acquire anatomic and flow information for analysis. There are known limitations in some of the modalities that can affect the accuracy of results and caution need be taken in comparing results of aortic flow studies that have employed different modalities for data acquisition. Notwithstanding the limitations, these studies have been instrumental in the development of flow models for the assessment and analysis of aortic flow and a few of these studies will be discussed in detail below.

2.3.1 Systemic and Regional Analysis of a Constricted (Stenosed) Aorta

In investigating flow patterns, Ahmed and Giddens (1983a, 1983b, 1984) in experimental studies found that the extent to which flow is disturbed is dependent on the inlet Reynolds number (Re) and the flow conditions proximal to the stenosis. Ojha et al., also found discrete frequency velocity oscillation turbulence and variations in measured wall shear stress downstream of the stenosis with high values recorded after peak flow. They also found as expected that the velocity profiles in pulsatile flows were relatively blunt when the Womersley number, \( \alpha \), (which is the ratio of unsteady forces to the viscous forces) is large compared to the parabolic flow in a Poiseuille flow. Similarly, it was observed and noted (Nichols et al., 2005) that with increase in Womersley number from 3.34 to 6.67, the velocity profile became progressively flatter.
2.3.2 Turbulence in normal and abnormal subjects

Because of the possibility that turbulence may play a role in a variety of pathophysiological processes, it is important to determine whether turbulent flow, in fact, occurs within the human body (Stein and Sabbah, 1976). The study by Stein and Sabbah, and many other experimental studies including Mustard et al., (1962), Smith et al., (1972) investigated the existence of turbulence in the aorta. The quantitative relationship between turbulence induced thrombosis (albeit in dogs) and the magnitude of turbulence have been investigated (Stein and Sabbah (1974). Further, on the possibility of turbulence in the human body, Stein and Sabbah (1976) investigated the nature of flow in the ascending aorta of subjects with normal and diseased aortic valves, by using hot film anemometry to measure point velocity in the human aortic valve region and along the ascending thoracic aorta and innominate artery. This study showed that highly disturbed flow occurred in the ascending aorta of normal subjects, and that turbulent flow occurred within the ascending aorta of normal subjects under some circumstances, such as during states of high cardiac output. Stein & Sabbah (1976), also reported observing, disturbed and turbulent flow in subjects with abnormal, bicuspid aortic (BAV) valve function. They observed that this disturbed, turbulent flow phenomenon was consistent in subjects with abnormal valve function. Further, Kilner et al., (1993), Bogren et al., (1995a) and other recent studies have reported consistent, disturbed and turbulent flow in subjects with abnormal valve function. Turbulent flow in the ascending aorta was routinely observed in subjects with aortic valvular disease and the magnitude of turbulence, as judged by the energy of the fluctuations (turbulent energy density) was found to be highest in subjects with aortic stenosis.

2.4 Computational Modelling of Aortic Flow

In order to gain more understanding of the local haemodynamics of the human aorta, and to obtain haemodynamic indicators that are impossible to measure, recent studies have applied and used PC MRI and CFD to further investigate blood flow in the human aortic thoracic aorta. Tan et al., (2009) and Cheng et al., (2010) used in vivo aorta anatomic and flow data acquired from PC-MRI. CFD studies have used both idealised and realistic 2D and 3D geometry models. Through robust equipment design and improved pulse sequencing, PC MRI capabilities for acquiring anatomic and directional velocities have become highly developed with increasingly accurate results obtainable from PC MRI and CFD studies. These studies (using direct or indirect velocity mapping) have shown that there is turbulent flow in the human aorta. However, conceptualizing and mathematically describing and modelling the thoracic aorta require a strong understanding of the physics and physical model for simulation. It is necessary to critically assess the assumptions applied in simplified models of the thoracic aorta and arch branches, because the complex aortic flow structure and pressure are influenced by conditions imposed at the outlet boundaries. In case the assumptions applied in the
If a simplified model does not hold true, then a number of complex numerical strategies need be implemented to deal with the coupled problem.

Recent studies by Cheng et al., (2010), Cheng et al., (2015), and reviews by Morbiducci et al., (2015) have shown evidence that the implementation of methods for obtaining reliable subject-specific coupled models of the thoracic aorta is a challenging issue, and one that typically requires very expensive tuning of several parameters to obtain the correct flow rate distribution at all outlets; or requires measurement, often invasively, of both the flow rates and pressures at each of the terminal vessels. It is for the highlighted reasons that several authors including Grinberg and Karniadakis, (2008), Morbiducci et al., (2013), and Cheng et al., (2015) recommend or use, when possible, the imposition of clinically measured hemodynamic quantities. For the outlet BCs, the prescription of loss coefficients is suggested by Benim et al., (2011), who investigated extracorporeal and physiologic circulations in the human aorta by CFD. For the extracorporeal circulation conditions, a (corresponding) state analysis was applied, whilst for the physiologic circulation the pulsatile flow analysis was used. Blood was modelled as Newtonian and the SST model for turbulence was employed in all cases. This study showed that the SST model could provide a coherent treatment of flows with Reynolds numbers encompassing the transitional regime. Further in analysis, for physiologic circulation, the study observed that the time-averaged velocity field of pulsatile flow did not show remarkable differences to steady-state results, Benim et al., (2011).

### 2.4.1 Boundary Conditions

Boundary conditions (BCs) are an essential part of a CFD model and they dictate the amount of flow and specify fluxes like mass, momentum and energy into the fluid domain. For the physical boundaries (geometry location boundaries) there are three types of BCs namely, inlet, outlet and wall. The reliability and results of a simulation are strongly dependent on the correctness of the BCs imposed. A poorly defined BC can have a significant impact on the solution obtained. Careful consideration of BCs is needed to ensure physiologically relevant results. Morbiducci et al., (2013) recently examined the influence of assumptions made on BCs extracted from PC-MRI. This together with many other studies, including Moyle et al., (2006), Taylor et al., (2010) and Gallo et al., (2012), have shown that the way BCs are imposed in patient-specific models can influence the predicted haemodynamic scenario.

For subject-specific studies, inlet BCs are usually derived from measured volumetric flow rate waveforms. In general, the knowledge of flow rate waveform taken at the inlet section of the fluid domain (e.g. thoracic aorta) is in itself not sufficient to guarantee the existence and uniqueness of the solution in computational haemodynamics. This factor is a limiting one in a situation where subject-
specific simulations represent a powerful tool to complement the information given by clinical images and for this reason, Morbiducci et al., (2013) emphasised and recommended the prescription of additional constraints at boundaries for a well posed computational problem. One of the common ways to overcome this problem is to use a theoretically deduced velocity profile fitting the measured flow rate, which effectively turns a defective boundary data problem into a classical Dirichlet problem. In order to partially reduce some of the limitations arising from the imposition of defective BCs, Tan et al., (2012) acquired PC-MRI flow maps above the aortic root and proximal to the sinotubular junction (STJ) and used these data to obtain pixel-based time varying axial velocities to be prescribed at the inlet, while neglecting the in-plane velocity components. Morbiducci et al., (2013) compared different strategies for prescription of BCs and found that BCs “even when measured and specific–to-the-subject, might lead to misleading numerical representations of the aortic hemodynamics”. The first strategy they used was the application of measured PC MRI velocity profiles at the inlet section of the ascending aorta (AAo). This involved acquiring three components of the velocity at the AAo inlet section, and processing the phase images to extract velocity vectors for every voxel of the inlet section. They generated and compared two different inflow conditions: (1) PC MRI measured 3D velocity profiles; (2) PC MRI measured 1D velocity profiles - obtained by using the measured velocity component that is orthogonal to the inlet plane (i.e. the axial velocity component). Cheng et al., (2010, 2015) also successfully applied 3D velocity profiles at the inlet of AAo, similar to the strategy applied by Morbiducci et al (2013).

Turbulence Intensity is an additional parameter required as part of the inlet BC for turbulent models. Previous studies, e.g. Tan et al., (2008), applied an inlet turbulence level of 1.5% to represent initial perturbation in the flow, which would allow for natural and realistic transition to occur. It has been found that moderately low Tu values between 1.5% and 2% were able to capture experimental data well. Tu values above 2% were found to cause too rapid a flow recovery in post-stenotic regions, whilst Tu values below 1.5% caused flow to behave as a laminar flow. A recent study, Kousera et al., (2013), made a good attempt to find a suitable level of turbulence intensity at the inlet of the ascending aorta that could be used for the SST-Tran model.

Outlet boundary conditions are used to represent the exit conditions prior to the solution of the flow problem. Measured pressures or velocities are usually specified at the outlet. When there is more than one outlet in a CFD model, mass flow split among multiple outlets is commonly used. Benim et al., (2011) modelled blood flow in the human aorta under Newtonian flow conditions and employed the SST model for turbulence for all their model cases in order to provide a coherent treatment of the flows exhibiting Reynolds numbers encompassing the transitional regime.
**Wall boundary condition** is required in CFD simulations and it prescribes the state of the wall. Often, the wall is modelled as rigid, with no slip.

**Other Simulation Considerations and Assumptions**

Both laminar and turbulent flow regimes occur within the thoracic aorta, and these change both spatially and temporally. The varying and changing flow patterns cause the flow characteristics to vary widely throughout the flow domain and bring about a lot of complexity in solving the flow problem. In order to make an already complex system like the thoracic aorta together with its arch branches a more tractable problem, simulation models usually involve a number of assumptions. These assumptions may and often include Newtonian fluid, incompressible flow, and rigid wall and no slip conditions. These conditions and assumptions are further explained below.

**Newtonian viscosity:** Though blood is generally non-Newtonian, it can be assumed to be Newtonian in large arteries like the aorta, where shear rate is high. The molecular viscosity is assumed constant for a Newtonian fluid.

**Incompressible fluid:** Blood, like most liquids, can be assumed to be incompressible with a constant density. For an incompressible fluid, its density does not change for isothermal problems.

**Rigid wall:** the boundary wall is assumed to be solid, rigid, with a no-slip condition, which dictates that due to fluid friction there is no slip between the wall and fluid (e.g. between the arterial surface and blood) and \( u = v = w = 0 \).

These assumptions reduce the complexity of the system to a manageable level whilst preserving the salient features of the problem in hand. Further, these assumptions are usually justifiable and acceptable, except the assumption of rigid wall which is unrealistic as aortic walls are compliant and they expand and contract with the pulsating pressure. This limitation will be discussed in detail later.

### 2.4.2 Flow Patterns in the Aorta

Flow in the aorta is pulsatile with complex patterns, which may undergo transition from laminar to turbulent flow and relaminarisation during a cardiac cycle. The spatio-temporal variation is quite significant in the aorta and studies have shown substantial geometric and flow phase differences amongst individuals. These differences are better appreciated through CFD simulations of the thoracic aorta. Investigating flow patterns in the diseased aorta can be more difficult because of the high variety in morphology. A variety observed even in the normal aorta (Kilner et al., 1983). For a clearer understanding of the flow phenomena, analysing aortic flow using *in vivo* subject-specific data from PC MRI is desirable for aortic quantification and characterization. This is because flow patterns
vary with geometry, and for precise flow description and quantification it is best to prescribe the flow
data to its related geometry. The heart rate and the geometric angles, valve types and topologies
influence the flow and pressure waveforms, which are all important in determining the haemodynamic
patterns, characteristic quantities and condition of the aorta. In order to improve our understanding of
the patho-physiological aorta, there have been many investigations and visualizations of blood flow
patterns in the human aorta through experimental studies and CFD simulations. Blood flow studies of
the normal and diseased aortas have been carried out using idealised (phantoms), and real geometries
with both experimental data and subject-specific flow data applied in simulations. The velocity
mapping technique has become useful for providing realistic inflow BCs (inlet velocity profiles and
values), as shown by Torii et al., (2011) and Cheng et al., (2015). Helical flow and retrograde flows,
observed as common and consistent features of aortic flow in healthy cases (Kilner et al., 1993), occur
partly due to the geometry (curvature) of the arch and pulsatility of flow. These flow features may be
significant components of the circulatory dynamics that may be related to aortic diseases, e.g.
pathogenesis of atheroma in the arch. Morbiducci et al., (2006) investigated if the commonly
observed helical flow might be a signature of the blood dynamics of vein graft anastomosis. In a
recent study of the aortic valve dynamics by Moore et al., (2014), heart rates have been found to
influence vortex formation and development in the sinuses and these vortexes influence the
directionality and strength of shear stresses along the base of the leaflet.

In diseased aortas, previous and recent studies including Singh et al., (2015) and Cheng et al., (2010,
2015) have shown disturbed flow features in abnormal aortas. Flow pattern in the dissected aorta has
been found to be extremely complex with disturbed and recirculating flow dominating in both the true
and false lumen, Cheng et al., (2010). It is interesting to note that some other studies (investigating
fluid dynamics and valve design) have linked recirculation regions and stress levels, and it is
suspected that recirculation regions may promote thrombus formation, Simon et al., (2007). In their
study, Simon et al., used spatio-temporal averaging of the sustained loading on blood elements for
estimating induced blood damaged potential.

Recent CFD studies of the human aorta have shown that turbulent flow does occur naturally in the
thoracic aorta of subjects with normal valve functions. Canstein et al., (2008) used in vivo data in their
CFD investigations and showed the need for subject-specific models in haemodynamic investigations
of the human aorta. Importantly, subject-specific data and models allow for more refined and realistic
boundary conditions in CFD simulations. A number of studies that combined PC MRI and CFD to
study the aorta, have found haemodynamic parameters and variables that are associated with thoracic
aorta diseases. These parameters include wall shear stress (WSS) and flow reversal ratio (FRR)
amongst others. A study investigating blood flow in the thoracic aorta of normal volunteers has found
genometry to be a major determinant of flow reversal in the proximal and hypothesised that ascending
aorta (AA) backward flow (BF) and forward flow (FF) could be relevant markers of subclinical arterial wall age-related alterations, (Bensalah et al., 2014).

Generally, flow regimes in the aorta vary between laminar and turbulent at a range of Reynolds numbers. Studies on turbulence usually involve examining the dynamics in regions of vortical flow. These deterministic studies have collectively focused either on the large-scale vortices and their interactions, or on how the large-scale vortices interact with the small-scale vorticity field (George and Hussein, 1991; Hussein and George, 1990). Turbulence in high Reynolds number flows is a process through which energy is transferred from high-scales of motion to increasingly low scales of motion until the energy is dissipated by viscous effects at the wall. Further, turbulent fluctuations always have a three-dimensional spatial character, even in flows where the mean velocities and pressures vary in only one or two dimensions.

**Turbulent Kinetic Energy** (TKE) has been identified as a useful parameter in diagnosis of aortic coarctation. It has recently been found by Dyverfeldt et al., (2008) that it is possible to use MRI to estimate TKE. Following on from this, preliminary investigations by Lantz et al., (2013) showed that CFD modelling can provide additional insights with significantly higher resolutions compared with MRI. In the presence of coarctation of the aorta, Lantz et al in their findings emphasized that MR-based TKE measurements showed good agreement with TKE results from CFD and that the TKE measurements might serve as a useful marker when evaluating intervention outcome.

**Flow reversal ratio** (FRR), essentially the ratio of retrograde to antegrade flow, has been suggested to be a key determinant of renal syndrome and failure according to a recent study by Hashimoto and Ito (2015) who found that FRR was the strongest determinant of estimated glomerular filtration rate, and that higher FRR was associated with lower intrarenal forward flow velocities. Their results suggested that an increase in aortic flow reversal (i.e. retrograde flow from the descending thoracic aorta toward the aortic arch), caused by aortic stiffening and impedance mismatch, could reduce antegrade flow into the kidney and consequently deteriorate renal FRR.

### 2.4.3 Wall Shear Stress (WSS) in the Aorta

Barker et al., (2010) performed a pilot study examining WSS in BAV patients. In order to validate WSS measurement, the smallest eligible ascending aorta (AAo) with a diameter of 10 mm was chosen to build a flow phantom. A sinusoidal flow of ± 4.2 L/min was prescribed to a long straight tube (~ 1 Hz, Fig. 1 a) and the resulting temporal velocity fields were measured. The Womersley solution to the Navier-Stokes equations was employed to calculate the theoretical axial velocity profile and WSS. They found that the spatial distribution and magnitude of systolic WSS in BAV patients (~ 6.7 ± 4.3 dynes/cm²) differed significantly from control patients (~ 11.5 ± 6.6 dynes/cm², p = 0.03). The results
showed the shear rate index (SRI) metric, a measure of shear symmetry along the lumen circumference, to be significantly different ($p = 0.006$) and indicated a heterogenic pattern of dilatation in the BAV patients. It has been found that regardless of the initial mechanism driving aortic dilatation in BAV patients, an enlarged aorta will further alter spatial velocity gradients and therefore WSS at the aortic wall. WSS is a known pathophysiological stimulus leading to altered gene expression and extracellular matrix remodeling. As a consequence, the quantification of WSS is important in order to fully understand the progression of this disease at the cellular level.

Very few studies have used combined MRI and CFD to look into the effect of BAV on flow patterns. Wendell et al., (2013) in their study of BAV models with aortic coarctation showed that the impact of AoV could be included in CFD simulations to identify regions of altered flow and deleterious hemodynamics. In their study, all simulations were initially run with a time-varying plug velocity profile across the entire inlet face and the results were compared with simulations where the inflow profile was restricted by the time varying area delineated from MR images. There was evidence of altered flow patterns in BAV compared with TAV (Meierhofer et al., (2013).

2.5 Summary

The aorta is a complex 3D structure with nonplanar curvature, bends and branching, which give rise to complex multidirectional flow. For the purpose of computational modelling, the aorta is a large artery where blood can be assumed to behave like a homogeneous fluid, and the Navier-Stokes equations, i.e. the continuity (mass conservation) and momentum equations can be used to describe the fluid motion. Due to the functional importance of the aorta, accurate representation of the geometry and flow conditions is needed in modelling and simulations. As flow in the aorta is known to be naturally transitional and in the laminar-turbulent regime, it is crucial in CFD simulations to use suitable transport models and appropriate boundary conditions. The correlation-based SST-Trans model (Menter et al., 2006) has been tested and applied to normal and diseased aorta in a limited number of cases. This model will be employed in the present study and further tested for simulation of flow in aortas of TAV and BAV subjects. Details of the computational model will be described in the next chapter.
Chapter 3

3 Methodology

3.1 Introduction

This chapter details the methods and materials used in this study. On the basis of the existing literature about flow in the human aorta, a better understanding of blood flow in the thoracic aorta is sought through subject-specific CFD modelling and comparison of the thoracic aortic flow in subjects with tricuspid aortic valve (TAV) and bicuspid aortic valve (BAV). In vivo anatomic and flow images of the thoracic aorta of eight volunteers were acquired non-invasively by phase contrast magnetic resonance imaging. Seven of the volunteers have TAV, whilst one has a BAV. A physiologically relevant mathematical model for the thoracic aorta flow problem is developed along with the required boundary conditions. Details of data acquisition, image processing and computational models are given below.

3.2 Medical Data Acquisition

Eight volunteers were recruited for imaging of the thoracic aorta. Seven of the volunteers presented with normal tricuspid aortic valve (TAV), whilst one presented with abnormal bicuspid aortic valve (BAV).

Both the anatomical and flow images of the thoracic aorta were acquired using MRI. To ensure consistency, similar imaging protocols were adopted for all subjects. The subjects’ data for this study were provided by clinical researchers at the Royal Brompton Hospital and Hammersmith Hospital, London, UK. A 3Tesla (for 3 subjects) Magnetom Skyra (Siemens) and 1.5Tesla (for 5 subjects) Philips Medical System (Achieva) were used to acquire cine PC MR images. Details of the MRI sequence parameters are given in sub-section 3.2.1. The use of consistent imaging parameters can reduce possible inherent imaging and measurement errors, according to the study by Gatehouse et al., (2010), who evaluated offset errors for 3 MR scanners.

3.2.1 MRI Protocols

Pulse sequences are patterns of radiofrequency pulses and magnetic gradients that are used to produce an image. Various pulse sequences of cardiac MRI have been developed to reproduce arterial geometry and blood flow. These can be divided into two broad categories - the black blood (for
anatomy) and bright blood techniques.

**The Black Blood** technique engages spin echo (SE) sequences. The acquisition time of this sequence is generally longer compared to the gradient echo sequences used in bright blood. There is relatively little metal artifact in SE sequences and high resolution images obtained are often used to study the anatomy of the heart, thoracic aorta and other great vessels like the pulmonary vein.

**The Bright Blood** technique uses gradient echo (GE) sequences. Bright blood is usually for dynamic imaging and angiography. GE has fast imaging speed compared to spin echo. It is however, more susceptible to artifacts. Amongst its many other uses, GE is generally employed to assess blood velocity, flow, valvular disease and ventricular function. Phase contrast magnetic resonance imaging (PC MRI) uses GE sequences and is suitable for flow analysis. There are various modifications of GE imaging that are used to produce bright blood images with excellent contrast between the blood and myocardium. The steady state free precision (SSFP) is a set of GE sequences that is used in cine MRI. The SSFP is further enhanced in the sequence set called true fast imaging with steady state precision (TrueFISP). The SSFP TrueFISP sequence provides high temporal resolution and excellent contrast.

2D PC MRI provides a good access to all segments of the aortic and pulmonary system and is considered the standard for evaluating blood flow. However, it is limited to velocity analysis in 2D planes and, in most cases, to single direction velocity measurement which may be inadequate to characterize the complex 3D haemodynamics in the thoracic aorta. 4D PC MRI, on the other hand, has more coverage as it provides simultaneous assessment of 3D flow characteristics within a 3D volume and offers the ability to quantify blood flow parameters at selectable regions of interest retrospectively. Both 2D MRI and 4D (i.e. three spatial and one temporal dimensions) PC MRI acquisitions have been used in this study, and subject-specific images for both geometric and flow data required for the CFD analysis were obtained by the same (or similar) set of MRI techniques. For image segmentation, the MRI sequences used in this study included the half-Fourier acquisition single-shot turbo spin-echo (HASTE), and true fast imaging with steady state precision (TrueFISP). Flow mapping was carried out at various transverse planes in one or three directions. Sample images used in this study are shown in Figure 3.1 and Figure 3.2. The HASTE images (Figure 3.1) were used for delineation of the thoracic aorta geometry. Typical imaging parameters and relevant information about the scan sequences adopted in the study are summarized in Table 3.1.
**Figure 3.1:** Sample MRI HASTE axial cross-sectional images showing (a) the ascending and descending thoracic aorta (b) the aortic arch – used for aorta geometry delineation and segmentation.

(a) ![Sample MRI Image](image1)

(b) ![Sample MRI Image](image2)

**Figure 3.2:** Sample PC-MRI Images showing (a) magnitude image and (b) phase image.

(a) ![Sample MRI Image](image3)

(b) ![Sample MRI Image](image4)
### Table 3.1: PC MRI sequences used in this study

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Heart Rate (beats/min)</th>
<th>Venc (cm/s)</th>
<th>Scanning Sequences</th>
<th>Phase Encoding</th>
<th>Flip Angle (°)</th>
<th>MR Acquisition Type</th>
<th>Slice Thickness (mm)</th>
<th>Repetition Time, TR (ms)</th>
<th>Echo Time, TE (ms)</th>
<th>Imaging Frequency (MHz)</th>
<th>No of Phase encoding Steps</th>
<th>Echo Train Length (ETL)</th>
<th>Percent Sampling (%)</th>
<th>Percent Phase Field of View (%)</th>
<th>Patient Position</th>
<th>Pixel Bandwidth (Hz/pixel)</th>
<th>Pixel Spacing (mm²)</th>
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<tr>
<td>C1</td>
<td>C1 - 57</td>
<td>150</td>
<td>Thru Plane</td>
<td>COL</td>
<td>90</td>
<td>3D</td>
<td>2</td>
<td>4.8</td>
<td>2.39</td>
<td>63.89</td>
<td>260</td>
<td>1</td>
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<td>108.33</td>
<td>HFS</td>
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<tr>
<td>C2</td>
<td>C2 - 65</td>
<td>150</td>
<td>RL, AP &amp; Thru Plane</td>
<td>COL</td>
<td>20</td>
<td>2D</td>
<td>6</td>
<td>47.6</td>
<td>3.53</td>
<td>123.22</td>
<td>136</td>
<td>1</td>
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<td>68.75</td>
<td>HFS</td>
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<td>1.77 x 1.77</td>
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<td>150</td>
<td>Thru Plane</td>
<td>COL</td>
<td>15</td>
<td>2D</td>
<td>10</td>
<td>4.2</td>
<td>2.63</td>
<td>63.87</td>
<td>114</td>
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<td>2D</td>
<td>10</td>
<td>70</td>
<td>2</td>
<td>63.68</td>
<td>158</td>
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<td>100</td>
<td>68.75</td>
<td>HFS</td>
<td>700</td>
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<tr>
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<td>100</td>
<td>68.75</td>
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<td>68.75</td>
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</table>
3.2.2 Phase Contrast Magnetic Resonance Imaging (PC MRI)

The cine PC MRI velocity mapping technique provides information on velocities within the imaging plane of the thoracic aorta at any point of the cardiac cycle, and multiple slices can be obtained within one acquisition. 3D cine phase contrast MRI (also known as flow sensitive 4D MRI) was used for detailed examination and visualization of complex flow patterns in the aorta (Kilner et al., 1993; Barker et al., 2010). 4D flow is obtained by time resolved PC MRI velocity encoding along three flow directions in a 3D anatomic coverage. 4D MRI allows for comprehensive evaluation of complex flow patterns in the aorta, and has been applied in the investigation and assessment of the thoracic aorta.

As summarized in Table 3.1, thoracic aorta image acquisitions were performed with the 3-Tesla CMR (Siemens) scanner for three of the TAV subjects, and with the 1.5-Tesla CMR (Siemens) scanner for the other four TAV subjects, as well as the one BAV subject. PC MRI datasets were acquired for each of the seven health subjects with (normal) TAV, and one abnormal BAV subject. For 4D MRI, flow was acquired in the foot to head (FH), right to left (RL) and anterior posterior (AP) directions at selected locations in the aorta. PC-MRI was performed at three cutting planes as defined in Figure 3.3.

![Figure 3.3: Sample case reconstructed geometry showing the thoracic aorta and locations of imaging planes.](image)

Plane 1A is at an oblique angle at the sinotubular junction, whilst plane 1 is located at mid ascending thoracic aorta. Plane 3, encompassing the three aortic branches, cuts across the branches at a position approximately 1-3 cm above the top most part of the arch, and plane 2 is located in mid descending
thoracic aorta. Fig. 3.2 (a) shows the flow image acquired at plane 1A, which provided the data for inlet flow profile, allowing the influence of aortic valve topology to be captured in subject-specific CFD simulations. The PC-MRI data from plane 2 was used to evaluate the amount of flow leaving through the arch branches. It can also be used to compare with the simulation results for validation purpose.

The PC MRI acquisition sequences were similar but varied in the number of slices, timing and slice thickness. As summarized in Table 3.1, the slice thickness was 2 mm for four of the TAV cases (C1, C2, C6, and C7) and 6 mm for the other three TAV subjects (C3, C4 and C5) and the one BAV case. At the imaging planes 1, 2 and 3, encoding velocity, $V_{enc}$ applied was 150 mm/s for the IS (inferior–superior) or FH direction and 150 mm/s for AP (anterior-posterior) and RL (right-left) directions.

PC MRI provides two sets of information as explained by Lotz et al., (2002). The magnitude image (Figure 3.2 a) resembles a normal bright blood image and is used for anatomic area delineation and orientation, whilst the phase image (Figure 3.2 b) is the velocity image, with the grey value of each pixel giving the velocity information of that voxel. PC MRI is capable of providing sufficient anatomical and flow data for realistic and fully personalized flow simulations (Cheng et al., 2010 and 2014, Canstein et al., 2008, Stalder et al., 2008; Tan et al., 2008 and Taylor et al., 2010). In order to convert the images acquired with PC MRI to velocity values, the images were processed using, an in-house Matlab program that was developed and validated previously (Cheng et al., 2010). The thoracic aorta and region of interest (ROI) were segmented from the magnitude images and then mapped on to the corresponding phase images; the grey scale of the pixels within the ROI was converted into velocity information according to the applied encoding sequence of the scanner.

### 3.3 Model Construction

Multislice anatomical (HASTE) images of the aorta were processed using Mimics (14.0, 15.0), while PC-MR images were processed using an in-house programme. ANSYS ICEM CFD (14.0, 15.0) was adopted to generate computation mesh for the reconstructed 3D flow domain, and ANSYS CFX 15.0, a finite volume method-based CFD solver, was used to solve the flow equations, under subject-specific boundary conditions.

#### 3.3.1 Geometry Reconstruction and Computational Mesh

The 2D series of MR images for each subject stored in the DICOM format were extracted and segmented. Using the digital header recordings, the images were sorted into categories as necessary for identification and processing. A number of image segmentation techniques including filtering,
thresholding, dynamic region growing, and smoothing (available in Mimics) were used. The segmented 2D planar slices were stacked up and integrated to construct the 3D geometry of the thoracic aorta for each subject.

In discretizing the geometries, both structured and unstructured meshing was adopted but structured meshing was preferred and used for most of the geometries. With structured meshing, the flow domain corresponding to each subject-specific aorta was discretized using structured hexahedral (hexa) mesh. The structured hexahedral mesh was chosen as it is best suited for the flow solver, ANSYS CFX. Considerable attention was paid to the control of mesh quality and density. It is essential that the boundary layer near the wall is well resolved, and for this reason, 12 to 15 prism layers were set in the near wall region with a growth factor of 1.2 (i.e. the thickness of each prism layer decreased exponentially towards the wall). Figure 3.4 shows the computational mesh around the aortic arch and at the inlet.

![Image of mesh around aortic arch](image)

**Figure 3.4:** (a) Sample hexahedral mesh of a reconstructed aorta (arch area) (b) Sample hexahedral mesh (at inlet location).

The Delauney and Octree algorithms (ANSYS ICEM CFD 14.0 Tutorial Manual) were employed in mesh refinement and to resolve the geometry. The Octree algorithm was particularly useful for a robust solution at sharp corners and to guarantee quality in 3D. The mesh size function was based on several factors including: the curvature and local geometric features, numerical error estimates (based on adaptive solver) and other user specified constraints, e.g. node location, distance function and the use of Laplacian smoothing (function by which node locations are iteratively moving closer to the average of neighbours) whilst ensuring good element quality. It is worth noting that a high quality image segmentation helps to ensure a quick hexa mesh generation, a process that could be very time consuming with poorly resolved pixilation and geometries. The number of mesh elements was between 222,270 and 1.1 million depending on the individual shape and size of the aorta. The subject-
specific meshes were tested for grid sensitivity and optimised to ensure that the difference in terms of maximum wall shear stress and flow velocity between two consecutive test results was less than 2%. Unstructured mesh was used in discretizing one of the geometries (C4) because a good quality and sufficiently fine structured mesh was not obtainable due to poor image quality.

3.3.2 Velocity Segmentation

The acquired PC MRI images consisted of paired magnitude and phase images that contain spatial and temporal flow information. Each pair of images corresponds to a specific location and time in the cardiac cycle. The magnitude images were used to delineate the flow area, whilst the phase images were used to derive velocities within each pixel. The segmented flow area and velocity maps were co-registered using an in-house Matlab code.

Velocity images acquired at Plane 1 were processed using the procedure described above and the extracted pixel-based velocities were used as inlet boundary conditions. This involved registering the PC MRI derived velocity on the inlet mesh of the thoracic aorta using MRI derived spatial coordinates and linear interpolation of pixel-based velocities in space to obtain velocities at each computational node. Since PC MRI flow mapping was acquired at around 20 to 30 time points in a cardiac cycle, temporal interpolation of velocities was also performed to obtain instantaneous velocities at the time points required in CFD simulations (usually 900-1000 time points per cardiac cycle).

3.3.3 Flow Models

For a flow problem, there is a need to specify the conservation of mass and the conservation of linear momentum. Further, blood flow in the aorta is both a characteristic-value problem and boundary-value problem. The characteristic value problem of aortic flow is expressed in terms of characteristic functions that are periodic. The function equations are best described in form of second-order homogeneous differential equations. The Navier-Stokes equations for Newtonian, incompressible flow are used to govern flow in the aorta.

3.3.4 Basic Conservation Equations

The fundamental and basic equations for CFD are the governing equations that describe fluid motion. These are the mass and momentum balances expressed as

Continuity equation: $$\frac{\partial p}{\partial t} + \nabla \cdot (\rho u) = 0 \quad (3.1)$$
Momentum equation:
\[
\frac{\partial u}{\partial t} + (u \cdot \nabla) u = \frac{1}{\rho} \nabla p + F + \frac{\mu}{\rho} \nabla^2 u
\] (3.2)
where \( u \) is the velocity vector, \( p \) is the static pressure relative to a datum level, and \( \rho \) and \( \mu \) are the density and dynamic viscosity of the fluid, respectively. \( F \) is the external force per unit mass.

For an incompressible, isothermal and Newtonian fluid, the Navier-Stokes equations can be written as:
Continuity Equation:
\[
\nabla \cdot u = 0
\] (3.3)

Momentum Equation:
\[
\rho \frac{\partial u}{\partial t} - \mu \nabla^2 u + \rho (u \cdot \nabla) u + \nabla p = 0
\] (3.4)

Since recent studies have found that flow in the aorta can be turbulent during part of the cardiac cycle (e.g. Cheng et al., (2010), Kousera et al., (2013)), the shear stress transport model (SST-Tran), which is a correlation-based transitional version of Menter’s hybrid \( k-\varepsilon/k-\omega \), (Menter et al., 2006), was adopted to simulate possible transition to turbulent flow. This choice was also based on calculations of the peak Reynolds number and Womersley parameter using subject-specific data, and preliminary assessment of flow states using existing criteria as performed by Kousera et al., (2013). Details of the SST-Tran model are given below.

3.3.4.1 The Two-Equation Shear Stress Transport (SST) Model
The two-equation transport model, i.e. the \( k-\varepsilon \) and \( k-\omega \) model by definition includes two extra transport equations that account for the turbulent properties of flow. The essential variables are turbulent kinetic energy, \( \kappa \), and dissipation, \( \varepsilon \) or specific dissipation, \( \omega \). The first variable, \( \kappa \) measures the actual amount of turbulent energy whilst the second variable (\( \varepsilon \) or \( \omega \)) determines the scale of turbulence. Menter’s SST model employs the original \( k-\omega \) model of Wilcox in the inner region of the boundary layer, and switches to the \( k-\varepsilon \) model in the outer region and in the free shear flows. This two-equation model is more advanced than the zero and one equation model because it solves for both the velocity and length scale by using two separate equations. It is highly recommended over the one-equation model and widely used because it is more robust and capable of capturing turbulence more reliably for similar class of flows like pipe flow or arterial flow, and case-by-case examination. The two-equation model allows for account of history effects like convection and diffusion of turbulent energy.

The SST \( k-\varepsilon/k-\omega \) model
In this hybrid SST \( k-\varepsilon/k-\omega \) model the turbulence viscosity (\( \mu_t \)) is assumed to be linked to turbulence
kinetic energy and turbulence frequency or specific dissipation rate, \( \omega \) through:

\[
\mu_t = \rho \frac{\kappa}{\omega}
\]

(3.5)

This model solves two transport equations, with one equation for \( k \) and another one for \( \omega \). The equation for \( k \) is:

\[
\frac{\partial k}{\partial t} + \rho U_j \frac{\partial k}{\partial x_j} = \tau_{ij} \frac{\partial U_i}{\partial x_j} - \beta \rho \kappa \omega + \frac{\partial}{\partial x_j} \left[ (\mu + \sigma^e \mu_t) \frac{\partial k}{\partial x_j} \right]
\]

(3.6)

while the specific dissipation rate equation, \( \omega \) is as such,

\[
\frac{\partial \omega}{\partial t} + \rho U_j \frac{\partial \omega}{\partial x_j} = \alpha \frac{\omega}{k} \tau_{ij} \frac{\partial U_i}{\partial x_j} - \beta \rho \omega^2 + \frac{\partial}{\partial x_j} \left[ (\mu + \sigma_\omega \mu_t) \frac{\partial \omega}{\partial x_j} \right] + 2(1 - F_1) \rho \sigma_{\omega^2} \frac{1}{\omega} \frac{\partial k}{\partial x_j} \frac{\partial \omega}{\partial x_j}
\]

(3.7)

A limiter is incorporated into the kinematic eddy-viscosity, \( \nu_t \) formula of this model. i.e.

\[
\nu_t = \frac{a_1 k}{\max(a_1 \omega, \Omega F_2)}
\]

(3.8)

\( F_1 \) and \( F_2 \) are blending functions where,

\[
F_1 = \tanh(\text{arg}_1^4)
\]

(3.9)

where,

\[
\text{arg}_1 = \min \left( \max \left( \sqrt{k}, \frac{500 \nu}{y^2 \omega} \right), \frac{4 \rho \sigma_{\omega^2} k}{CD_{k\omega} y^2} \right)
\]

(3.10)

where, \( y \) is the distance to the nearest wall and \( \nu \) is the kinematic viscosity and

\[
CD_{k\omega} = \max \left( 2 \rho \sigma_{\omega^2} \frac{1}{\omega} \frac{\partial k}{\partial x_j} \frac{\partial \omega}{\partial x_j}, 10^{-10} \right)
\]

(3.11)
\[ F_2 = \tanh (arg_2^2) \]  
(3.12)

with

\[ arg_2 = \max \left( \frac{2\sqrt{k}}{0.09\omega y'}, \frac{500\nu}{y^2\omega} \right) \]  
(3.13)

Close to the walls, the blending function, \( F_1 \) is zero thus leading to the standard \( \omega \) equation. The blending function is unity and corresponds to the standard \( \varepsilon \) equation when far from the walls, (Menter, 1994). \( F_2 \) restricts the limiter to the wall boundary layer. \( \Omega \) is the absolute value of the vorticity. The model constants are: \( \alpha = 5/9, \beta = 0.075, \sigma_\omega = 0.5, \sigma_{\omega_2} = 0.856 \), and \( a_1 = 0.31 \).

### Transitional SST Hybrid \( \kappa-\epsilon/\kappa-\omega \) Model

The transport equation for intermittency, \( \gamma \) is given below:

\[
\frac{\partial (\rho \gamma)}{\partial t} + \frac{\partial (U_j \rho \gamma)}{\partial x_j} = P_{\gamma 1} - E_{\gamma 1} + P_{\gamma 2} - E_{\gamma 2} + \frac{\partial}{\partial x_j} \left[ \left( \mu + \mu_t \right) \frac{\partial \gamma}{\partial x_j} \right]
\]  
(3.14)

The transition sources are defined as \( P_{\gamma 1} = 2F_{\text{length}} \rho S |\gamma F_{\text{onset}}| \gamma^3 \) and \( E_{\gamma 1} = P_{\gamma 1} \gamma \). \( S \) is the strain magnitude, i.e. absolute value of the strain rate, while \( F_{\text{length}} \) is an empirical correlation that controls the length of the transition region. The destruction/re laminarization sources are \( P_{\gamma 2} = (2C_{\gamma 1}) \rho \Omega \gamma F_{\text{turb}} \) and \( E_{\gamma 2} = c_{\gamma 2} P_{\gamma 2} \gamma \) where \( \Omega \) is the vorticity magnitude. The transition onset is controlled by the following functions:

\[
Re_v = \frac{\rho y^2 S}{\mu}; \quad R_T = \frac{\rho k}{\mu \omega}
\]  
(3.15)

\[
F_{\text{onset} 1} = \frac{Re_v}{2.193 \cdot Re_{bc}}
\]  
(3.16)

\[
F_{\text{onset} 2} = \min(\max(F_{\text{onset} 1}, F_{\text{onset} 1}^4), 2.0),
\]  
(3.17)
\[ F_{\text{onset} \, 3} = \max \left( 1 - \left( \frac{R_T}{2.5} \right)^3, 0 \right), \]  
\[ F_{\text{onset} \, 1} = \max (F_{\text{onset} \, 2} - F_{\text{onset} \, 3}, 0), \]  
\[ F_{\text{onset}} = \max (F_{\text{onset} \, 2} - F_{\text{onset} \, 3}, 0), \]  
(3.18)  
(3.19)  

\[ F_{\text{turb}} \] is a function used to deactivate the destruction/relaminarisation source when the flow is fully turbulent:  
\[ F_{\text{turb}} = e^{-\left( \frac{R_T}{4} \right)^4} \]  
(3.20)  

where,  
\[ Re_y \] is the strain rate or vorticity rate Reynolds number,  
\[ R_T \] is the turbulent Reynolds number and  
\[ Re_{\theta c} \] is the critical Reynolds number where the intermittency first starts to increase in the boundary layer. The constants for these equations are:  
\[ C_{y1} = 0.03, C_{y2} = 50, C_{y3} = 0.5 \quad \text{and} \quad \sigma_y = 1.0. \]  
The modification separation-induced transition is as indicated  
\[ \gamma_{\text{sep}} = \min \left( 2 \cdot \max \left[ \frac{Re_y}{3.235Re_{\theta c}} - 1, 0 \right] F_{\text{reattach}}, 2 \right) F_{\theta t}, \]  
(3.21)  
\[ F_{\text{reattach}} = e^{-\left( \frac{R_T}{20} \right)^4}, \]  
(3.22)  
\[ \gamma_{\text{eff}} = \max (\gamma, \gamma_{\text{sep}}). \]  
(3.23)  
The boundary condition for \( \gamma \) at a wall is zero normal flux, while for the inlet \( \gamma \) is equal to 1.0.  
The transport equation for the transition momentum thickness Reynolds number, \( \bar{Re}_{\theta t} \) is  
\[ \frac{\partial (\rho \bar{Re}_{\theta t})}{\partial t} + \frac{\partial (U_j \rho \bar{Re}_{\theta t})}{\partial x_j} = P_{\theta t} + \frac{\partial}{\partial x_j} \left[ \sigma_{\theta t} (\mu + \mu_t) \frac{\partial \bar{Re}_{\theta t}}{\partial x_j} \right], \]  
(3.24)
The source term is defined as:

\[ p_{\theta t} = c_{\theta t} \frac{\rho}{t} (Re_{\theta t} - \overline{Re_{\theta t}})(1.0 - F_{\theta t}); \quad t = \frac{500\mu}{\rho U^2}, \]  

(3.25)

\[ F_{\theta t} = \min \left( \max \left( F_{wake} \cdot e^{\left(\frac{\gamma}{5}\right)^4}, 1.0 - \left( \frac{y - 1/50}{1.0 - 1/50} \right)^2 \right), 1.0 \right), \]  

(3.26)

\[ \theta_{BL} = \frac{\overline{Re_{\theta t}}}{\rho U}; \quad \delta_{BL} = \frac{15}{2} \theta_{BL}; \quad \delta = \frac{50\Omega y}{U}; \delta_{BL}, \]  

(3.27)

\[ Re_\omega = \frac{\rho \omega y^2}{\mu}; \quad F_{wake} = e^{-\left(\frac{Re_\omega}{10^5}\right)^2} \]  

(3.28)

The constants for the equation are: \( c_{\theta t} = 0.03 \) and \( \sigma_{\theta t} = 2.0 \). The boundary condition for \( Re_{\theta t} \) at an inlet is calculated from the empirical correlation based on the inlet turbulence intensity.

\[ \frac{\partial (\rho k)}{\partial t} + \frac{\partial (U_j \rho k)}{\partial x_j} = \tilde{P}_k - \tilde{D}_k + \frac{\partial}{\partial x_j} \left[ (\mu + \sigma_k \mu_t) \frac{\partial k}{\partial x_j} \right] \]  

(3.29)

\[ \tilde{P}_k = \gamma_{eff} P_k; \quad \tilde{D}_k = \min \left( \max \left( \gamma_{eff}, 0.1 \right), 1.0 \right) D_k, \]  

(3.30)

\[ R_y = \frac{\rho y \sqrt{\kappa}}{\mu}; \quad F_3 = e^{-\left(\frac{R_y}{120}\right)^8}; \quad F_1 = \max \left( F_{1orig}, F_3 \right) \]  

(3.31)

### 3.3.5 Boundary Conditions

In order to capture individual flow characteristics in the aorta, subject-specific information should be incorporated in CFD simulations and this includes heart rate (cycle time), 3-D geometries and pulsatile flow waveform. According to many studies, amongst them Tan et al., (2009) and Cotrufo...
and Della (2009), aortic valve (AoV) morphology and function have a strong influence on the progression of disease in the ascending aorta (AAo). Cotrufo and Della (2009) observed that aneurysm formation and aortic dilatation in patients with aortic valve disease tended to occur at the sinotubular junction (STJ). Tan et al., (2009) have computationally investigated the influence of aortic valve on the AAo haemodynamics using simplified TAV and BAV models. According to Wendell et al., (2013), imposing subject-specific blood flow velocities corresponding to the subject’s own AoV dynamics is important for subject-specific simulations. Further, from a clinical perspective, differences in the AAo due to valve morphology could aid in determining which patterns should be closely monitored as a result of adverse haemodynamic conditions introduced due to abnormal aortic valves. Hence, choosing appropriate boundary conditions is an essential part of this study. Figure 3.5 shows a representative aorta model and its physical boundaries. For the models considered in this study, three types of boundaries are present, namely, inlet, outlet and wall.

At inlet flow boundaries, mass flow or velocities can be specified. Mass flow boundaries can be set at both inlet and outlet of the models as either fractional flow rates or directly specified values. Previous studies have found that the shape of velocity profile at the inlet section can influence the entire numerical solution (Tan et al., 2012), and based on this understanding, two strategies were adopted for the velocity inlet profile: a flat profile and a realistic profile. In the first strategy, a flat velocity profile was imposed in all the TAV cases, while in the second strategy, velocity profiles extracted from MR images were applied. In both strategies, subject-specific flow rate derived from MR images were used. According to Li et al., (2015), a turbulence intensity level of 1.5% was specified at the inlet. For the outlet boundaries, with three in the arch branches and one main outlet in the descending thoracic aorta, different boundary conditions were applied. The combined outflow from the three arch branches was assumed as 30% of the inflow measured at plane 1A or 1 (defined in Figure 3.3), and the percentage outflow from each of the aortic arch branch (i.e. the brachiocephalic artery, the left common carotid artery (CCA) and left subclavian artery) was determined based on their sizes. Flow images acquired at plane 2 were also processed and the derived flow was compared with the assumed percentage flow. At the main outlet in the descending aorta, zero pressure was applied. The thoracic aorta wall was assumed to be rigid with no slip conditions.
Figure 3.5: A representative model of thoracic aorta showing boundary conditions.

3.3.6 Numerical Methods

The governing equations were discretized spatially and temporally by the second order upwind scheme and the implicit backward Euler scheme respectively (Barth et al., 1989). ANSYS CFX 15 (ANSYS Inc., Canonsburg, PA) was used to perform all the CFD simulations presented in this thesis, employing the boundary conditions and subject-specific geometries described above. In the CFD models, blood was treated as Newtonian with a constant density of 1060 kg m\(^{-3}\) and dynamic viscosity of 0.004 Pa.s. A fixed time step of 1 millisecond (0.001 s) was specified for the transient simulation and typically 3 cycles were required to reach a periodic solution. Convergence of the numerical solutions was controlled by monitoring the residual RMS error, which was set to be \(10^{-6}\).


3.4 Geometric Parameters

For reliable assessment and comparison of the complex geometric features of the aorta, a consistent approach is needed for the measurement of basic geometric parameters, such as aortic diameter, tortuosity and arch angles. Before any measurement was taken, the region of interest was examined and defined precisely relative to an anatomic landmark (serving as a consistent reference point for taking measurements). This is a necessary step because of large individual variations in geometry and potential intra- and inter-observer errors. For this purpose, the use of distance measurement alone may not be adequate, as the position of an anatomic feature relative to another is rarely the same for any two individuals. The landmarks used are similar to those used by Mongeon et al., (2016).

In order to achieve reproducible measurements, a set of consistent steps was devised and followed in this study. This involved searching, finding, delineating and segmentation of the anatomic landmarks from the HASTE images. Anatomical features used as landmarks included the coronary arteries, the highest aortic arch point, and the sinotubular junction (STJ). After locating the landmarks in the segmented geometry, they were used for measurements of defined geometric features.

Using the procedure described above, a number of geometric parameters were measured and evaluated, including aortic diameters at various locations, tortuosity and arch angles. Definitions of these parameters are given below. Each measurement was made three times and the average of the three measurements was taken.

3.4.1 Diameters

Diameters were measured at six locations along the thoracic aorta starting from the mid sinuses of Valsalva. Three measurements of the best fit diameter at each location (with 1 mm distance between two consecutive measurements) were obtained using Mimics and the average value for each location was then recorded.

3.4.2 Tortuosity

Tortuosity is described as a measure of the twists and turns of an artery. There is evidence that vessel tortuosity is related to many cardiovascular diseases such as hypertension (Diedrich et al., 2011). Tortuosity of the aorta is a significant feature for investigation, which when quantified and calibrated can be used as a marker in clinical assessment of the aorta. Tortuosity (T), however, has been recognized as a term that lacks a commonly accepted definition (Wood et al., 2006), but has been used to summarize information about curvature at individual points on the centerline of a vessel segment. It is defined in this study as:
\[ T = 1 - \frac{C}{L} \]  

(3.32)

where \( L \) is the distance along a curve (curve length) and \( C \) is the straight line distance between the ends of a curve (or chord length). Tortuosity of the thoracic aorta was measured in all the cases included in this study. An example of tortuosity measurement is shown in Figure 3.6, where tortuosity measured from the ventriculo-arterial junction (VAJ) to the end descending thoracic aorta (DTA) was 0.51, whereas the measurement taken from the inferior (tip) end sinuses to the end descending thoracic aorta was 0.58.

![Figure 3.6: Examples of tortuosity measurement.](image)

**Figure 3.6: Examples of tortuosity measurement.**

### 3.4.3 Arch Angles

Towards reproducible measurements, the location of the left coronary artery and the arch outer and inner curvature extreme points were used as level references in angle measurements, as shown in Figure 3.7. The angle definition adopted here is similar to that used by Yoshii et al., (1988). For consistency in measuring the arch angles, the same topological orientation was adopted for all the subjects, and the arch angles were defined by the relationship between the ascending and descending arch legs. The measurements can be input as workflow within the Mimics software (3-matic function), and ANSYS ICEM CFD. The arch angles \( X \) and \( Y \) in perspective can be used as a measure of the distortion of the arch, and can be related to arch curvature similar to other methods adopted in previous phantom and experimental studies (Kilner et al., 1993).
3.5 Flow Parameters used in Analysis

For a comprehensive evaluation of the flow parameters, it was necessary for the flow field to be monitored throughout the cardiac cycle. Three important time points were chosen for detailed analysis and comparison: at mid-acceleration, peak flow and mid-deceleration. A number of defined flow parameters were identified and used to describe the flow patterns for characterization of the thoracic aorta. Velocity contours taken at sectional planes with instantaneous velocity streamlines at mid acceleration, peak and mid deceleration were used to provide visualisation of the flow. 3D streamlines display flows with local velocities at various time points in the entire thoracic aorta. 2D vector fields and contours (showing on 2D planes) extracted from the 3D thoracic volumes were used to display velocity vectors. The predicted velocity profiles were compared with in vivo data acquired by PC MRI.

In addition to visualisation of flow patterns, a number of flow-derived parameters were also
evaluated. These included time average wall shear stress (TAWSS), oscillating shear index (OSI) and helicity parameters. Wall shear stress (WSS) is determined by local velocity gradient and blood viscosity. It is sensitive to local changes in geometry and flow pattern. TAWSS, which is commonly used to evaluate the shear stress experienced at the wall during a cardiac cycle, is defined as:

\[
TAWSS = \frac{1}{T} \int_{0}^{T} |\tau_w| \, dt
\]  

(3.33)

where \( T \) is the cycle period and \( \tau_w \) is the instantaneous wall shear stress.

Oscillatory Shear Index, (OSI) is used to describe the cyclic departure or shift of wall shear stress vector from its predominant axial alignment. It is defined as:

\[
OSI = 0.5 \left( 1 - \left( \frac{1}{T} \int_{0}^{T} \tau_w \, dt \right) \right)
\]  

(3.34)

The OSI values range between 0 and 0.5.

Turbulence Intensity (Tu) is the ratio of root-mean-square value of the fluctuating components of velocity to the mean velocity, and it is defined as:

\[
Tu = \frac{\sqrt{\frac{2}{3} k}}{V}
\]  

(3.35)

where \( k \) is the turbulence kinetic energy and \( V \) is the mean velocity. An initial turbulence intensity of 1.5% was applied at the model inlet.

If a fluid rotates about an axis parallel to the main direction of flow, it will have a helical flow component. The helicity \((H)\) in fluid flow is defined as the integrated scalar product of the local velocity vector \( \mathbf{u}(r,t) \) and the vorticity vector \( \mathbf{\omega}(r,t) \), in 3D Euclidean space \((\mathbb{R}^3)\).

\[
H = \int \mathbf{u}(r,t) \cdot \mathbf{\omega}(r,t) \, dV
\]  

(3.36)

where the vorticity vector filed is defined as the curl of the velocity vector field, as:
\[ \mathbf{\omega} (r, t) = \nabla \times (r, t) \] (3.37)

Helicity is a conservative quantity, and it remains unchanged for incompressible fluids with zero viscosity and homogeneous density. The dot product of the velocity and vorticity vectors describes the helicity density \( H_d \):

\[ H_d = \mathbf{u}(r, t) \cdot \mathbf{\omega}(r, t) \] (3.38)

Both the helicity and helicity density are pseudo scalar quantities. In the case of forward flow (i.e. directed from the heart to the aorta), the signs provide information on the direction of rotation of the fluid (either clockwise or counterclockwise). The angle \( \alpha \) (the cosine of the angle) between the velocity and vorticity vectors is referred to as the relative helicity or relative helicity density \( H_r \):

\[ H_r = \frac{\mathbf{u}(r, t) \cdot \mathbf{\omega}(r, t)}{||\mathbf{u}(r, t)|| \cdot ||\mathbf{\omega}(r, t)||} \] (3.39)

Alternatively, helicity density can be expressed as helical flow index (HFI) and used as a measure of blood flow complexity. Morbiducci et al., (2011) and Cheng et al., (2015) in related studies evaluated HFI from the velocity field resulting from the interpolation of PC MRI measurement to obtain a measure of the helical structure in the blood flow.

Further, HFI can be determined using the local normalized helicity (LNH) as a basic quantity computed along a particle trajectory,

\[ LNH_{(s; t)} = \frac{V(s; t) \cdot \omega(s; t)}{||V(s; t)|| \cdot ||\omega(s; t)||} \quad -1 \leq LNH \leq 1 \] (3.40)

where \( s \) is the location and \( t \) is the time in a flow field of velocity vector, \( \mathbf{V} \). The non-dimensional quantity LNH is a function of space and time, and it is the local value of the cosine of the angle between the velocity and vorticity vectors.

Finally, the flow reversal ratio (FRR) is used to quantify bulk flow derangement. The degree of retrograde flow at systole was calculated by the following relationship (Barker et al., 2010) for FRR, expressed as a percentage:

\[ FRR = \frac{|Q_{\text{negative}}(t_{\text{systole}})|}{Q_{\text{positive}}(t_{\text{systole}})} \times 100 \] (3.41)
Where $Q_{\text{positive}}(t_{\text{systole}})$ and $Q_{\text{negative}}(t_{\text{systole}})$ represent the forward and reverse flow at peak systolic flow.

Determination of FRR is important, as it has been suggested that FRR is a key determinant of renal syndrome and failure (Hashimoto and Ito; 2015).
Chapter 4

4 Subject-Specific Normal Thoracic Aorta Study: Multiple Cases with Tricuspid Aortic Valve (TAV)

4.1 Introduction

In this chapter, the morphological and flow patterns in the thoracic aortas of seven healthy normal volunteers with tricuspid aortic valve (TAV) were examined and analyzed using a combination of PC MRI and CFD techniques. Information on subject recruitment and PC MRI data acquisition is given in Section 4.2, with the reconstructed 3D models of the thoracic aortas presented in Section 4.3. Anatomic features including local diameters, tortuosity and arch angulation were measured and compared among the subjects. In the subject-specific CFD models for aortic flow, two types of inlet boundary conditions were tested: the assumption of flat velocity profile and realistic velocity profiles derived from MR images. Details about the two types of inlet boundary conditions can be found in Section 4.4. Numerical results are described in Section 4.5, where spatio-temporal haemodynamic patterns and parameters in the normal aortas are analyzed, including helicity, wall shear stress (WSS), and other WSS-based indices.

4.2 Subject Information

Seven volunteers (6 males, 1 female) were recruited with their consent and the approval of the local ethics committee. All participants (aged 25-55 years) were normal, fit and with no known medical conditions. The volunteers have been anonymized and the subjects in this study are referred to as C1, C2, C3, C4, C5, C6, and C7. Data for subjects C1 to C5 were provided by the Royal Brompton Hospital London, whilst St Mary’s Hospital in collaboration with Hammersmith Hospital, Imperial College Healthcare NHS Trust, provided the other two data sets. The MR images acquired for C3, C4 and C5 were more complete and have been selected for detailed flow analysis.

4.3 Model Reconstruction and Computational Mesh

The Haste images were imported directly from DICOM into Mimics for anatomic image segmentation. The images were filtered, cropped, segmented, smoothed and reconstructed into 3D aorta models. The reconstruction process involved a multi-plane reconstruction of axial, sagittal and coronal images. The volume rendered 3D model geometries were then measured (using the landmarks
previously explained in Chapter 3), to obtain geometric parameters, including diameter, angle and tortuosity.

In order to perform CFD simulations on the reconstructed geometry, each aorta model was divided into a structured mesh consisting of hexahedral elements. To obtain a fine mesh of the complex fluid domain, the geometry was divided into multiple blocks. The first block was created and its leading face was extruded to build a new block, and subsequent blocks were created in a similar way and joined up to complete the model topology. The multi-block surfaces, curves, edges and vertices were associated in a structured manner. In order to resolve the momentum boundary layer adequately, twelve layers of prismatic elements were placed adjacent to the luminal wall. Mesh independence test was carried out on each aorta model.

As an exception, an unstructured mesh was generated and adopted for case C4 because MR images had relatively poor quality and low resolution in this case. The geometry was more tortuous and because of this complexity, a high quality and robust structured mesh could not be generated. To satisfy the turbulent flow model requirement for a fine resolution near the wall, the wall boundary layer element $y^+$ was kept at less than 2, where $y^+$ is the dimensionless height of the elements based on the turbulent wall boundary layer coordinates (ANSYS ICEM CFD 15). The unstructured mesh for C4 was found to be adequate.

4.4 Flow Models and Computational Details

4.4.1 MR Velocity Image Processing

The acquired PC MRI velocity images (the magnitude and phase image pairs) were segmented. The cine 2D PC MRI datasets and 4D flow sequences obtained by routine clinical protocols provided the velocity-encoded images. The 2D PC MRI acquisition was performed with a single direction through-plane velocity mapping. The 4D images were acquired with three-directional mapping i.e. foot to head, FH (through plane velocity encoding), right to left (RL) and anterior-posterior (AP) directions. In the through-plane flow mapping, the imaging plane was placed perpendicular to the local vessel centerline and the acquired flow data contained velocities in a single-direction (i.e. axial) that is orthogonal to the 2D (through-plane) imaging slice. The 4D flow images included velocity encoding of all the three spatial directions for a cardiac cycle. The acquisition from the time-resolved cine 3D sequence provided the magnitude and phase data for vessel contour and three velocity components in three orthogonal directions, i.e. velocities in the RL, AP and FH encoding directions respectively (Figure 4.1).
The segmented 4D MRI datasets produced a spatio-temporal description of the velocity profile in the thoracic aorta at selected time points in a cardiac cycle, as shown in Figure 4.2. This information was used in CFD simulations to obtain flow patterns in the entire thoracic aorta. The PC MRI through plane images were segmented to derive the time-varying flow rate. The flow rate was obtained by performing Gaussian integration over the imaging plane and the obtained volumetric flow rate was then applied at the model inlet assuming a flat velocity profile.
**Figure 4.2:** Sample PC MRI velocity map in the FH direction.

**Figure 4.3:** Cross-sectional velocities derived from MR flow imaging.
4.4.2 Flow Models and Boundary Conditions

The SST-Tran model was used in CFD simulations for all aorta models. This model was chosen based on initial assessment of the flow state, and the success in applying SST-Tran model to physiological flows in recent studies by Tan et al., (2008), Cheng et al., (2015) and Li et al., (2015) gave a high level of confidence in using this model. The inlet location corresponded to the PC MRI measurement plane. The mean and maximum velocities and best-fit diameter at the inlet for each of the subjects were used to calculate the corresponding Reynolds numbers (Re), and the peak Re ranged between 3000 and 8000 for all the cases included in this study. As shown in Table 4.1 (a) and Figure 4.4, the peak Re values were sufficiently high for flow to be considered as disturbed, hence justifying the need for the SST-Tran model.

The blood was assumed to be homogeneous, incompressible and Newtonian with a dynamic viscosity of 0.004 Pa.s and a density of 1060 kg m\(^{-3}\). The aortic wall was assumed to be rigid and a no-slip condition was applied at the wall. Two strategies were used for the inflow boundary condition: flat velocity profiles based on subject-specific flow rate derived from 2D PC-MR images or 3D realistic velocity profiles derived from 4D MR flow mapping. These were applied at the model inlet corresponding to the imaging plane 1A, as shown in Figure 4.5 (a). Flat velocity profiles were used initially to observe the flow patterns and qualitative trend in the TAV cases whilst the mapped realistic 3D velocity profiles provided more specificity to each case for quantitative analysis and assessment.
Table 4.1: Mean and maximum velocities and calculated Reynolds number (Re) and Womersley number (α) together with cycle period T (s)

<table>
<thead>
<tr>
<th>TAV Cases/Age (Years)</th>
<th>Mean velocity (m/s)</th>
<th>Maximum velocity (m/s)</th>
<th>Mean Re</th>
<th>Peak Re</th>
<th>T (s)</th>
<th>α</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1/35</td>
<td>0.11</td>
<td>0.43</td>
<td>839</td>
<td>3290</td>
<td>1.1</td>
<td>18</td>
</tr>
<tr>
<td>C2/25</td>
<td>0.16</td>
<td>0.73</td>
<td>902</td>
<td>4176</td>
<td>0.9</td>
<td>15</td>
</tr>
<tr>
<td>C3/31</td>
<td>0.16</td>
<td>0.80</td>
<td>1172</td>
<td>5874</td>
<td>0.9</td>
<td>19</td>
</tr>
<tr>
<td>C4/43</td>
<td>0.15</td>
<td>0.85</td>
<td>1110</td>
<td>6234</td>
<td>0.9</td>
<td>18</td>
</tr>
<tr>
<td>C5/26</td>
<td>0.17</td>
<td>0.93</td>
<td>1208</td>
<td>6742</td>
<td>0.9</td>
<td>17</td>
</tr>
<tr>
<td>C6/50</td>
<td>0.19</td>
<td>1.00</td>
<td>1484</td>
<td>7868</td>
<td>1.0</td>
<td>19</td>
</tr>
<tr>
<td>C7/55</td>
<td>0.06</td>
<td>0.44</td>
<td>595</td>
<td>4169</td>
<td>1.0</td>
<td>23</td>
</tr>
</tbody>
</table>

Figure 4.4: Peak Reynolds number (Re) versus Womersley number (α).
In order to represent the mapped 3D inflow velocity accurately in the flow model, the geometric model inlet was orientated to overlap the PC MR imaging plane. As depicted in Figure 4.6, the CFD model was translated and orientated such that the inlet corresponded to the imaging plane coordinates, and the inlet (surface) point coordinates (arbitrarily selected at the periphery) were then related to the MRI matrix. The CFD inlet nodes 1, 2, 3 and centre point (x) were mapped to the velocity plot coordinates (i.e. at points 1, 2 and 3 and centre respectively) of the PC MR image.
Figure 4.6: Sample case CFD model (left) and the pixilated PC MRI image (right).

For all the CFD simulations, a uniform time step of 0.001 s was specified and three cardiac cycles were run to ensure that the solution reached periodicity. Solutions obtained from the first two cycles were used to initialize the simulation in the third cycle. The analysis of results was based on solutions obtained from the third cycle. The maximum RMS residual of $10^{-6}$ was imposed as the criterion for convergence.

4.5 Results and Discussion

In the following sections, the segmented geometric models, morphologic parameters and the haemodynamic results obtained from the combined PC-MRI and CFD simulations are presented and discussed. The analysis focused on flow patterns, regional velocities, wall shear stress as well as velocity and shear-dependent descriptors, e.g. HFI and SRI (previously defined in Chapter 3) to describe and characterize the local and global flow structures and hemodynamic environment of normal aortas with TAV.

4.5.1 Morphology

The reconstructed aortas for the seven healthy subjects, including the three major arch branches, the
brachiocephalic, the left common carotid and the left subclavian arteries, are presented in Figure 4.7. The reconstructed aortas show individual variations in arch curvature, tapering and arch branches. It is noteworthy to mention the fact that the arch branches of cases C1, C2, C6 and C7 were reconstructed more faithfully as a result of higher spatial resolutions in the original MR images for these cases.

Figure 4.7: Reconstructed 3D geometries of the normal (TAV) thoracic aorta.

Subject–specific measurements of aortic diameters, arch angles and tortuosity (defined in Chapter 3), are summarised in Table 4.2 and Table 4.3. The diameters and arch angle measurements show a range of values for the measured features that can be correlated with age. Table 4.2 gives the diameters of mid sinuses of valsalva (SoV) in the range of 30.8-36.7 mm with a mean of 32.5±2.1mm, and the
distal descending aorta (DAo) in the range of 16.1-23.6 mm with a mean of 20.8±2.5 mm. These values show that there is a marked difference in vessel diameter from the aortic root to the descending aorta with a distinct tapering of the aorta. Although there is limited information available on age-specific morphological properties and measurements of human thoracic aorta, the diameter values obtained in this study show good agreement with those available in the literature. Burman et al., (2008) used MRI and manual planimetry to take aortic root measurements in both male and female volunteers aged between 20 and 80 years, and they reported similar values for the sinus plane (i.e. mid-SoV) diameter in normal aortic roots. Mao et al., (2008) examined the ascending aorta diameter of a large population by using 64 Multi-Detector Computed Tomography (MDCT) and Electron Beam Computed Tomography (EBT), and they found the ascending aorta diameter (mean±SD (mm)) for age (years) 20-40 to be 29.0±3.3 and 30.8±3.5 for females and males respectively, and the descending aorta diameter (mean±SD (mm)) for age range 41-60 to be 30.7±3.8 for females and 33.3±3.6 for males. The ascending aorta diameter measurements reported by Mao et al., (2008) are in good agreement with the corresponding diameter measurement obtained in this study.

Furthermore, using the mid SoV to distal DAo measurements in Table 4.2, the tapering (observed in Figure 4.7) was found to be in the range of 30.1-48.1%. The percentage of tapering from the ascending aorta to the beginning of descending aorta for each subject was less than 50%, which is within the range of tapering reported in similar studies, e.g. Wolak et al., (2008) where measurements of the thoracic aorta were taken from more than 4000 adults (aged 26 to 92 years) with the mean diameters for the (normal, low risk subjects’) ascending and descending thoracic aorta being $33 \pm 4$ mm and $24 \pm 3$ mm, respectively. Using these values gave an average tapering of about 28%. Comparing diameters at the STJ to that at the end-descending aorta, a mean reduction of 25% was found for the TAV cases. The tapering in case C5 was relatively small at 18%, which is expected in young subjects (26 years), as tapering is known to increase with age. The diameters at the sinotubular junction (STJ) ranged between 22.0 to 31.5 mm, with the smallest in the youngest subject and largest in the oldest subject.

The arch angles were measured based on the definitions illustrated in Figure 4.8 (a), which shows the arch being sectioned and defined as the Minor Arch, the 1st Major Arch and 2nd Major Arch. Arch angle X is defined as the angle between the ascending aorta and the ascending arch leg, and angle Y is defined as the angle between the ascending and descending arch legs. Figure 4.8 (c) defines the minor arch angle $X1$ ($\angle BAD$) and major arch angle $Y1$ ($\angle DAE$). $X1$ is the angle subtended at the arch, at A (the highest point) by B and D, where B is the start point of the ascending leg of the first major arch and D is the start point of the ascending leg of the second major arch), while $Y1$ is the angle between the ascending and descending legs of the second major arch.
Figure 4.8: Definition of (a) arch sections, (b) angles X and Y, and (c) minor arch angle BAD and major arch angle DAE.

For the measured arch angles, as shown in Figure 4.8 and summarised in Table 4.3, the angles X and Y were smaller in C7 than in C5 and C2. In a study by Agnoletti et al., (2008), it was found that sharper angulation of the aortic arch was associated with early pulse wave reflection, dilatation of the
ascending aorta, and aortic regurgitation after the arterial switch operation for transposition of the 
great arteries. In view of anatomic measurements and changes being naturally related to age, gender 
and size, it may be necessary for future studies to revisit the association between arch angle and 
dilatation.

An examination of the arch geometries showed the aortic arch branch take-off angles and distances 
between the branches were different for each subject. Aortic arch branch take-off angles were not 
measured here because image resolutions were insufficient for reliable measurements on some 
subjects (e.g. C3, C4 and C5).
### Table 4.2: Anatomical measurements of normal thoracic aortas

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Location</th>
<th>Cases</th>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Location</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C1</td>
<td>C2</td>
<td>C3</td>
</tr>
<tr>
<td>Mid SoV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31.5</td>
<td>31.0</td>
<td>33.0</td>
</tr>
<tr>
<td>STJ</td>
<td>29.0</td>
<td>22.0</td>
<td>27.3</td>
</tr>
<tr>
<td>Proximal AAo</td>
<td>28.9</td>
<td>22.1</td>
<td>30.6</td>
</tr>
<tr>
<td></td>
<td>29.4</td>
<td>22.7</td>
<td>30.3</td>
</tr>
<tr>
<td>Distal AAo</td>
<td>22.5</td>
<td>18.3</td>
<td>22.0</td>
</tr>
<tr>
<td></td>
<td>19.1</td>
<td>16.1</td>
<td>21.7</td>
</tr>
<tr>
<td>Mid SoV to DAo (%) Diff.</td>
<td>39.4</td>
<td>48.1</td>
<td>34.3</td>
</tr>
<tr>
<td></td>
<td>34.2</td>
<td>26.8</td>
<td>20.6</td>
</tr>
<tr>
<td>STJ to DAo (%) Diff.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHORD LENGTH (mm)</td>
<td>Arch</td>
<td>91.7</td>
<td>64.8</td>
</tr>
</tbody>
</table>

**Legend:** Aorta = Ao, D = Diameter, SoV = Sinuses of Valsalva, STJ = Sinotubular Junction, AAo = Ascending Aorta, DAo = Descending Aorta, Arch = Aortic Arch, STJ to DAo % Diff = STJ to DAo percentage difference in diameter measurements, Chord length = the widest Aortic Arch width (mm).
Table 4.3: Measurements of arch angles in normal aortas

<table>
<thead>
<tr>
<th>Case</th>
<th>Defined Arch Angles (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
</tr>
<tr>
<td>C1</td>
<td>115.93</td>
</tr>
<tr>
<td>C2</td>
<td>129.82</td>
</tr>
<tr>
<td>C3</td>
<td>101.07</td>
</tr>
<tr>
<td>C4</td>
<td>117.49</td>
</tr>
<tr>
<td>C5</td>
<td>118.92</td>
</tr>
<tr>
<td>C6</td>
<td>104.65</td>
</tr>
<tr>
<td>C7</td>
<td>104.98</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>113.27±1</td>
</tr>
</tbody>
</table>

Legend: D = Diameter at the sinotubular junction (STJ), Mean = Mean of the defined angles, SD = Standard Deviation of the defined angles.

4.5.2 Flow Patterns

The flow patterns obtained using flat inlet velocity profiles were analyzed first. Using ANSYS Post and Ensight it was possible to generate interactive 3D models of the thoracic aorta for analysis. The results obtained based on the flat inflow assumption were used as a first approximation to show the qualitative flow patterns. Flow waveforms for all the TAV cases are shown in Figure 4.9, which displays substantial variations in peak and mean flow rates. In comparison, the peak flow rates of cases C1 and C2 were similar at 16 - 17 L/min, whereas the peak flow rates of cases C3, C4, C5 and C7 were in a higher range between 26 - 33 L/min. However, compared to all other TAV cases, the peak flow rate of case C6 was the highest at about 42 L/min. These differences may be related to age, gender, and the size of individual aorta. The similarity in flow rate values of cases C3, C4 and C5 (aged 26 - 43 years) was notable and these subjects were also scanned using the same PC MRI sequences on the same scanner. The corresponding cardiac output was 6.2, 5.7 and 6.5 (L/min) for
cases C3, C4 and C5 respectively, and these are within the expected range (5 - 6 litres/min) for a normal aorta at resting conditions.

**Figure 4.9:** Aortic flow rate waveforms for all TAV cases C1 to C7.

In order to examine the aortic flow patterns, 3D streamlines and time-resolved particle traces along with helical flow iso-surfaces were visualized. Figures 4.10 shows 3D streamlines for cases C3 and C5 based on results obtained using flat velocity profiles at the inlet.
Figure 4.10: Instantaneous streamlines in the aortic arch for C3 (left) and C5 (right).

The high velocity observed in the left common carotid artery of C3 in Figure 4.10 is noteworthy. This high velocity can be attributed to a number of factors, including low image resolution in the branch bifurcation (borders) region, leading to inadequate and limiting delineation/segmentation in this branch. A segmentation resulting in a smaller branch orifice (than actual) would effect a higher velocity than expected. For accurate characterization of the arch branches, there is need for dedicated imaging of the region.
Figure 4.11: Particle trajectories for C5 at (a) T1, (b) T2, (c) T3, (d) T4 and (e) T5. The particles were emitted from the inlet plane.

The numerical results showed that flow patterns and qualitative features of flow in the aortic arch were similar for all TAV cases, but there were quantitative differences. Figure 4.10 shows that the flow was laminar and organized in early systole but became disturbed in the mid-acceleration phase, especially along the inner bend of the arch and in the proximal descending aorta. In Figure 4.11, the particle trajectories show dominant helical and bi-helical structures in the aorta. These results however, as stated earlier, were only for preliminary analysis and should be regarded as a first approximation of the flow phenomena in a normal thoracic aorta.
Further flow simulations using realistic inlet velocity profiles derived from MR flow mapping were performed for increased case-specificity and quantitative assessment. Figure 4.12 shows the MR-derived velocity profiles at the inlet of a normal aorta. The spatio-temporal velocity profiles are shown in three directions (FH, AP, and RL), i.e. the through-plane and in-plane velocity components.

Figure 4.12: Spatio-temporal profiles of the axial and in-plane velocities at the inlet of a normal aorta. The corresponding maximum velocities are also given in each panel.

The velocity profiles are presented at five characteristic time points in systole, i.e. at T1 at the start of systole, T2 at mid-acceleration, T3 at the peak, and T4 and T5 in the deceleration phase. The FH (through-plane) velocities were always higher than the in-plane velocities. AP velocities were the lowest at all time points in comparison with FH and RL velocities. For all the velocity components, their magnitude increased sharply from early acceleration to peak, however it was observed that after T3 (peak systole), velocity patterns were different with the through-plane component maintaining a peak value of 1.1 m/s to T4 before falling by about 17% between T4 and T5, whilst the AP component decelerated by about 27% between T3 and T4 before the peak velocity rose again by about 27% between T4 and T5. On the other hand, the peak RL velocity increased from T3 at 0.36 m/s to 0.37 m/s.
peak at T4 with a velocity of 0.40 m/s (an increase of 12% between T3 and T4) before falling off. The fluctuating velocity gradients at the inlet are expected to affect the flow patterns in the aorta. Figure 4.12 also shows that the through-plane (FH) velocity profiles have a similar shape with fairly uniform velocities in the lumen and low or negative velocities near the wall.

Predicted flow fields were analyzed in terms of instantaneous streamlines and particle trajectories, as described previously. Figure 4.13 shows the instantaneous streamlines for subjects C3 and C5 at 5 different time points along a cycle. The streamlines show the flow patterns to be similar and comparable amongst the TAV subjects. The flow at the outer curvature of the descending aorta (DAo) was more streamlined, uniform and mostly undisturbed at mid-acceleration and peak systole. However, subtle but potentially significant differences were observed between C3 and C5, e.g. C3 showed flow recirculation immediately distal to the inlet along the outer curvature of the ascending aorta at T3 and T4 while C5 showed highly skewed flow towards the inner curvature of the ascending aorta. C3 also showed lower velocities compared to C5 owing to geometric differences: C3 had a larger aorta than C5. At T2, the streamlines were regular and more organized, but there was evidence of disturbed flow from T3, especially at T4 and T5 (mid-deceleration) in both C3 and C5.
Further examination of flow patterns was performed by superimposing secondary velocity vectors on through-plane velocity contours on selected planes between the mid-ascending aorta and the descending thoracic aorta. This would allow the in-plane velocity components to be examined along with the through-plane velocity. Figure 4.14 shows the velocity vectors for subject C3. The results are
displayed at 5 different time points in the cycle: early systole (0.01 s), mid-acceleration (0.06 s), peak systole (0.13 s), early deceleration (0.95 s) and mid-deceleration (0.20 s). It shows that flow patterns in the mid-ascending aorta changed rapidly during systole, with the development of disturbed flow especially prominent during systolic deceleration. In early systole (T1), the rotation of flow was already clear from plane 1 to plane 3, whereas there was little rotation after plane 3 in the descending aorta. At peak systole (T3), a large recirculation zone was observed at plane 1, which was also present at T4 and T5, and extended to plane 2 in systolic deceleration. No vortex was observed on planes 3, 4 and 5 at T2 and T3.
For comparison, Figure 4.15 shows the velocity vectors for C3 and C5 at peak systole. It can be observed that there were more and stronger vortices in C5 than in C3 at this time point, especially on the arch planes 3 and 4 and in the proximal descending aorta at plane 5; whereas these vortices were not developed in C3 until later in systolic deceleration as shown in Figure 4.14 (d) and (e). The locations of vortices were different, which is expected as they depend strongly on the curvature and non-planarity of the aortic arch. The different flow patterns described above can be attributed to differences in aortic flow rate and geometric features between the two subjects.
Figure 4.15: Velocity vectors at peak systole (T3) in C3 (top) and C5 (bottom).

In order to validate the predicted flow patterns, comparisons of axial velocity contours at different time points along the cardiac cycle were made between the simulation results and MR velocity data in the descending aorta (DAo) of two selected subjects.
Figure 4.16 shows comparison of the PC MRI velocity data and CFD simulation results for the FH velocity component in the descending aorta at four time points in the cardiac cycle, i.e. at mid acceleration, peak systole, mid deceleration and early diastole for both C3 and C5. The velocity contour maps are spatio-temporally similar with negative on the colour scale indicating forward flow into the descending aorta and positive indicating retrograde flow. The MR data and simulation results are shown in the same scale for the same time point, and different colour scales are used for different time points.

The same scale was chosen for C3 and C5 for comparison. The plane is viewed in the inferior-superior direction. The MRI data and CFD simulation results show good agreement in both the direction and magnitude of velocities at all time points. Flow was mainly in the forward direction at mid-acceleration. Low velocities were observed on the anterior side in C3 and anterior-left side in C5 at peak systole and mid-deceleration. There was no retrograde flow at mid acceleration and peak systole but by mid systolic deceleration and early diastole, there was evidence of retrograde flow. The retrograde flow contours, showing in the anterior side in C3 and anterior left in C5, were similar in both MRI data and simulation results. The magnitude of retrograde flow was smaller compared to the main forward flow.

Although MRI data and CFD results were comparable, there were differences between the measured and simulated velocities from one case to the other. For example, at mid deceleration, the velocities for C3 were higher for the MRI data compared to the simulation results, whereas the velocities for C5 were smaller in magnitude for MRI data compared to the simulation results. This inconsistency in the pattern from one case to the other at this time point may be due to differences in local geometry and resolution problems. The observation, i.e. note of lower velocities of MRI data compared to higher velocities of CFD result for C5 at mid deceleration, was again observed for both C3 and C5 in diastole. The differences observed between MRI and CFD at this time point may be attributed to overestimation, possibly due to the rigid wall assumption in the CFD model. However, the retrograde flow was very small compared to the main forward flow. Importantly, both forward and retrograde flow distributions were spatio-temporally comparable in MRI and CFD, albeit with differences between the measured and simulated velocities, particularly at mid deceleration and in diastole. There is good evidence that the CFD model simulations have reasonably resolved the arterial flow field.
Figure 4.16: Comparison of axial velocity contours at different time points along the cardiac cycle between the simulation results and MR velocity data (in m/s) in the descending aorta (DAo) of C3 (top) and C5 (lower).

4.5.3 Helical Flow Structure

Helical flow is an important feature of the aorta. It has been found to occur naturally in normal aortas and varies continuously during a cardiac cycle (Kilner et al., 1993). It is challenging to quantify and compare helical flow. Many studies have used 2D vector plots, 3D streamlines or pathlines and isosurfaces to visualize helical flow in the aorta. However, it is difficult to use these methods for quantitative comparison among different subjects. A parameter that describes helical flow structure throughout the entire aorta and cardiac cycle would be needed and for this reason the helicity flow index (HFI) was adopted in this study. The derived HFI values are definitive spatio-temporal flow descriptors, suitable for regional and global aortic flow characterization. In order to determine HFI, particle trajectories are required which can be calculated from the predicted velocities. Figure 4.17 shows the particle trajectories for C3 obtained by releasing uniformly distributed particles from the inlet plane at five injection times during systole. The same interval was maintained between each time point and the total travel time of each particle in the luminal domain was between the injection time and the end of systole.
Figure 4.17: Particle trajectories at T1, T2, T3, T4 and T5 for C3.

HFI is derived from calculations that use local normalized helicity (LNH) obtained from particle trajectory analysis of the flow. LNH is defined as:

$$LNH = \frac{V(s, t) \cdot \omega(s, t)}{|V(s, t)| \cdot |\omega(s, t)|} \quad -1 \leq LNH \leq 1$$ \hspace{1cm} (4.1)

where $s$ is the location and $t$ is the time. The sign of LNH indicates the direction of the rotational flow and it is positive for clockwise rotation (CW) and negative for anticlockwise rotation. The sign of LNH changes across a separation or attachment line, making it very useful for locating these lines and secondary vortices (Morbiducci et al., 2011). Based on the recorded LNH of each particle trajectory, the time-averaged value of LNH experienced by the $k$th particle moving along its trajectory during a specified time interval can be evaluated as:

$$HFI_k = \frac{1}{(T_k^{end} - T_k^{start})} \int_{T_k^{start}}^{T_k^{end}} |LNH_k(\zeta)| d\zeta \quad 0 \leq HFI_k \leq 1$$ \hspace{1cm} (4.2)
For a total of $N_p$ particles moving in the flow domain, the HFI can be calculated as:

$$HFI = \frac{1}{N_p} \sum_{k=1}^{N_p} HFI_k \quad 0 \leq HFI \leq 1$$

(4.3)

Figure 4.18 shows a comparison of average HFI values for cases C3 and C5 at the five particle injection points. The HFI values were higher in early systole and decreased steadily from T1 to T5. It was also noted that HFI values were less variable in C3 than in C5.

![Figure 4.18: HFI values versus particle sets released for each subject at 5 time points.](image)

In addition, the mean value of HFI was calculated for C3 and C5. This was determined as:

$$\bar{HFI} = \frac{1}{N_T} \sum_{j=1}^{N_T} HFI_j \quad 0 \leq HFI \leq 1$$

(4.4)

where $N_T$ is the number of time points at which particles are released ($N_T = 5$ in this case). The values for HFI were 0.42 for C2 and 0.43 for C5, both in agreement with the values reported in the literature (Cheng et al., 2015).

Further information on the helical flow structure can be appreciated by examining helicity density isosurfaces shown in Figure 4.19. An important common feature between the two cases was that the aortic arch had the highest helicity density, with both clockwise and anti-clockwise rotations. This can be attributed to the non-planarity of the aortic arch. Differences were also clear in that helical flow
dominated a larger portion of the arch in C5 than in C3, although the average HFI values differed very little between the two cases.

![Helicity density isosurfaces at peak systole for C3 (left) and C5 (right). Red represents clockwise rotation and blue represents anti-clockwise rotation.](image)

**Figure 4.19:** Helicity density isosurfaces at peak systole for C3 (left) and C5 (right). Red represents clockwise rotation and blue represents anti-clockwise rotation.

### 4.5.4 Wall Shear Stress

It is widely recognized that wall shear stress (WSS) influences endothelial cell function, gene expression and is associated with vascular remodeling (Malek et al., 1999). WSS is sensitive to local geometry and varies with the pulsatile flow. In this study, WSS was analyzed in terms of time averaged wall shear stress (TAWSS), oscillatory shear index (OSI) and shear range index (SRI).

Contours of TAWSS and OSI for selected cases are shown in Figure 4.20. TAWSS was different for each case and varied regionally over the thoracic aorta. Generally low TAWSS was found in cases C1 and C7 along the entire thoracic aorta, while other cases displayed more spatial variations with relatively high TAWSS along the inner bend of the aortic arch and in arch branches. Although TAWSS was observed to be low in most regions of the aorta, it was high in some cases in regions immediately distal to the inlet, and at bends in the arch region and particularly in narrow sections. TAWSS contours in C4 showed large spatial variation in the arch region and in the left common carotid (LCC). C4 also had the highest TAWSS value at 23.29 Pa. This relatively high value could be ascribed to the geometry of C4, particularly to the arch curvature and the very small diameter of the LCC that caused high velocities. Though different for each aorta, TAWSS values were fairly close amongst the normal cases and the mean for all the TAV cases was 18.41 Pa.
The maximum values of TAWSS are given in Table 4.4, which also shows the comparison of results obtained with the two different types of inlet boundary conditions (i.e. flat and 3D realistic velocity profiles). Comparison of TAWSS between the flat and 3D velocity boundary conditions showed much higher maximum values for the latter in all cases except for C5. The difference in each case was at least 20% higher with the 3D velocity boundary condition, and the difference was particularly significant in C4, demonstrating the importance of inlet flow boundary conditions in determining flow patterns and wall shear stress. It was not possible to make similar comparisons for C1 and C2 due to data limitations, as only the through-plane velocity data were acquired on these subjects.
Figure 4.20: Time-averaged wall shear stress (TAWSS) and oscillatory shear index (OSI) for (a) C1 and C2, (b) C3 and C4, (c) C5, C6 and C7.

Table 4.4: Maximum TAWSS for cases with both flat and 3D velocity profiles at inlet

<table>
<thead>
<tr>
<th>Shear Parameters</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C1</td>
</tr>
<tr>
<td>TAWSS$\text{max}_{\text{Pa}}$</td>
<td>Flat inlet velocity profile</td>
</tr>
<tr>
<td></td>
<td>3D inlet velocity profile</td>
</tr>
</tbody>
</table>

Legend: N/A – Not sufficient flow data available.

Spatial distributions of OSI are also displayed in Figure 4.20, which shows a similar pattern in most cases (C1, C2, C5, C6 and C7), with high OSI areas co-localizing with areas of low TAWSS. By
definition, OSI is limited within the range of 0 and 0.5. The results showed that the maximum value of 0.5 was reached in some areas, where frequent directional changes of wall shear stress took place.

4.5.5 Shear Range Index (SRI)

While TAWSS provides spatial mapping of cycle-averaged shear stress on the luminal surface of the entire thoracic aorta, detailed examination of local wall shear stress variations can reveal additional information and facilitate easy comparison among different cases. For this purpose, shear stress index (SRI) was evaluated to measure the degree of flow derangement at the vessel wall.

SRI is defined as:

\[
SRI = \frac{\max[\tau_{\text{max}(\theta,t)} - \tau_{\text{min}(\theta,t)}]}{\tau_{\text{t-avg}}}
\]  \hspace{1cm} (4.5)

It is a parameter that measures circumferential WSS asymmetry along the lumen and has been used in related studies (Cheng et al., 2015). SRI was calculated for a series of planes along the aorta as defined in Figure 4.21. The SRI patterns and values during one cardiac cycle on each of the analysis planes for cases C3 and C5 are shown in Figure 4.22.

![Figure 4.21: Locations of planes 1 to 16 for SRI calculations in C3 (left) and C5 (right).](image)
Figure 4.22: SRI for C3 (top panel) and C5 (lower panel) calculated on the planes 1 to 16 at different time points.
SRI is a dynamic descriptor varying both spatially and temporally. Figure 4.22 shows that SRI values were low at T1, but increased with the increase in flow. At T1, SRI profile was relatively flat showing small variations along the thoracic aorta. Large fluctuations in SRI were observed at other time points, and the peak SRI values were reached at peak systole (T3) or mid-deceleration (T4). In both C3 and C5, SRI was the highest in the arch region (plane 7-8), reaching 16.5 for C3 and 28.08 for C5, but there was an additional peak in C3 in the proximal ascending aorta (plane 2). Compared to SRI values in the ascending aorta (planes 1-6 in C3 and planes 1-5 in C5), SRI was less variable along the descending aorta (planes 9-16).

Table 4.5 shows the average shear range indices (SRI) for different regions of the thoracic aorta. SRI ranged from high values in the ascending aorta and arch regions to comparatively lower values in the descending aorta. The highest SRI was in the arch region and the lowest value was in the distal descending aorta.

Table 4.5: Average values of Shear Range Index (SRI) in different regions of the thoracic aorta for C3 and C5

<table>
<thead>
<tr>
<th>Case / Aorta Region</th>
<th>C3</th>
<th>C5</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAo</td>
<td>5.60</td>
<td>9.65</td>
</tr>
<tr>
<td>Arch</td>
<td>5.71</td>
<td>11.69</td>
</tr>
<tr>
<td>DAo (Proximal)</td>
<td>3.10</td>
<td>4.72</td>
</tr>
<tr>
<td>DAo (Distal)</td>
<td>1.45</td>
<td>3.53</td>
</tr>
</tbody>
</table>

Legend: AAo = Ascending aorta, Arch = Aortic arch, DAo = Descending Aorta.
4.6 Summary

The objective was to characterize morphological and flow features in normal thoracic aortas with TAV by using a combination of MRI and CFD. A systematic approach was developed for MR image acquisition, image processing, 3D geometric reconstruction, patient-specific CFD simulation, as well as measurement and analysis of morphological and haemodynamic parameters.

The morphologies of the TAV thoracic aortas were similar with small differences in measured diameters. The measured diameters varied from 29.1±4.4 (mm) in the proximal ascending aorta to 20.8±2.5 (mm) in the distal descending aorta, and the arch (chord) length was 90.7±14.4 mm. These values are consistent with values reported in the literature (e.g. Burman et al., 2008), and are within the expected range for normal aorta. The arch angles showed more variations among the subjects, with arch angles X and Y in the range of 105 -130° and 74 - 99° respectively. Arch angles have been found to be age dependent (Devereux et al., 2012), and the range of variations obtained in this study is expected given the age range of the subjects concerned.

Flow patterns in normal aortas are very complex with highly helical flow. Helical flow predominates throughout the ascending aorta and the arch, as observed by Kilner et al., (1993). The helical flow described by the helicity density was in both clockwise and anticlockwise directions. The average helicity flow index (HFI) obtained for all the TAV cases was 0.425, which is in agreement with data in the literature (Cheng et al., 2015). The difference between cases was less than 2%. The flow patterns showed more turbulent characteristics and spatio-temporally evolving vortices in the ascending thoracic aorta and arch, especially at peak flow and flow deceleration phase. Generally, compared to other thoracic regions the flow patterns in the distal descending thoracic aorta appeared more organized and laminar-like. These characteristic features and values agree with those obtained for normal aortas by Cheng et al., (2015). The results obtained in this study show that the numerical model strategies employed can adequately capture: (1) the spatio-temporal distribution of velocities in the thoracic aorta, (2) the helical flow patterns and shear rate indices, (3) vortex evolution and locations.

The anatomic and flow information obtained from the combination of MRI and CFD simulations have permitted the interrogation and assessment of the thoracic aorta throughout the cardiac cycle. The wall shear stress (WSS) distribution pattern amongst TAVs was qualitatively similar, regardless of the shape of inlet velocity profiles (flat or realistic), but notable quantitative differences were found. On average, models with realistic 3D inlet velocity profiles predicted high TAWSS than those with a flat profile, demonstrating the influence of inlet flow boundary conditions on aortic flow patterns and wall shear stress. In all cases, TAWSS in the thoracic aorta was generally low, except at bends, in the
arch region and arch branches where isolated patches of high TAWSS values were found. Wall shear stress is strongly influenced by the blood flow rate of each individual.

The derived SRI and multi-plane analysis showed large spatial and temporal variations of WSS in the thoracic aorta, with the highest SRI in the arch. On the basis of the circumferential WSS derangement reflected by SRI and the helical flow structure described by HFI, it is evident the flow environment is significantly different between the ascending thoracic aorta, the arch and the descending thoracic aorta.

In summary, the haemodynamic conditions of the normal aortas examined in this study are highly comparable with subtle differences in quantitative measures that are ascribable to differences in aortic geometric configuration and dimensions. Geometry has been found to impose a significant influence on flow patterns and dynamics.
Chapter 5

5 Patient-Specific Abnormal Thoracic Aorta Study: Case with Bicuspid Aortic Valve (BAV) in comparison with normal TAV

This chapter details the case study of an abnormal human thoracic aorta with bicuspid aortic valve (BAV). Subject-specific anatomic and flow data obtained using MRI were used to build a realistic model for CFD simulations in order to determine flow patterns, wall shear stress (WSS) distributions and other important flow parameters in a BAV aorta. Section 5.1 provides the patient information and Section 5.2 describes the reconstructed 3-D model and flow data, together with the modeling procedures. Section 5.3 provides an account of the interplay between the morphological features and haemodynamic patterns. The results are presented in Section 5.4 with detailed analysis of the BAV aorta in terms of velocity profiles, time-averaged wall shear stress, turbulent intensity, and helical flow density and flow reversal ratios in the thoracic aorta.

5.1 Patient Information

A 34-year-old male patient with a BAV was recruited with consent and approval of the local ethics committee. The patient data were acquired at the Royal Brompton Hospital London, by routine clinical MR imaging protocol and sequences. Details of the imaging parameters are presented in Table 5.1. Patient’s images were anonymized before further analysis.

<table>
<thead>
<tr>
<th>Venc (cm/s)</th>
<th>Flip Angle (°)</th>
<th>Slice Thickness (mm)</th>
<th>FOV (mm)</th>
<th>Pixel Spacing</th>
<th>TR (ms)</th>
<th>TE (ms)</th>
<th>Number of Images</th>
</tr>
</thead>
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<tr>
<td>150</td>
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<td>6.0</td>
<td>255 x 340</td>
<td>1.25 x 1.25</td>
<td>800</td>
<td>42</td>
<td>35</td>
</tr>
</tbody>
</table>

Legend: FOV = Field of View, TR = Repetition Time, TE = Echo Time.

5.2 Reconstructed 3-D Model

Haste images (35 in total) were segmented to reconstruct the 3-D geometric model and the PC MRI magnitude and phase images (20 pairs) acquired at the inlet plane were segmented to derive the flow
data and velocity profiles. Figures 5.1 (a) and (b) show the sample Haste images and the reconstructed 3-D model respectively. Due to resolution limitations, it was only possible to reconstruct a short section of the arch branches, with a length of approximately 3 cm from their origins on the arch. In order to minimize the influence of artificial boundary conditions imposed at the branch outlets, each arch branch was further extended by at least 5 times the lumen diameter.

Figure 5.1: Reconstruction of the thoracic aorta with BAV: (a) Sample Haste image from which the segmented 3D volume (lumen) was obtained, (b) Geometric 3D model.

5.3 Flow Model and Computational Details

Based on the methodology described in Chapter 3 and experience gained from the earlier simulations of the TAV cases (Chapter 4), blood was assumed to be homogeneous, incompressible and Newtonian with a dynamic viscosity of 0.004 Pa.s and a density of 1060 kg m$^{-3}$. The aortic wall was assumed rigid with no-slip conditions at the wall. The boundary condition imposed at the model inlet was generated from PC-MRI measured flow, as described in Chapter 4 for the TAV cases. Examples of the acquired MR images and segmented axial (orthogonal) velocity profiles are shown in Figure 5.2. Figure 5.3 (a) shows the volumetric flow waveform extracted from MR flow images obtained on the same BAV patient. Figure 5.3 (b) shows the waveform from CFD simulations for the same BAV patient.
Figure 5.2: (a) PC MRI magnitude and phase images - (AAo outlined in blue), and (b) Sample axial (through plane) velocity map on 2D Plane (left) and 3D view (right).
Figure 5.3: (a) MR-derived volumetric flow rate at the inlet plane in the ascending aorta of the BAV patient. (b) Mass flow rate from CFD simulations of the BAV patient.

The segmented through-plane velocity data were imposed at the inlet of the computational domain, by mapping between the 3D model inlet and the imaging plane using the same method described in Chapter 4. The mean Reynolds number (Re) (derived from the calculated mean velocity and inlet
diameter) was 880.5 and the peak Re, based on the peak velocity and inlet diameter, was 4055 and the Womersley number was 17.86. Based on the stability line shown in Figure 4.4, flow in the BAV aorta was disturbed, justifying the need for the SST-Tran model. Computational details were similar to those adopted for the TAV cases, i.e. a uniform time step of 0.001 s was specified and three cardiac cycles were run to ensure a periodic solution. The solution obtained from the previous cycle was used to initialize the next cycle, and the analysis was based on results from the final (third) cycle. The flow waveform for the simulation is shown in Figure 5.3 (b).

The derived peak flow in Figure 5.3 (a) of 24.6 L/min is comparable to the simulation peak flow (mass flow of 0.33 (kg/s)), equivalent to 18.7 L/min. However, there is a shortfall of 24.1% between the calculated volumetric flow and simulation flow results. This difference may be attributable to a combination of factors, e.g. underestimation of the simulation peak flow due the low image resolution, and simulation round off errors.

5.4 Results and Discussion

In what follows, the morpho-haemodynamic results of the 3D thoracic aorta for a BAV patient are presented. The results from the flow simulations were evaluated with a focus on the characteristic flow patterns and shear stress environment; these include instantaneous streamlines, isosurfaces and contours of TAWSS, OSI, turbulence intensity (Tu) and helical flow densities ($H_d$).

5.4.1 Morphology

The reconstructed thoracic aorta geometry of BAV is depicted in Figure 5.4, showing the measured diameters at different locations. The diameter at the STJ was 34.02 mm. The AAo diameter increased to a maximum of 34.59 mm immediately downstream of the STJ, before it gradually reduced to a minimum of about 29 mm in the proximal arch region.
Figure 5.4: Reconstructed 3D geometry of the thoracic aorta with BAV depicting the changing diameter along the aorta.

The diameter downstream of the aortic root ranged between 34.59 mm and 19.42 mm, from the ascending aorta to the end of descending thoracic aorta. The largest diameter in the ascending thoracic aorta was recorded at a location between the sinotubular junction and the proximal ascending aorta, where enlargement was observed. Beyond the enlarged portion and into the descending aorta, there was a subtle but definite tapering of the thoracic aorta. BAV diameter measurements between the STJ to distal DAo showed a tapering of 42.92%. The amount of tapering from the ascending aorta to the beginning of descending aorta was less than 50% in this BAV case but within the range of tapering reported in other studies (Wolak et al., 2008).

Further, more measurements were taken downstream of the STJ in the mid-ascending aorta area and within two measurements set 1 to 2 mm apart (taken between two planes in the axial direction), there
was a 4% incremental change in the ascending aorta (AAo) diameter. This diameter increase is probably only a local expansion and not an indication of the reported aortic dilation usually seen in BAV, which has been suggested as a cofactor in the development of diseases like aneurysm and dissection (La Canna et al., 2006; Cecconi et al., 2005). Though these studies have demonstrated that aortic diameter and the rates of dilatation in BAVs are statistically greater than in subjects with a normal TAV, it is important to note that these studies did not find any correlation between aortic dimensions and aortic valve morphology (Cecconi et al., 2005).

As described and determined for the TAV cases, the BAV arch angles were also measured and depicted in Figure 5.5. A summary of BAV diameters and arch angles is given in Table 5.2.

Figure 5.5: Definition of arch angles as previously defined in Chapter 4. (a) X is ABD and Y is BAC (b) minor arch angle BAD and major arch angle DAE.
Table 5.2: Summary of measured diameters and arch angles for the BAV aorta

<table>
<thead>
<tr>
<th>BAV1 Location Measurements</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diameter (mm)</strong></td>
<td></td>
</tr>
<tr>
<td>Sinotubular Junction (STJ)</td>
<td>34.02</td>
</tr>
<tr>
<td>Mid-Ascending Aorta (AAo)</td>
<td>34.59</td>
</tr>
<tr>
<td>Proximal Ascending Aorta (AAo)</td>
<td>34.02</td>
</tr>
<tr>
<td>Distal Ascending Aorta (AAo)</td>
<td>31.59</td>
</tr>
<tr>
<td>Proximal Descending Aorta (DAo)</td>
<td>22.30</td>
</tr>
<tr>
<td>Distal Descending Aorta (DAo)</td>
<td>19.42</td>
</tr>
<tr>
<td><strong>Chord (mm)</strong></td>
<td></td>
</tr>
<tr>
<td>Arch Chord Length, C</td>
<td>95.94</td>
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<tr>
<td><strong>Angle (°)</strong></td>
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<tr>
<td>Arch Angle X</td>
<td>133.96</td>
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<tr>
<td>Arch Angle X₁</td>
<td>24.57</td>
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<tr>
<td>Arch Angle Y</td>
<td>55.11</td>
</tr>
<tr>
<td>Arch Angle Y₁</td>
<td>33.61</td>
</tr>
</tbody>
</table>
5.4.2 Flow Patterns

Instantaneous streamlines in the thoracic aorta for the BAV case are presented in Figure 5.6 at five different time points in systole corresponding to the start (T1), mid acceleration (T2), peak (T3), fast deceleration phase (T4) and mid deceleration (T5). Further visualization of flow patterns is given through velocity vectors on highlighted planes in Figure 5.7, and particle trajectories in Figure 5.8. BAV1 streamlines in Figure 5.6 at T1 were quite ordered with a low velocity range. The onset of disturbed flow could be seen as the flow spatio-temporally evolved. In early systole, the flow was organized and appeared laminar, however, the streamlines showed signs of helical flow in the proximal ascending aorta (AAo) at T1, T2, and at T3. The spiral and helical flow became more pronounced as flow started to decelerate. From the streamlines in Figure 5.6 and the corresponding velocity maps in Figure 5.7 at T4 and T5, it is observed that the helical flow pattern has become predominant in the ascending aorta, the arch and proximal descending aorta. The helical patterns were more prominent along the inner curvature of the thoracic aorta. By early and mid-deceleration, the helical pattern was observed to be bi-directional, in clockwise and anticlockwise directions, along the whole of the ascending aorta (AAo), in the arch and proximal descending aorta (DAo). Combining the streamlines and particle trajectories in Figure 5.6 and Figure 5.8 respectively, some areas of recirculating flow can be observed, particularly at T4 and T5 in the ascending aorta and along the inner curvature of the arch and proximal DAo. In Figure 5.7, the velocity contours (through-plane velocity components only) changed as flow traversed the constantly changing thoracic topology, with low velocity flow skewed towards the inner curvature of the aorta at T4 and T5. There is a correspondence in the location of the helical pattern observed in Figure 5.6 and the velocity contours in Figure 5.7.
Figure 5.6: Instantaneous streamlines in the thoracic aorta for BAV1 at different times in the cardiac cycle.
The influence of BAV was pronounced and apparent at the inlet in the proximal ascending aorta. From the streamlines, flow at the inlet was skewed in the anterolateral direction, possibly as a result of the BAV. At this time point, T1, the flow was eccentric with high velocities in the anterior aspect and low velocities in the posterior aspect. The flow pattern was highly asymmetric and the observation compared favorably with that of Barker et al., (2010) for BAV aortas and for diseased aortas reported by Cheng et al., (2015). The velocities increased from a maximum of 0.4 m/s at T1 to 0.91 m/s and 1.1 m/s at T2 and T3 respectively. The highest velocities were along the outer curvature and in the arch region during most of the systolic phase. The maximum velocities decreased to 0.9 m/s and 0.8 m/s at T4 and T5. Flow patterns at T1, T2 and T3 were more organized compared to those during T4 and T5. The velocities were higher anterolaterally in the AAo, centrally and posteriorly in the arch and posteriorly at the outer curvature in the DAo at T4 and T5. Secondary flows were observed in the ascending aorta, arch section and proximal descending aorta during T4 and T5.

Until recent times, there have been very few studies on BAV haemodynamics, and the related studies were mainly experimental, sparse on data and have provided mainly qualitative assessment. However, previous experimental studies have been pivotal to recent and new studies, which have become more subject/patient-specific, and provided both qualitative and quantitative assessment of aortic flow.
Figure 5.7: Velocity vectors (m/s) on selected planes (orthogonal to flow direction) along the thoracic aorta, at six characteristic time points in systole as indicated in panels.
5.4.3 Turbulence Intensity

To examine the possible occurrence of turbulence, turbulence intensity $Tu$, defined as the ratio of the root-mean-square value of the fluctuating components of velocity to the mean velocity, was plotted as isosurfaces. Turbulence intensity isosurfaces of two TAV cases are depicted in Figure 5.9. Further, for comparative analysis, isosurfaces and turbulence kinetic energy values of TAV and BAV cases are presented in Figure 5.10.
Figure 5.9: C5 (left) and C6 (right) showing turbulence intensity isosurfaces at mid-systolic deceleration.
There was little or no evidence of turbulence observed at the start, mid-acceleration and peak systolic phase but at mid deceleration turbulence was apparent, with a range of intensities depicted in Figure 5.9. The turbulence intensity, $Tu$, was different and varied in magnitude in and amongst the individual TAV cases. High $Tu$ levels of up to 50% were found in the descending thoracic aorta, especially in the proximal DAo at mid deceleration and end systole. However, analyzing the turbulence kinetic energy (TKE) maps in Figure 5.10, high TKE levels were found in the ascending and descending thoracic aortas of both TAV and BAV at mid deceleration and end systole.
Further, it was observed that the area experiencing high TKE in the ascending aorta was larger in the BAV aorta than that in the TAV aorta. Conversely, the region experiencing high TKE in the descending thoracic aorta was smaller in the BAV aorta than that in the TAV case. The low-high range of velocities along with rapid spatio-temporal changes influenced the levels of turbulence intensity and turbulent kinetic energy.

5.4.4 Helical Flow Structure

The bulk flow structures and particularly helical flow, was an important focus feature for observation, spatio-temporal analysis and quantification in the investigation of BAV, because helical flow has been demonstrated to be a natural occurrence in the aorta (Kilner et al., 1993). Results for helicity density, evaluated at five different time points in a cycle are displayed in Figure 5.11, which revealed the evolving helical flow direction, and changes in magnitude during the systolic phase. No appreciable helicity was observed at the start of systole and very low values were observable at mid-acceleration in the arch. There was increased helicity in both clockwise and anti-clockwise directions in the arch at peak and mid-deceleration with the highest value recorded at mid-deceleration. It is particularly interesting that in the BAV aorta there was some increase in absolute peak relative helicity at mid-deceleration during systole, and a heterogeneous distribution of mean helicity within the thoracic aorta. Helical flow was observed mainly in the ascending aorta and arch regions, and was largely absent in the descending aorta. The helicity flow index, HFI, depicted in Figure 5.12 shows a low and fluctuating range between 0.28 and 0.33 with the highest value at peak systole.
Figure 5.11: Helical flow in the clockwise (red) and anticlockwise (blue) direction during systole for the BAV case.
**Figure 5.12:** HFI values for BAV1 calculated from particle traces taken at the inlet plane for five injection periods in systole. Average HFI = 0.30

### 5.4.5 Wall Shear Stress

The importance of wall shear stress (WSS) in vascular biology and arterial diseases has been mentioned in the preceding chapters. Figure 5.13 shows the time averaged wall shear stress (TAWSS) contours for the BAV case analyzed here. Generally, TAWSS ranged between 0.02 and 7.39 Pa. TAWSS magnitude varied along the thoracic aorta with low values in the anterior and right regions of the ascending thoracic aorta and in the descending aorta. TAWSS was slightly higher on the right than on the left. Higher values in the range of 2.51 to 3.75 Pa were found in the ascending aorta (AAo) and arch region. Along with localized high TAWSS values in the arch region, very low values between 0.02 and 1.26 Pa were also observed in some areas, e.g. band of low TAWSS observed between the LCC and brachiocephalic arteries. Further, in Figure 5.13, in the AAo, TAWSS values were higher left compared to the right. TAWSS values greater than 3.75 Pa were found near the junctions of the arch branches. TAWSS values were low in the descending thoracic aorta.

The impact of inflow boundary condition on the thoracic aorta haemodynamics has been evaluated particularly in terms of TAWSS distribution on the luminal surface, and helical flow structures in a study by Morbiducci et al., (2013). Results obtained in this study are comparable to those of Morbiducci et al.
The oscillatory shear index (OSI) was also investigated and areas of high OSI were found to coincide with areas of low TAWSS indicating a localized flow reversal or a varying flow direction (similar to findings in the TAV discussed and highlighted in Chapter 4).

5.4.6 Shear Range Index (SRI)

Shear Range Index (SRI) is another index used in the assessment of flow derangement at the arterial wall. As previously defined and explained in Chapter 4, SRI is derived from wall shear stress and is used to measure the circumferential WSS asymmetry along the BAV luminal wall. Figure 5.14 shows the derived SRI at five characteristic time points in systole on a number of analysis planes defined along the BAV thoracic aorta. The regional SRI values for BAV1 are given in Table 5.3.
Figure 5.14: SRI for BAV1 derived at different time points in systole.

Table 5.3: Average values of wall shear range index (SRI) in difference regions of the aorta in the BAV case

<table>
<thead>
<tr>
<th>Aorta Region</th>
<th>AAo</th>
<th>Arch</th>
<th>DAo (Proximal)</th>
<th>DAo (Distal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shear Range Index (SRI)</td>
<td>2.52</td>
<td>6.80</td>
<td>3.20</td>
<td>2.52</td>
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</tbody>
</table>

Legend: AAo = Ascending aorta, Arch = Aortic arch, DAo = Descending Aorta.

5.5 Comparison with normal TAV aorta

In this section, morphological and flow features of the BAV aorta are compared with those of normal thoracic aortas obtained from subjects with a TAV. Mean values of geometric dimensions of the TAV
aortas (evaluated in Chapter 4) were compared with the corresponding dimensions of the BAV case. For a fair comparison of flow parameters, flow in C5 (TAV) was reanalysed using the same type of inlet boundary condition as adopted in the BAV case, and the obtained results were compared with those for BAV1.

### 5.5.1 Geometric Features

The geometric measurements of the TAV and BAV1 subjects were taken at selected locations as depicted in Figure 5.15. Table 5.4 shows the comparison of the mean values for normal TAV aortas and the BAV aorta.

![Image](image_url)  

**Figure 5.15:** Definitions of selected locations of the thoracic aorta used for geometric measurements in the TAV and BAV models.

The diameters measured along the thoracic aorta at similar locations for both TAV and BAV (Table 5.4) showed marked differences between the two valve types. In comparison, TAV diameters were smaller at all locations except in the descending aorta where the BAV diameter was slightly smaller, indicating that the ascending aorta of the BAV subject was dilated.
Comparing the mean TAV and BAV1 arch angles in Table 5.4, there were differences between the two valve types, with arch angle X being considerably wider and larger by 15.4%, and angle Y much smaller by 60.9% in the BAV1 aorta.

Table 5.4: Comparison of key geometric measures between TAV and BAV aortas

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Location</th>
<th>Cases</th>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAV</td>
<td></td>
<td>BAV1</td>
</tr>
<tr>
<td></td>
<td>Mean± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D (mm)</td>
<td>Mid SoV</td>
<td>32.5±2.1</td>
<td>34.5</td>
</tr>
<tr>
<td></td>
<td>STJ</td>
<td>27.8±3.0</td>
<td>34.0</td>
</tr>
<tr>
<td></td>
<td>Proximal AAo</td>
<td>29.1±4.4</td>
<td>34.0</td>
</tr>
<tr>
<td></td>
<td>Distal AAo</td>
<td>29.5±4.4</td>
<td>31.6</td>
</tr>
<tr>
<td></td>
<td>Proximal DAo</td>
<td>23.3±2.6</td>
<td>22.3</td>
</tr>
<tr>
<td></td>
<td>Distal DAo</td>
<td>20.8±2.5</td>
<td>19.4</td>
</tr>
<tr>
<td>Chord Length</td>
<td>Arch</td>
<td>90.7±14.4</td>
<td>95.9</td>
</tr>
<tr>
<td>(mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arch Angle</td>
<td>X</td>
<td>113.27±10.19</td>
<td>133.96</td>
</tr>
<tr>
<td></td>
<td>X1</td>
<td>25.07±3.57</td>
<td>24.57</td>
</tr>
<tr>
<td></td>
<td>Y</td>
<td>88.67±11.88</td>
<td>55.11</td>
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<tr>
<td></td>
<td>Y1</td>
<td>54.27±9.33</td>
<td>33.61</td>
</tr>
</tbody>
</table>
5.5.2 Flow Features

The subject-specific MR images were used to derive the inlet flow parameters. Figure 5.16 shows the imaging planes (used as inlet for the corresponding CFD model) and their geometric dimensions. It is clear that the BAV aorta is much larger than the TAV aorta at this location. Volumetric flow rate waveforms for the TAV and BAV cases are shown in Figure 5.17. Although they were similar in shape, the maximum flow rate in TAV (32.2 L/min) was much higher than that of BAV (24.6 L/min). The mean cardiac output of the TAV case at 6.13 L/min was also higher than of the BAV at 4.8 L/min. These flow rates and values compare favourably with results from other studies of similar nature, e.g. Barker et al., (2010), Cheng et al., (2010).

![MR images of the inlet plane](image)

**Figure 5.16**: MR images of the inlet plane: (a) TAV aorta (C5): \( D = 0.02892 \text{ m}, A = 0.000657 \text{ m}^2 \) (b) BAV aorta: \( D = 0.03527 \text{ m}, A = 0.000977 \text{ m}^2 \).
Figure 5.17: Flow waveforms for a TAV (C5) and BAV aorta.

Figure 5.18: Velocity profiles at the inlet of C5 (top row) and BAV1 (bottom row) at nine time points, T1 to T9.
Differences in velocity profiles at the inlet and their temporal variations can be appreciated through the 3D velocity profiles shown in Figure 5.18. It is clear that inlet velocity profiles in the TAV case were more uniform and less skewed compared to those in the BAV aorta. There were high velocities at T2, T3, T4 and T5 in both aortas with the velocities at these time points higher and more axially directed in TAV than BAV. Further analysis of flow was done by calculating the flow reversal ratio.

**Flow Reversal Ratio**

The flow reversal ratio (FRR), previously defined in Chapter 3 (equation 3.41) is a percentage value used to quantify flow derangement. The degree of retrograde flow in systole was calculated for each case as in equation (3.41) i.e.

\[
\text{FRR} = \left| \frac{Q_{\text{negative}(t_{\text{systole})}}}{Q_{\text{positive}(t_{\text{systole})}}} \right| \times 100\%
\]

where \(Q_{\text{positive}(t_{\text{systole})}}\) and \(Q_{\text{negative}(t_{\text{systole})}}\) represent the forward and reverse flow at peak systole.

Table 5.5 shows the FRR values obtained for three TAV subjects and one BAV subject. FRR values in TAV models were found to be much smaller compared to the BAV aorta. The FRR values for the TAVs at less than 10% show good consistency with results of Barker et al., (2010). Furthermore, the BAV1 case showed relatively low retrograde flow, which appears to be in the low retrograde category of <10% FRR for BAV aortas as reported by Barker et al., (2010). Moreover, FFR has been highlighted to be a useful parameter for the planning of extracorporeal (EC) procedures, in which blood is taken from a patient’s circulation to undergoing a specific process before being returned to the normal circulation. It has also been found that excessive and persistent retrograde flow can be detrimental as it can reduce antegrade flow into other (smaller) arteries. It is a factor significantly associated with perfusion. Bensalah et al., (2014) examined aortic geometric parameters and haemodynamics, and found a strong relationship between aortic backward flow and age. However, in this study, due to data limitation (one dataset available) such a relationship cannot be drawn.
Table 5.5: Comparison of flow reversal ratio (FRR) between TAV and BAV cases

<table>
<thead>
<tr>
<th>Subject</th>
<th>C3</th>
<th>C4</th>
<th>C5</th>
<th>TAV Mean± SD</th>
<th>BAV1</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRR (%)</td>
<td>2.70</td>
<td>3.03</td>
<td>2.10</td>
<td>2.61±0.47</td>
<td>8.30</td>
</tr>
</tbody>
</table>

Comparisons of velocity contours on defined planes along the thoracic aorta are depicted in Figure 5.19 (a) at early systole and (b) peak systole, respectively. To further highlight the spatio-temporal flow patterns of the TAV and BAV, Figure 5.20 depicts the velocity vector plots on corresponding planes in the ascending aorta, arch region, and descending thoracic aorta. The axial velocities along the thoracic aorta are depicted at six characteristic time points in systole, i.e. at start, mid acceleration, peak, early deceleration, mid deceleration and late deceleration. Disturbed flows were observed in the thoracic aortas of both TAV and BAV cases, particularly along the inner curvature. Recirculation was first noticed at peak, and was found to be stronger in systolic deceleration. The disturbed flow may be due to the combined effects of strong aortic curvature and instability caused by flow deceleration. There was a clear and marked difference in flow patterns between the TAV and BAV aortas, especially in the ascending aorta at mid deceleration and late deceleration where flow and velocities were very low. The maximum TAV velocity was 21% higher than the maximum BAV velocity at late systole. Flow was more skewed in BAV than in TAV during late systole.
Figure 5.19: Comparisons of velocity contours (m/s) at sixteen defined analysis planes along the entire thoracic aorta of a TAV (left) and BAV (right) at (a) early start systole (b) peak systole. Colour maps in (m/s).
Comparison of velocity vectors (m/s) on selected planes (orthogonal to flow direction) along the thoracic aorta of a TAV left) and BAV (right) subject, at six characteristic time points (top to bottom). Continued below:
Comparison of velocity vectors (m/s) on selected planes (orthogonal to flow direction) along the thoracic aorta of a TAV (left) and BAV (right) subject, at six characteristic time points (top to bottom). Continued below:
Figure 5.20: Comparison of velocity vectors (m/s) on selected planes (orthogonal to flow direction) along the thoracic aorta of a TAV left) and BAV (right) subject, at six characteristic time points (top to bottom).
Helicity Density

With the same number of particles released and the same period of tracking in both TAV and BAV, comparisons were made between the two groups. Comparisons of particle trajectories between the TAV and BAV cases are given in Figure 5.21, Figure 5.22 and Figure 5.23. At T1 and T2 in early systole there was swirling in both the TAV and BAV aortas, but it was more pronounced in the ascending aorta of the BAV case, appear more loosely wrapped, with less tortion compared to TAV. The particle trajectories were obtained by tracking the motion of 400 particles released at the inlet over one cardiac cycle, extents were longer in TAV compared to BAV. The figures together show the evolution of the helical patterns with both clockwise and anticlockwise directions and changing strengths of the flow. With the varying velocities, the extent and length of the trajectories were changing. As the systolic cycle progressed and flow reduced, the trajectories reduced in extent. The spiral helical patterns changed in direction with the fluctuating velocities as the pathlines twisted, wrapped and coiled around each other. Helicity is the degree to which the velocity field twists and turns. The TAV aorta showed more helical forms along the inner curvature whereas BAV helixes were more dense in the outer aorta curve region, particularly in the proximal ascending aorta areas owing to the strongly skewed velocity profile at the inlet.
Figure 5.21: Particle trajectories at T1 and T2 for the TAV aorta (left) and BAV aorta (right).
**Figure 5.22:** Particle trajectories at T3 and T4 for the TAV aorta (left) and BAV aorta (right).
Comaprison of helicity flow indices are shown in Figure 5.24. HFI was higher for TAV than for BAV at all time periods covered. Over the systolic phase interval (for which the particle traces were clustered and analysed), HFI was 20% higher in TAV than BAV. Helical flow structures and magnitudes are further revealed in Figure 5.25 (a, b, c,) showing the evolution of helical flow during systole. Both TAV and BAV showed clockwise and anti clockwise rotations. The helicity values depicted are relative and it was observed that the helical flow was denser in the TAV than BAV. Further, the helical flow structures were more extensive in the TAV than in the BAV. This difference in depth and quantity can be ascribed to differences in flow volume, velocity and energies within the two types of aortas. Importantly, helical flow does occur in both normal and abnormal aortas.

**Figure 5.23:** Particle trajectories at T5 for the TAV aorta (left) and BAV aorta (right).

![Velocity vs Time Graph](image)

**Figure 5.24:** Comparison of HFI between TAV (C5) and BAV1 calculated from particle traces taken at the inlet plane for 5 injection periods in systole. Average HFI: C5 = 0.37 and BAV1 = 0.30
Helicity Density (HD): 
- **Clockwise** (Positive Value)
- **Anticlockwise** (Negative Value)

(a)
Figure 5.25: Comparison of helical flow in the clockwise and anticlockwise direction at different time points in systole between TAV (left) and BAV (right). Showing (a) start and mid acceleration, (b) peak and early deceleration and (c) mid deceleration. Maximum helicity density (HD) values are indicated (i.e. positive clockwise, and negative anticlockwise) on the colour bar.

Wall Shear Stress (WSS)
In comparison with the TAV cases discussed in Chapter 4, TAWSS in the BAV aorta was lower, and this could be expected in view of both the larger aortic diameter of BAV, and the comparatively lower cardiac output/flowrate. The cardiac output was 4.8 L/min in BAV compared to mean CO of 6.13 L/min in TAV.
Shear range index (SRI)

The spatio-temporal variation in circumferential shear range index (SRI\textsubscript{circumferential}) has been shown previously in Figure 5.14 for the BAV aorta, which is qualitatively similar to that of the TAV aorta. Quantitative comparisons are given in Table 5.6, which shows that SRI was comparable between TAV and BAV with the highest values in the arch region and lowest in the distal DAo. The very low SRI in the distal DAo is as expected considering the low velocities and laminar nature of flow in this region. The range of SRI values for the TAV aorta obtained in this study agree with the values reported by Cheng et al., 2015, who also found the highest SRI in the aortic arch.

Table 5.6: Comparison of average values of shear range index (SRI) in different regions of the thoracic aorta for TAV (C3 and C5) and BAV cases during systolic phase

<table>
<thead>
<tr>
<th>Case /Aorta Region</th>
<th>C3</th>
<th>C5</th>
<th>BAV1</th>
</tr>
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<tbody>
<tr>
<td>AAo</td>
<td>5.60</td>
<td>9.65</td>
<td>2.52</td>
</tr>
<tr>
<td>Arch</td>
<td>5.71</td>
<td>11.69</td>
<td>6.80</td>
</tr>
<tr>
<td>DAo (proximal)</td>
<td>3.10</td>
<td>4.72</td>
<td>3.20</td>
</tr>
<tr>
<td>DAo (distal)</td>
<td>1.45</td>
<td>3.53</td>
<td>2.52</td>
</tr>
</tbody>
</table>

Legend: AAo = Ascending aorta, Arch = Aortic arch, DAo = Descending Aorta.
5.6 Summary

The geometry and haemodynamics of the TAV and BAV aortas were compared. The morphological analysis of both groups showed spatial variations along the entire thoracic aorta. Comparing level by level, diameters in the ascending thoracic aorta were larger in BAV than in TAV. Tapering in the descending aorta was evident in both groups but it was higher in BAV at 42.92% compared to TAV with a mean tapering of 25%. These differences in thoracic aorta diameters between the TAV and BAV could be due to the valve type. It has been suggested that there is a difference in the structure and strength of collagen fibres and other tissue components of the aortic wall between TAV and BAV aortas. The continuous impingement on the aortic wall by a skewed flow along with a weakened aortic wall will have a degenerative effect on the wall, causing endothelium denudation that may lead to aneurysm or dissection over time.

Although flow patterns in the TAV and BAV aortas exhibited qualitatively similar features, there were quantitative differences. The flow rate waveforms were similar, but both peak and mean flows in the BAV aorta were lower than those in the TAV aorta. Moreover, TAV aortas were found to have lower flow reversl ratio (2.61%) compared to BAV (8.30%). Turbulent vortices were observed along the inner curvature of the thoracic aorta in both the TAV and BAV particularly at mid and late deceleration. This was similar to observations by Tokuda et al., (2008). The flow field was asymmetric and with helical flow observed in both TAV and BAV. The helical flow index for TAV was higher at 0.425 compared to 0.30 for BAV. The shear range index was generally low in the thoracic aorta with the highest value obtained in the arch region.

Work presented in this chapter demonstrates that 3D cine PC MRI and CFD have been successfully combined and employed to obtain spatial and temporal flow descriptors and assessment of a BAV aorta. By using subject-specific geometric and flow data from MRI in CFD simulations, it is possible to obtain haemodynamic indicators to assess normal and disturbed flows in the aorta, which may be useful for the assessment, treatment and management of aortic diseases for individual patients.
Chapter 6

6 Conclusion and Recommendations

6.1 Main Conclusions

The aim of this project was to develop a magnetic resonance imaging (MRI) based computational fluid dynamics (CFD) model of the human thoracic aorta, for quantitative analysis of morphological and haemodynamic parameters. The model can be used to assess and compare haemodynamic functions of the aorta amongst individual subjects. The ultimate aim is to have a modelling tool that will aid in clinical diagnosis, treatment and management of thoracic aortic diseases. In order to do this, MR images containing anatomic and flow information of the thoracic aorta were processed and used to build patient-specific CFD models for detailed flow analysis. Since blood flow in the aorta can undergo transition from laminar to turbulent during part of the cardiac cycle, in addition to the Reynolds averaged Navier-Stokes equations, the shear stress transport transitional (SST-Tran) model was chosen to simulate and evaluate flow in patient-specific models of the thoracic aorta. Seven normal aortas with tricuspid aortic valves (TAV) and one abnormal aorta with a bicuspid aortic valve (BAV) were included in this study. The main findings of this study are summarised below.

6.1.1 Morphological Features

The normal thoracic aortas (with TAV) were similar in shape with subject-to-subject variations in branching angle, curvature and geometric dimensions reflected in the differences in diameter and angle measurements. The aortic diameter in the TAV subjects was 32.5±2.1 mm in the mid sinus of Valsalva (SoV), whilst diameters measured from the sinotubular junction (STJ) to distal descending aorta (DAo) ranged between 27.8±3.0 mm and 20.8±2.5 mm. The TAV aortic diameter was largest at the (SoV). The mean tapering from the STJ to distal DAo was 25.3±5.5%. Though the number of subjects studied was small, it was interesting to note that the smallest STJ diameter was recorded in the youngest subject (25 years) and the largest value in the oldest subject.

Aortic diameters in the BAV subject varied from 34.5 mm at the STJ to 19.4 mm in the distal DAo. In comparison to TAV aortas, the ascending aorta of the BAV subject was larger especially in the mid-ascending aorta.
The tapering from the STJ to distal DAo was 42.92%, which was more distinct compared to the aortas in TAV subjects. The larger ascending aorta diameter in the BAV subject is expected, and can be ascribed to the valve type which causes highly skewed velocity profile at the valve plane, resulting flow impingement in the mid-ascending aorta causing local dilatation.

The measured arch angles showed smaller variation amongst individuals with differences ranging from 10 to 12% for angles X, X1 and Y. However, for angle Y1, the difference was higher at up to 20%. The BAV aorta had a larger arch angle X which was 133.96° compared to 113.27° in the TAV aorta. However, angles Y and Y1 were smaller in the BAV aorta compared to the equivalent TAV angles by a difference of 37.8% and 38.1%, respectively. The differences between TAV and BAV were larger than that found amongst the TAV subjects for angles X, Y and Y1. For angle X1, which captures the non-planarity of the thoracic aorta, the difference between TAV and BAV (2%) was smaller than the difference amongst the TAV subjects.

It should be borne in mind that individual variations in the geometry of the thoracic aorta can also be ascribed to body size, age, gender, and many other factors such as the biomechanical environment.

6.1.2 Hemodynamic Features

CFD simulations based on patient-specific MRI derived geometries and flow conditions provided detailed results that were used to examine the aortic flow pattern, helical flow structure, turbulence and wall shear stress. The main findings from the flow analyses are summarised below.

The flow patterns were qualitatively similar in the TAV and BAV aortas with quantitative differences. The MR-derived volumetric flow rates in the ascending aorta of the TAV subjects were similar in shape, but their mean and peak values varied substantially from subject to subject. The cardiac output for TAV subjects ranged from 5.7 to 6.5 (L/min). The mean cardiac output for TAV subjects was 6.13 L/min, which is in good agreement with generally accepted value of 5 to 6 L/min for a normal aorta at resting conditions. The cardiac output for the BAV subject was 4.8 L/min. The BAV cardiac output compared to the mean CO for TAV subjects is smaller (with a difference of 21.7%). However, this value is fair, as it is close to the cardiac output range for TAV subjects.

The flow in the thoracic aorta was found to be characteristically complex with spatio-temporally changing flow patterns along the thoracic aorta. Disturbed flow was observed in some regions of the aorta, particularly in the arch region during systolic deceleration, whilst it was mainly organised and laminar like in the distal descending aorta. Turbulent features were captured by the SST-Tran model,
with the highest turbulence intensity (up to 50%) occurring in deceleration phase. The velocities within the thoracic aorta were rapidly changing. The vortices were substantial and observed to be interacting and spatio-temporally evolving at different scales. Flow in the descending aorta, particularly in the distal descending aorta was less disturbed than in the ascending aorta. There was evidence of fluctuating velocity gradients and increased anisotropic features of turbulence within the spatially changing aorta. The helicity density ($H_d$) was found to be higher in the TAV aorta than in the BAV aorta.

In addition to the flow parameters and characterization, flow reversal ratio (FRR) was evaluated and compared between the TAV and BAV aortas. The amount of reversed flow obtained in this study was notably different between the two valve types: FRR was 2.6% for the TAV, and 8.3% for the BAV aorta.

Wall shear stress (WSS) is not constant in the human thoracic aorta and significant changes were observed. WSS in the thoracic aorta varied from region to region, with the highest values occurring in regions around the three major arch branches. The circumferential WSS values in the TAV aortas were different within and amongst individuals. The range of WSS obtained within the thoracic aorta was wide, with minimum values close to 0 Pa in the descending aorta region, and maximum values of up to 3.75 Pa in the ascending aorta, arch, and descending aorta regions. However, there were small areas in the ascending aorta and arch with WSS close to 0 Pa. There were small areas with higher WSS up to 5 Pa found in the inlet area, inner curve of the arch region, and after the left subclavian (around the isthmus of the aorta), at the arch bend in the proximal descending aorta. Areas of high WSS, (range 15.22 to 23.29 Pa) were found in the TAV around the arch branches. The regionally changing and varying WSS distribution was observed in both TAV and BAV. WSS was higher in the TAV aorta than in the BAV aorta. The mean maximum time averaged wall shear stress (TAWSS) for TAV aorta was 18.42 Pa whilst that in the maximum TAWSS for the one BAV aorta was 7.39 Pa. The shear range index (SRI) was generally low in the thoracic aorta with the highest value obtained in the arch region. The mean SRI for the TAV aortas was 8.57, and it was 6.80 for the BAV aorta.

Finally, The flow data extracted from in vivo 3D phase-contrast magnetic resonance images and CFD simulation results were compared and a good agreement was obtained in terms of velocity contours and magnitude. The good correspondence between PC-MRI measurements and CFD predictions demonstrated that the subject-specific model was credible and suitable for further application, and investigation of the thoracic aorta.
6.2 Model Limitations

This study involves a number of limitations, which are outlined below.

- **Data acquisition, quality and subject population** – First, some MR images had low spatial resolution, making image segmentation and reconstruction of the aorta challenging, particularly in the aortic arch branch region. Second, the required and complete 3D MR flow data sets for study were only available for a limited number of cases, and as images were acquired at different hospitals using different MR scanners there were differences due to acquisition variables and techniques. Third, there was only one BAV (patient) data available for investigation owing to a lack of volunteers for this category of patient. It is generally a hard and long procedure to recruit volunteers and obtain ethics approval for required patient images.

- **CFD model and assumptions** – The aortic wall was assumed to be rigid, which is considered the most significant limitation of the present study. The flow was simulated using Reynolds-averaged Navier-Stokes (RANS) equations coupled with a correlation-based transitional flow model. Though the SST-Tran model employed did capture important characteristic flow features and appeared more attractive than computationally intensive approaches (such as large eddy simulation), a more comprehensive model may be required to capture the full scales of helical flows and vortices.

- **Boundary Conditions** – A fixed flow split was specified at the outlets of the arch branches. This might not be physiologically true, as flow through each branch is likely to vary with time and brain activities. The fixed pressure assumption applied at the main outlet in the descending aorta is also non-physiological, but this assumption has been widely accepted for rigid wall models.

6.3 Suggestions for Future Work

1. **Possible alternative turbulence model** – the SST-Tran (i.e. $\kappa$-$\varepsilon$/$\kappa$-$\omega$) model has been used in the present study and turbulence has been observed at various time points and locations. It is possible that the spatial extent and time scales have not been accurately captured and it is suggested to employ large eddy simulation (LES) in the future and compare findings with those from this study and other studies based on the SST-Tran model. LES may be able to capture the large eddies and the turbulent scales better. The difference (if any) in findings (e.g. WSS and helicity density, $H_d$, and turbulence intensity, $T_u$ etc.) will enhance the understanding of the aorta and encourage the development and use of combined MRI and CFD techniques as a clinical tool in
the management and treatment of cardiovascular diseases.

2. **Physiological Boundary Conditions** - With the fact that the thoracic circulation is pulsatile, physiological boundary conditions should be applied. 3-D *in vivo* data would be preferred and should be acquired for future full flow field study. At the model outlets, the lumped parameter models, such as the 3-element Windkessel model may offer an improved and better alternative for modeling the outlet.

3. **Compliant Wall** - The need to accurately determine shear stress at the wall of the aorta remains a challenge, one that effectively continues to drive the numerical studies aimed at determining WSS and other aortic flow descriptors accurately for clinical use. A compliant fluid-structure interaction model (though a challenge in itself) may have to be considered and used in future CFD studies of the thoracic aorta.

4. **Incorporation of aortic tissue properties**: many studies have investigated and found the structure of the aortic tissue to be different in regions of the aorta. The reason for the difference in the regional ascending thoracic aorta diameter between a TAV and a BAV can be further examined through investigation of biomechanical properties (e.g. delamination strength and failure energy of collagen fibres) of aortic tissue. This investigation may further reveal and provide more insight into the different and varying local diameters in the proximal ascending aorta of BAV compared to that of TAV. The continuous pounding of the aortic wall by a skewed flow is likely to have a degenerative (or denudation) effect that may lead to aneurysm and dissection in time. A situation that a structurally defective and weak aortic wall will compound. This investigation can increase our understanding of the morpho-haemodynamic interplay and corelational activities that occur within the ascending thoracic aorta.

5. **A larger cohort study is needed.** This would enhance and expand the determined flow parameters and characterization of the thoracic aorta, with possible uptake and use of the determined parameters in clinical assessment and management of the aorta.


ANSYS CFX 15.0 Tutorial Manual (ANSYS Inc, Canonsburg, PA).


ANSYS ICEM CFD 15.0 Tutorial Manual (ANSYS Inc, Canonsburg, PA).


EnSight 10.0 Tutorials.


GOOGLE IMAGES. 2016. Google Inc.


SIU, S. C., SILVERSIDES, C. K. 2010. Bicuspid Aortic Valve Disease. *Journal of the American College of Cardiology*, 55, © 2010 by the American College of Cardiology Foundation ISSN 0735-1097/$36.00 Published by Elsevier Inc.


Appendix
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<td>Cardiovascular physiology concepts (Klabunde, 2009)</td>
<td>©1998-2016 Richard E. Klabunde <a href="http://www.cvphysiology.com">www.cvphysiology.com</a></td>
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<td>Davies et al., (2010)</td>
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<td>Figure 2.5: The ‘Aortic Annulus’ or aortic valve is a complex structure with many components. The aortic valve and supporting ventricular structures are depicted - the green ring 1 is the sino-tubular junction, green ring 2 is the virtual basal ring and red ring 3 is the anatomic ventriculo-aortic junction.</td>
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