

**Analysis of Blood Flow in Patient-specific Models
of Type B Aortic Dissection**

by

Zhuo CHENG

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Abstract

Aortic dissection is the most common acute catastrophic event affecting the aorta. The majority of patients presenting with an uncomplicated type B dissection are treated medically, but 25% of these patients develop subsequent dilatation and aortic aneurysm formation. The reasons behind the long-term outcomes of type B aortic dissection are poorly understood. As haemodynamic factors have been involved in the development and progression of a variety of cardiovascular diseases, the flow phenomena and environment in patient-specific models of type B aortic dissection have been studied in this thesis by applying computational fluid dynamics (CFD) to in vivo data. The present study aims to gain more detailed knowledge of the links between morphology, flow characteristics and clinical outcomes in type B dissection patients.

The thesis includes two parts of patient-specific study: a multiple case cross-sectional study and a single case longitudinal study. The multiple cases study involved a group of ten patients with classic type B aortic dissection with a focus on examining the flow characteristics as well as the role of morphological factors in determining the flow patterns and haemodynamic parameters. The single case study was based on a series of follow-up scans of a patient who has a stable dissection, with an aim to identify the specified haemodynamic factors that are associated with the progression of aortic dissection. Both studies were carried out based on computed tomography images acquired from the patients. 4D Phase-contrast magnetic resonance imaging was performed on a typical type B aortic dissection patient to provide detailed flow data for validation purpose. This was achieved by qualitative and quantitative comparisons of velocity-encoded images with simulation results of the CFD model.

The analysis of simulation results, including velocity, wall shear stress and turbulence intensity profiles, demonstrates certain correlations between the morphological features and haemodynamic factors, and also their effects on long-term outcomes of type B aortic dissections. The simulation results were in good agreement with in vivo MR flow data in the patient-specific validation case, giving credence to the application of the computational model to the study of flow conditions in aortic dissection. This study made an important contribution by identifying the role of certain morphological and haemodynamic factors in the development of type B aortic dissection, which may help provide a better guideline to assist surgeons in choosing optimal treatment protocol for individual patient.

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I personally think this section is the most difficult part of the thesis, as words are always too pale to express human's motion.

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Declaration

I hereby certify that the work presented in this thesis is the result of my own investigation carried out at Imperial College London during the period from October 2007 to March 2011, except where otherwise stated.

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Notation

Abbreviations

AAS	Acute Aortic Syndrome
IRAD	International Registry of Aortic Dissection
INSTEAD	Investigation of STEnt Grafts in Aortic Dissection
WSS	Wall Shear Stress
CFD	Computational Fluid Dynamics
ECG	Electrocardiogram
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
TTE	Transthoracic Echocardiography
TEE	Transesophageal Echocardiography
RF	Radio Frequency
TR	Repetition Time
TE	Echo Time
SSFP	Steady-state Free Precession
PCMRI	Phase Contrast Magnetic Resonance Imaging
TAWSS	Time Averaged Wall Shear Stress
OSI	Oscillatory Shear Index
FEM	Finite Element Method
FVM	Finite Volume Method
LDV	Laser Doppler Velocimetry
PIV	Particle Imaging Velocimetry
IVUS	Intravascular Ultrasound
AAA	Abdominal Aortic Aneurysm
FSI	Fluid-structure Interaction
ALE	Arbitrary Lagrangian-Eulerian
TAA	Thoracic Aortic Aneurysm
NURBS	Non-uniform Rational B-spline

ILT	Intraluminal Thrombus
PTFE	Polytetrafluoroethylene
PDMS	Polydimethylsiloxane
FH	Foot to Head
AP	Anterior to Posterior
RL	Right to Left
SNR	Signal-to-Noise Ratio
DICOM	Digital Image and Communication in Medicine
SST Tran	Shear Stress Transport Transitional
SST	Shear Stress Transport
FFT	Fast Fourier Transform
RMS	Root-mean-square
TEVAR	Thoracic Endovascular Aortic Repair
TA	Stanford Type A Dissection
AL	Ascending Aorta Lumen
DL	Descending Aorta Lumen
IA	Iliac Arteries
LONG	Longitudinal
SIG	Significance level
SMA	Superior Mesenteric Artery
ET	Entry Tear
TL	True Lumen
FL	False Lumen
TH	Thrombus
PT	Primary Entry Tear
TKE	Turbulence Kinetic Energy
RRT	Relative Residence Time
RMSD	Root-mean-square Deviation

Symbols

A_0	Mean velocity over a cardiac cycle
A_n	Fourier coefficients of the cos term
B_0	Applied main magnetic field strength
B_n	Fourier coefficients of the sin term
I	Grayscale of pixel
$I_{\max}$	Maximum grayscale value of phase image
$I_{\min}$	Minimum grayscale value of phase image
M	Net magnetic moment
r	Radial distance from the wall
R	Multiple coefficients
N	Degree of the trigonometric polynomials
Q	Volumetric flow rate
R	Radius of aorta
T	Temperature of the fluid
T_1	Longitudinal relaxation time
T_2	Transverse relaxation time
T	Cycle period
t_r	Particle residence time
t'_r	Particle relative residence time
V	Velocity parallel to the wall
V_{enc}	Velocity encoding
V_{pc}	Velocity value at pixel
V	Instantaneous local velocity
X	Independent variable
Y	Dependent variable
ω_0	Larmor frequency
γ	Gyromagnetic ratio
v	Velocity

Δm	Difference of first moment of the magnetic gradient time curve
$\Delta\phi$	Phase difference
τ_w	Wall shear stress
μ	Dynamic viscosity
τ_{mean}	Magnitude of the time-averaged wall shear stress.
u	Instantaneous velocity
ε	Thermodynamic internal energy
π	3.14
p	Instantaneous static pressure
ρ	Density
μ	Viscosity
K_H	Heat conduction coefficient
F	External force per unit mass
k	Turbulence kinetic energy
ω	Specific dissipation rate
ε	Dissipation per unit mass
δ	Fractional error in wall shear stress
β	Correspondent parameter
α	Constant parameter
δ	Cartesian distance
Re	Reynolds number
Tu	Turbulence intensity
y^+	Viscous wall unit

Chapter 1

Introduction

1.1 Clinical Background

1.1.1 Aortic dissection and the patient population

More than 200 years ago, Morgagni, the father of modern anatomical pathology, described a patient who developed a tear in the ascending aorta with subsequent rupture into the pericardial space in his masterpiece “The Seats and Causes of Disease”. This is the first time aortic dissection has been pathologically described in history. Since then, aortic dissection has been gradually unveiled to the medical world. In 1819, Laennec first used the term “aneurysme dissequant” to describe this disorder. Because of this ancient description, the disease had been referred to as “dissecting aneurysm” for more than a hundred years. However, as the affected aorta is infrequently aneurysmal, the simple term “aortic dissection” has been preferred since late 1900s, and widely used in both clinical and medical applications.

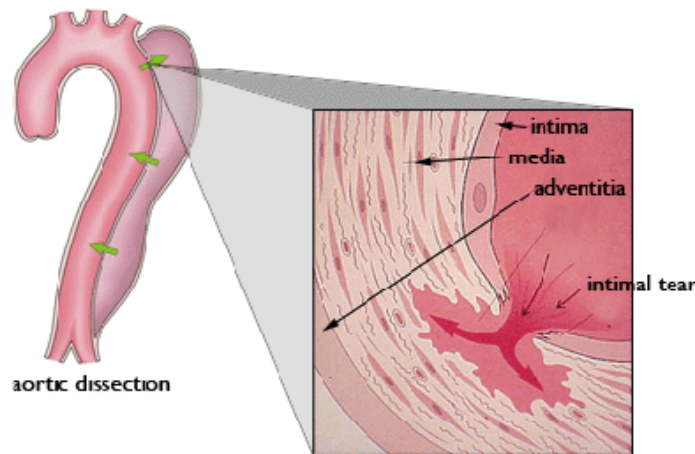


Figure 1.1: Proposed mechanism of initiation of aortic dissection (adopted from www.iradonline.org).

The initial event of classic aortic dissection is a sudden tear in the aortic intima that directly exposes an underlying diseased medial layer to the driving force of the intraluminal blood (see Figure 1.1). This is rapidly followed by a surge of blood into the diseased media layer. The blood cleaves the laminar plane of the media in two, and then separates the intima from the adventitia, thus dissecting the aortic wall (Wheat 1983). Most aortic dissections propagate distally from their point of origin driven by the forward force of aortic blood flow, but proximal extensions can also be seen (Benedikt 2000). The so-called false lumen, adventitially and partly medially bound, represents the blood-filled space between the dissected layers of the aortic wall, while the true lumen is bounded by the endothelium entirely and is the normal passageway of blood. The layer of intimal and part of media tissue separating the false lumen from the true lumen is known as the intimal flap. Typically, one or more tears in the intimal flap produce exit sites or additional entry sites allowing flow communication between the two lumens, thus maintaining false lumen patency.

Classic aortic dissection is one of the aortic pathologies of a new cardiovascular syndrome – acute aortic syndrome (AAS). AAS describes the acute presentation of patients with characteristic “aortic pain” caused by one of several life threatening thoracic aortic pathologies including classic aortic dissection, intramural haematoma, and penetrating atherosclerotic ulcer (Ahmad et al. 2006). The clinical profile of patients with intramural haematoma and aortic ulcer is similar to that of classic aortic dissection. Penetrating atherosclerotic ulcer is a condition in which ulceration of an aortic atherosclerotic lesion penetrates the internal elastic lamina into the media and may precipitate intramural haematoma (Vilacosta & San Roman 2001). Aortic intramural

haematoma represents a novel variant of aortic dissection characterised by the absence of an identifiable intimal tear (Vilacosta & San Roman 2001). Being different from classic aortic dissection, it begins with the rupture of vasa vasorum within the aortic media with the development of a hematoma followed by a secondary rupture through the intimal layer. Aortic ulcer and intramural haematoma are linked and may progress to the classic aortic dissection.

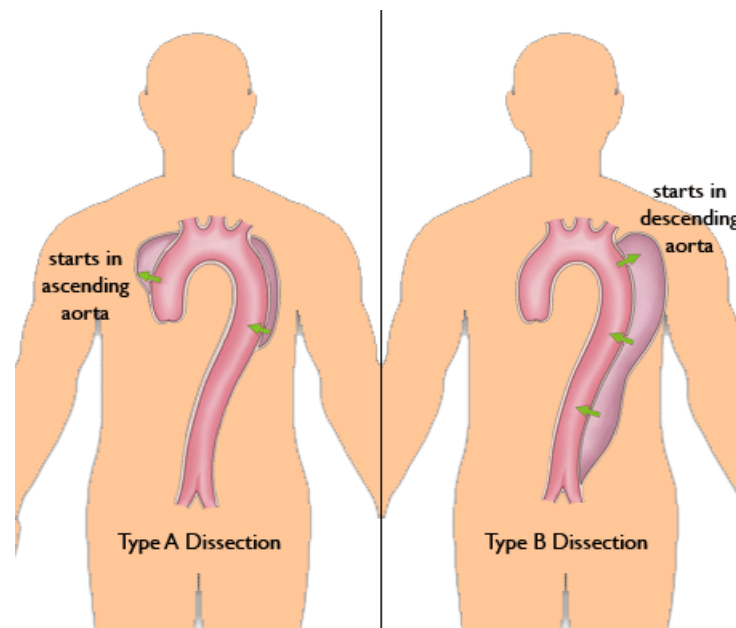


Figure 1.2: Commonly used Stanford classification system for aortic dissection with arrows demonstrating openings or communications between the true lumen and false lumen. Left: type A dissection; Right: type B dissection (adopted from www.iradonline.org).

Most classification schemes for aortic dissection are based upon its anatomic location and time from onset. These two variables play an important role in determining both therapy and prognosis. Anatomically, the vast majority of aortic dissections originate in one of two locations: (1) the ascending aorta, within several centimeters of the aortic valve, and (2) the descending aorta, just distal to the origin of the left subclavian artery at the site of the ligamentum arteriosum (Roberts 1981). Based on the site of origin and proximal or distal involvement, Stanford classification, which was proposed by Dailey and his colleagues from Stanford University in 1970, has been the most widely used (see Figure 1.2). Under this system, aortic dissection is grouped into Stanford type A, which involves the ascending aorta, and Stanford type B, which is confined to the descending aorta. Type A dissection is more common than type B and approximately sixty-five per cent of intimal tears occur in the ascending aorta (Crawford et al. 1990). In addition to

its location, aortic dissection is also subclassified based on its duration from symptom onset to medical evaluation. Acute dissection has traditionally been used to describe presentation within the first two weeks, while the term subacute is sometime used to describe the period between 2 weeks and 2 months. Chronic dissection is reserved for those patients presenting at more than two months following the initial event (Green & Kron 2003). At diagnosis, about two-thirds of aortic dissections are acute, and the remaining one-third are chronic (Spittell et al. 1993).

The true incidence of aortic dissection is difficult to estimate because of its rapid fatality and its ability to mimic other more common conditions (Hiratzka et al. 2010). As reported, it is not as common as some other cardiovascular diseases, such as aortic aneurysm and coronary artery diseases. Population-based studies suggest an incidence of aortic dissection of around 30 cases per million people per year, which corresponds to 6000 to 10 000 cases annually in the US. Among the patients, aortic dissection is more likely to affect males over 60 years old (Hagan et al. 2000). Although it is relative rare, aortic dissection is highly lethal causing more than twice as many deaths as attributed to ruptured abdominal aortic aneurysms (Svensson & Rodriguez 1997). Early mortality of aortic dissection was reported as high as 40 per cent and 1-2 per cent per hour thereafter (Hirst et al. 1958). Although survival may be significantly improved by the timely administration of appropriate medical and/or surgical therapy, the morbidity and mortality of this debilitating disease remain alarmingly high, with an overall in-hospital mortality of 27.4% reported by Hagan et al. (2000) from the International Registry of Aortic Dissection (IRAD). However, the in-hospital outcomes of type B dissection are far more acceptable than that of type A dissection, with 90% of patients surviving the initial episode (Klan & Nair 2002).

1.1.2 Treatment for aortic dissection

Because of its rapid lethality, aortic dissection is regarded as a medical emergency requiring immediate treatment. Therapy may include medical or surgical treatment, according to the type and complication level of dissection. Based on the report from IRAD (2000), the in-hospital mortality rate from type A patients treated with medical therapy alone was 55.9%. Successful surgery could significantly decrease the mortality rate (26.6%) of type A dissection, and is also associated with excellent 1- and 3-year follow-up survival rates (Tsai et al. 2006). As surgery has a clear prognostic advantage over medical treatment, type A dissections are considered as a surgical emergency,

mandating replacement of the ascending aorta and sometimes aortic valve to reduce the risk of death.

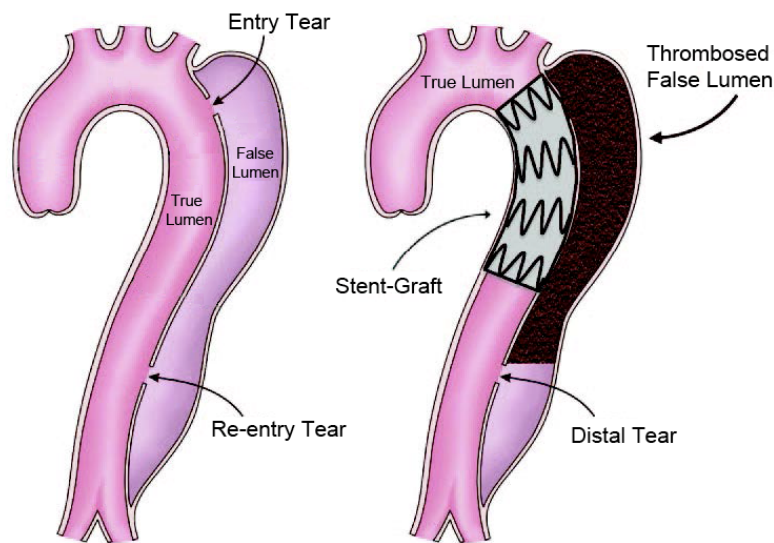


Figure 1.3: Endovascular stent graft in type B aortic dissection and the subsequent thrombosis in the false lumen (adopted from Nienaber et al. 2009).

The management of type B dissection classically depends on whether the dissection is considered complicated or not. For patients with uncomplicated type B dissections, medical management is usually advocated, because of its lower mortality than surgical intervention (Suzuki et al. 2003). Medical treatment focuses initially on haemodynamic monitoring, normalization of blood pressure, beta-blockers and on pain control with morphine sulfate (Ince & Nienaber 2007). However, type B dissection presenting with complications such as peripheral malperfusion syndromes and haemodynamic instability, requires intervention in the acute phase, owing to its high risk of subsequent death. Nevertheless, mortality rates for surgical intervention are extremely high that an overall in-hospital mortality rate of 29% has been reported from the IRAD database (Trimarchi et al. 2006). In 1990s, following the successful application of endovascular treatments in managing diseases of the coronary artery, abdominal aorta, and arteries of the legs, the concept of endovascular stenting and fenestration to treat aortic dissection became popular (Williams et al. 1997). The main approach is to place one or more covered stents over the intimal entry tears through which blood flows to the false lumen, hence, directing flow into the true lumen and promoting thrombosis in the false lumen (as shown in Figure 1.3). Endovascular treatment has now exceeded standard open surgery as the dominant procedure to treat complicated type B aortic dissections. Fattori and colleagues from IRAD (2008) stated that endovascular treatment could offer

better short-term outcomes in terms of mortality and associated complications than open repair.

The premise of endovascular treatment is that stent graft placement over the primary entry tear will prevent blood flow into the false lumen and stimulate aortic remodeling. Positive aortic modeling, defined as false lumen obliteration and true lumen recovery, often serves as a surrogate measure of treatment success in aortic dissection. The INSTEAD trial showed that aortic remodeling occurred in 91.3% of the patients who underwent thoracic endovascular aortic repair for uncomplicated acute Type B dissections compared to only 19.4% in patients under medical treatment ($P < .001$), which is suggestive of continued remodeling following stenting (Nienaber et al. 2009). Sayer et al. studied the early clinical outcome and morphological changes after endovascular stenting in both acute and chronic type B aortic dissection. They found that the acute group, which demonstrates significant aortic remodeling, presented better mid-term survival than the chronic group. (Sayer et al. 2008). Kim et al. found that aortic remodeling could occur as early as within days after stenting and remain predictable in long-term with continuous expansion of true lumen and regression of false lumen in acute complicated dissection. Failure in increasing the true lumen volume may lead to endoleaks or distal reperfusion (Kim et al. 2011).

1.1.3 Risk management for uncomplicated type B aortic dissection

Although uncomplicated type B aortic dissection has an acceptable in-hospital mortality rate of 10% with medical treatment, the long-term survival rates are not optimistic: 60% at five years and 40% at 10 years (Umana et al. 2002; Bernard et al. 2001). About 20% to 50% of patients with uncomplicated type B dissection will develop aneurysmal dilation within 1 to 5 years, eventually leading to the need for surgery repair to prevent aortic rupture (DiMusto et al. 2010). Once a patient develops complications, the prognosis can worsen significantly, with an in-hospital mortality of 50% or higher (Tang et al. 2009). Therefore, surgical intervention is classically reserved for those patients who evolve late complications in the chronic phase. As the in-hospital results of endovascular treatment in complicated type B dissection appear to be favourable, the use of covered stents for uncomplicated type B patients was proposed. However, the application of endovascular treatment of uncomplicated type B remains controversial.

Limited trial studies have been conducted to examine the use of endovascular treatment in uncomplicated type B dissections to prevent late complication of aneurysm development and rupture. Arts et al. (2007) suggested equivalent mortality in patients

with uncomplicated type B dissection who were treated medically or by endovascular stents combined with medical therapy at 1 year. The Investigation of STEnt grafts in patients with type B Aortic Dissection (INSTEAD) randomized trial, which was designed to compare covered stents with medical treatment alone for uncomplicated type B dissection, presented no improvement of endovascular treatment, with a 2-year cumulative survival rate of 95.6% with optional medical therapy versus 88.9% with covered stents (Nienaber et al. 2009). Although the long-term outcome of endovascular treatment in uncomplicated type B dissection is still unclear, those patients who will evolve late complications could benefit from early endovascular procedure by reducing the risk of mortality after complication onset. However, there is currently no reliable indicator which can predict the late dilatation or aneurysmal complications in type B dissection at early phase. Hence, choosing an optimal treatment, medical and/or endovascular therapy, for patients with uncomplicated type B is still a dilemma for surgeons.

1.2 Motivation for research

Although no reliable prognostic indicators are currently available, there is some evidence suggesting that certain geometrical and hemodynamic factors may help identify type B dissection patients who are at higher risk of developing complications and thus may benefit from early endovascular treatment.

Aortic diameter has long been associated with the risk of rupture. According to the early reviews from the Yale aortic database, median size at time of rupture for descending aorta is 7.2 cm, and the risk of rupture for an aorta larger than 7.0 cm is significant increased. A general guideline has also been proposed that operative intervention is recommended in asymptomatic patients with enlargement larger than 6.5 cm (Coady et al. 1997; Elefteriades et al. 1999). Another review from Davies et al. (2006) demonstrated that relative aortic size, defined as the aortic diameter divided by body surface area, was more important than absolute aortic size in predicting complications. Song et al. (2007) established that the upper descending thoracic aorta was the major site of late aneurysmal dilation, and a large diameter of this part portended late aneurysm and adverse outcome warranting early intervention. Patients with initial upper descending thoracic aorta diameter of larger than 22 mm were reported with higher event rate of aneurysm or death (Song et al. 2007). However, a report from IRAD in 2007 challenged the aortic diameter concept with data showing that majority of the

patients didn't fall within the current criteria, thus, indicators other than aortic size are needed to predict the risk of late complications (Pape et al. 2007).

In addition to aortic diameter, patency of the false lumen has been closely linked to false lumen expansion and rupture over time. Bernard et al. (2001) analysed data from 109 patients including type B dissections. Postoperative false lumen patency of the thoracic descending aorta in this group of patients was demonstrated as a predictor of late mortality, and was also suggested to be responsible for progressive aortic dilation. In a report of 101 patients with uncomplicated type B dissections, Marui et al. (1999) established that the independent predominant predictors for aortic enlargement in the chronic phase were a maximum aortic diameter of larger than 40 mm combined with a patent false lumen during the acute phase. The values of actuarial freedom from aortic enlargement in patients with a relative small maximum aortic diameter (< 40 mm) and a closed false lumen are much higher than those with a maximum aortic diameter of 40 mm and a patent false lumen at 1, 5, and 10 years (Marui et al. 1999). The impact of partial thrombosis of the false lumen in uncomplicated type B dissection was evaluated by IRAD (Tsai et al. 2007) based on a series of 201 dissection patients. Interestingly, the report demonstrated that partial thrombosis of the false lumen, compared to complete patency, was a significant independent predictor of mortality after hospital discharge. It was speculated that partial thrombus in the false lumen might occlude the re-entry tears, thus impeding outflow and increasing pressure in the false lumen. But the situation of lacking a distal tear in a dissected aorta with partial thrombosis is regarded as relatively uncommon (Tang et al. 2009).

Various previous studies have suggested that abnormal hemodynamic stresses, as well as recirculating and turbulent flow within the diseased aorta, are an important influence in the formation, degeneration, and ultimate rupture of aortic aneurysms, atherosclerosis, and other cardiovascular diseases (Malek et al. 1999; Thubrikar et al. 2001; Fillinger et al. 2002; Slager et al. 2005). Shear stress can affect endothelial cell functions, such as proliferation, apoptosis, migration, permeability, and remodelling (Lehoux et al. 2006; Li et al. 2005). Low shear stress may increase monocyte adhesion due to flow reattachment, and recirculating flow would enhance the delivery of monocytes to the vessel wall (Pritchard et al. 1995). On the other hand, high shear stresses in the bulk flow were found to activate platelets, which were then more likely to adhere to the wall in the recirculation regions immediately downstream (Ramstack et al. 1979). Disturbance and turbulence in the blood flow influence physiological parameters and processes, such as flow resistance, pressure, wall shear stress (WSS), wall

remodelling, inflammation, and mass transport from the blood to the vessel wall (Giddens et al. 1976). In the case of aneurysms, turbulence has also been suggested to result in wall vibration, with additional stresses on the aneurysmal wall, which can accelerate the progression of the aneurysm, and further increase the rate of wall dilation (Berguer et al. 2006; Khanafer et al. 2007). Hence, haemodynamic factors may potentially have a key role in the complicated degeneration of type B dissection during chronic phase.

To the best of the author's knowledge, no systematic study of flow patterns and haemodynamic factors in dissected aorta has been reported, owing to the complexity of the problem and uncertainties associated with the mechanical properties of the dissected wall layers. If the haemodynamic factors that are associated with late dilation and aneurysmal degeneration in uncomplicated type B aortic dissections could be identified, they may provide a more reliable guideline for predicting the long-term outcome of patients, and assist surgeons in choosing treatment protocol. In doing so, those patients who have high risk of developing late complications could be treated with endovascular therapy at early phase, thus improving their long-term survival rate.

1.3 Objectives of the study and research strategy

As pointed out previously, the lack of understanding of flow patterns and haemodynamic conditions in type B aortic dissection has motivated this study. The overall aim of the research is to gain detailed knowledge of the effect of morphology and flow characteristics on clinical outcomes in type B aortic dissection by combining computational fluid dynamics with patient-specific imaging. It is hoped that associations can be found between morphologic and haemodynamic factors and progression and long-term degeneration or stabilization of type B aortic dissection. As detailed fluid dynamics of dissected human aorta has not been studied previously, this work may offer the first quantitative data on the complex flow field in aortic dissection, thereby contributing to a better understanding of the role of haemodynamics in the progression of aortic dissection. In this study, a number of specific objectives have to be accomplished in order to achieve the overall aim. The objectives include:

- Determining the anatomical features, flow patterns and distribution of haemodynamic stresses in type B aortic dissection based on patient-specific data.
- Identifying the common geometrical characteristics of type B dissection and the key haemodynamic factors which have potential effects on the degeneration of dissected aorta.

- Examining the relationship between morphological factors and flow patterns in aortic dissection.
- Examining the effects of key haemodynamic factors on the long-term degeneration or stabilization of aortic dissection
- Evaluating the assumptions made in the image-based patient-specific aortic dissection flow model and validating the computational model using *in vivo* or *in vitro* data.

A research strategy has been developed to achieve these objectives. The patient-specific models are used to investigate anatomical and flow characteristics under physiologically realistic conditions using image data acquired from individual patients. First, data from a group of patients with type B dissection are analysed to investigate the characteristics of haemodynamic parameters. This subset of study demonstrates the complexity of geometry and flow in dissected aorta, and allows the key parameters to be identified. As the geometry varies from patient to patient, it is important to examine the role of morphological factors in determining the flow patterns and haemodynamic stresses. Subsequently, analysis is performed on a series of follow-up scans of a patient with an aim to assess whether any of the haemodynamic factors identified from the multi cases study can predict the progression of aortic dissection. Phase contrast magnetic resonance images, which contain patient-specific flow information, are utilized to evaluate the computational results from patient-specific simulations.

1.4 Plan of the thesis

The thesis contains seven chapters, which are organized in a logical sequence. In Chapter 2, a comprehensive literature survey is given for the research covering both medical and engineering aspects. In Chapter 3, the materials and methodology utilized to accomplish the objectives of the study are described. Chapter 4, 5 and 6 present the findings and analysis of results of patient-specific study. Chapter 4 includes the cross sectional study based on a series of type B aortic dissection subjects, and Chapter 5 is focusing on a single case with multiple follow ups. Chapter 6 subsequently presents the model validation work by comparing the simulation results to phase contrast MR data. Finally, conclusions and suggestions for future work are given in Chapter 7.

Chapter 2

Literature Review

2.1 Introduction

In this chapter, a comprehensive literature review is presented covering both medical and engineering aspects of the project. First, the relevant medical background is given which provides a brief introduction to the components and functions of the cardiovascular system. This is followed by the pathology and aetiology of aortic dissection for further understanding of the disease. The most common and latest diagnosis imaging methods of aortic dissection are introduced, followed by a review on previous studies of haemodynamic factors in aortic disease. The engineering background is focused on the basic knowledge of computational fluid dynamics (CFD) and its development and applications in physiological environments. Then, a brief review of wall mechanics studied of diseased aorta is given to understand the biomechanical behaviour of the aortic wall and finite element stress analysis. Relevant experimental studies of blood flow in aortic dissection are summarized in the third part.

2.2 Medical background

2.2.1 The human cardiovascular system

The cardiovascular system is a very important organ system to support human's life. Its primary function is the rapid convective transport of oxygen, nutrients and water to every organ and tissue; and the rapid washout of metabolic waste products from cells. It is also a control system, distributing hormones to the tissues and secretes a hormone itself, and a cooling system for body temperature regulation (Levick 2003). The

cardiovascular system consists of the pulmonary circuit and the systemic circuit (as shown in Figure 2.1). The pulmonary circuit, starting at the right ventricle and ending at the left atrium, is composed of arteries and veins that transport blood between the heart and the lungs. In the pulmonary circuit, deoxygenated blood enters the lungs via arteries, and oxygenated blood leaves the lungs in veins. The systemic circuit is the portion of the cardiovascular system between the heart and the other organs and tissues. It transports oxygenated blood away from the left ventricle to the rest of the body other than the pulmonary exchange surface, and returns deoxygenated blood to the right atrium. The systemic circuit is much longer than the pulmonary circuit, and contains about 84% of total blood volume at any moment.

The main components of cardiovascular system are: the heart, the blood vessels and the blood. The three parts, each with specific responsibilities, work together making up the functional network of the cardiovascular system.

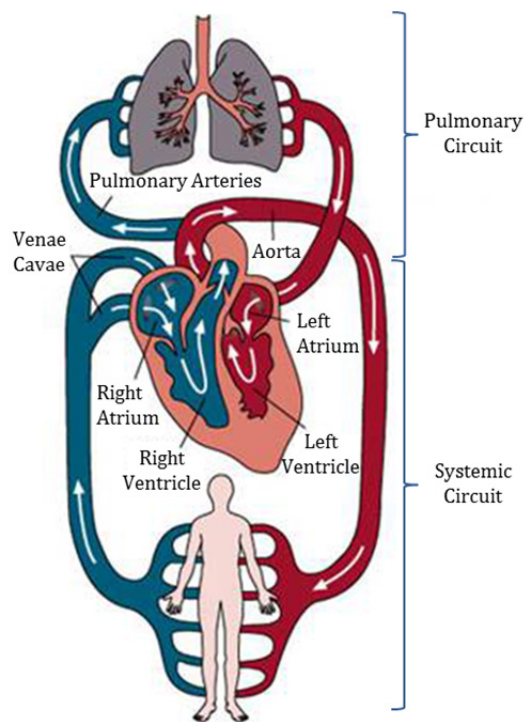


Figure 2.1: The human cardiovascular system (Courtesy from Revision World).

Heart

The heart is one of the critical organs in the body. It is a four-chambered organ that pumps oxygen-poor blood to the lungs and oxygen-rich blood to the organs and tissues (see Figure 2.2). The right atrium collects blood from the systemic circuit through the superior vena cava and inferior vena cava, and passes it to the right ventricle, which

pumps blood into the pulmonary circuit through pulmonary arteries. The left atrium then receives blood from the pulmonary circuit via pulmonary veins and transports it into the left ventricle, which pumps blood into the aorta, thus, entering the systemic circuit (Martini 2009).

The left ventricle is the largest chamber of the heart with thick walls that enable it to generate sufficient pressure to push blood through the whole systemic circuit. Blood leaves the left ventricle by passing through the aortic valve into the ascending aorta. The tricuspid aortic valve, which is located at the root of the aorta, prevents the backflow of blood from the aorta into the left ventricle. Each cusp of the aortic valve is adjacent to the aortic root which bulges out forming a saclike dilation (Martini 2009). The most common valve abnormalities include aortic stenosis in which the incompletely opened valve obstructs blood flow out from the heart, and aortic insufficiency in which the incompetence of valve induces wrong direction blood flow back to the heart.

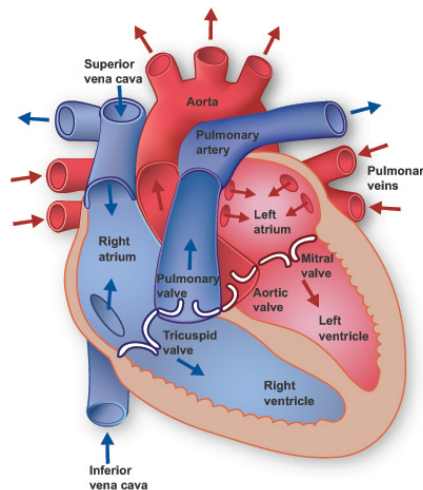


Figure 2.2: The front sectional anatomy of the heart, showing major landmarks and the path of blood flow marked by arrows (Courtesy from Texas Heart Institute Online).

The contraction of the heart is controlled by the electrical impulses conducted through the whole heart. The electrical events occurring in the heart can be detected on the surface of the body, and recorded as an electrocardiogram (or an ECG) (as shown in Figure 2.3). The ECG includes three features: P wave, QRS complex and T wave. The QRS wave is a relatively strong electrical signal, and is followed almost immediately by the onset of ventricular contraction (Levick 2003). The R wave is generally used as the trigger in ECG-gated medical imaging techniques, which aims to synchronize imaging process with a phase of the cardiac cycle. The techniques are useful to minimize motion

artifacts when data acquisition is too slow to accomplish during a short section of the cardiac cycle.

A cardiac cycle, which is the period between the starts of two continuous heartbeats, can be divided into two phases: systole and diastole. The systole is the period time when the heart contracts and pushes blood into the arterial trunk. It is followed by diastole which is the resting phase for the chambers to relax and prepare for the next heartbeat. When the cardiac cycle starts, the atria contract and push blood into the ventricle. After the atria's contraction, the ventricle which is completely filled with blood enter systole phase. When ventricular pressure exceeds arterial pressure, the outflow valves are forced open, and the blood is pushed through the systemic and pulmonary circuits and back to the atria. Three quarters of the blood is ejected in the first half of the ejection phase. Then the ventricle enters diastolic phase, and the whole heart keeps resting for the rest of the cardiac cycle. The ventricular diastolic phase lasts for almost two-thirds of a cardiac cycle (Martini 2009). Figure 2.3 illustrates the phases of the cardiac cycle based upon changes of pressure, volume and flow in aorta, ventricle and atrium.

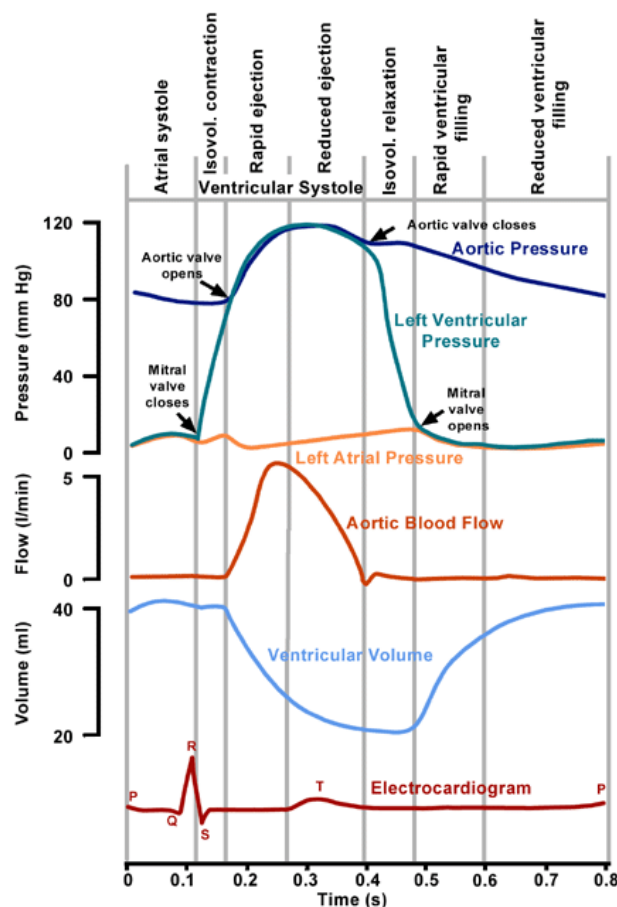


Figure 2.3: Changes in pressure, volume and flow in aorta, left ventricle and left atrium during human cardiac cycle (Courtesy from Mountain West Digital Library).

Aorta

The aorta is the largest artery in the systemic circuit, originating from the left ventricle, arching over the top of the heart and descending to the abdomen, where it branches off into the common iliac arteries (see Figure 2.4(a)). The aorta carries oxygen-rich blood away from the heart, and transports to connected arteries, thus, delivering to every organs and tissues. The main sections of the aorta are: the ascending aorta, aortic arch and descending aorta. The ascending aorta begins at the aortic valve of the left ventricle, and extends obliquely upward, forward, and to the right, in the direction of the heart's axis, presenting a slight curve in its course with a total length of approximately 5 cm. The aortic arch is situated across the superior surface of the heart in a shape of the handle of a cane. Three arteries, which are deriving from the aortic arch and delivering blood to the upper part of the body above the heart, are: the innominate artery, left common carotid artery, and left subclavian artery, from left to right along the arch. The descending aorta is continuous with the aortic arch. It can be divided into two sections by the diaphragm: the thoracic and abdominal aorta. Several groups of branches derive from the descending aorta servicing the tissues and organs in the body trunk. The terminal segment of the abdominal aorta divides to the right and left common iliac arteries which transport blood to the pelvis and lower limbs.

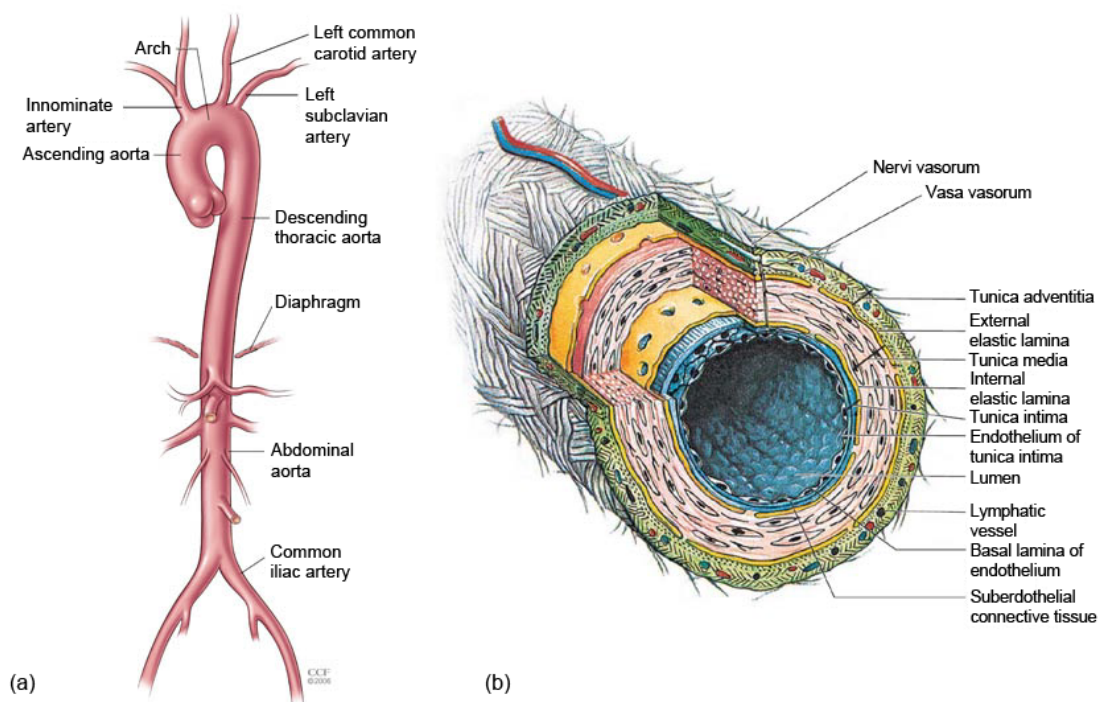


Figure 2.4: (a) The scheme of the aorta indicating the main branches and sections; (b) the principal structural features of the elastic artery (adapted from Gray's anatomy).

The wall of aorta contains three distinct layers: the tunica intima, tunica media, and tunica adventitia, from internal to external. Blood flows in the interior volume of the aorta known as the lumen (see Figure 2.4(b)). The tunica intima includes the endothelium and an underlying layer of connective tissue. The internal elastic membrane, which is a thick layer of elastic fibres, situates at the outer margin of the tunica intima. 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-haemostatic 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, usually the thickest layer, consists of concentric sheets of smooth muscle tissue and a high density of elastic fibres with the external elastic membrane at the outbound. The elastic fibres make the wall extremely resilient tolerating the pressure changes within cardiac cycle and smoothing the surging pressure and flow waves (windkessel function). The tunica adventitia is a connective tissue sheath including collagen fibres with scattered bands of elastic fibres. The diameter of aorta can reach up to 25 mm (Martini 2009). The thickness ratio of intima/media/adventitia in aorta is found to be 1/6/3 (Gao et al. 2006).

Blood

The blood circulating in the cardiovascular system provides nutrients, oxygen, and chemical instructions to each cell, as well as a way of removing wastes. Despite its transporting function, the blood also contributes to the regulation of the pH and ion composition of interstitial fluids, restriction of fluid losses at injury sites, defence against toxins and pathogens, and the stabilization of body temperature. Blood volume (litres) in a human body can be estimated by calculating 7% of the body weight (kilometres). It consists of plasma and formed elements. About 8% of the plasma is plasma proteins and other solutes, while the rest 92% is all water. Formed elements, which are produced through the process of hematopoiesis, compose of three types of blood cells: red blood cells, white blood cells, and platelets. Red blood cells consist 99.9% of the formed elements, and is responsible to transport oxygen in the blood. The white blood cells, although less numerous, play an important role in the body's defence mechanisms. Platelets are small, membrane-bound cell fragments which are important to the process of clotting (Martini 2009).

Hemostasis is the process that halts the loss of blood through the walls of damaged vessels and maintains the integrity of a closed, high-pressure circulatory system. The process starts with an injury in the vessel wall and the extravasation of blood from the circulation. The local smooth muscle fibres are subsequently contracting to stop the blood loss at the damage site. Afterwards, circulating platelets, which become a main component of the developing thrombus, are accumulated at the site of injury, and form a platelet plug. The attachment of platelets to the exposed surfaces is called adhesion, and the sticking bound between platelets is called aggregation. Then, the blood coagulation, initiated by tissue factor, culminates in the generation of thrombin and fibrin and forms a blood clot which efficiently seals off the wall damage (Martini 2009). When pathologic processes overwhelm the regulatory mechanisms of hemostasis, excessive quantities of thrombin is produced, thus, initiating thrombosis (Furie 2008). Thrombosis Exposed subendothelial collagen and tissue factor to the flowing blood are believed to be the trigger of the accumulation and activation of platelet, thus, initiating the formation of thrombus (see Figure 2.5). In the developing of thrombus, some platelets continue to accumulate at the site, whereas others separate from the thrombus. In the dynamic process of thrombus formation, haemodynamic factors, such as shear, flow, turbulence, and the number of platelets in the circulation, play an important role in the platelet adhesion and aggregation (Furie & Furie 2008; Fuster et al. 1990).

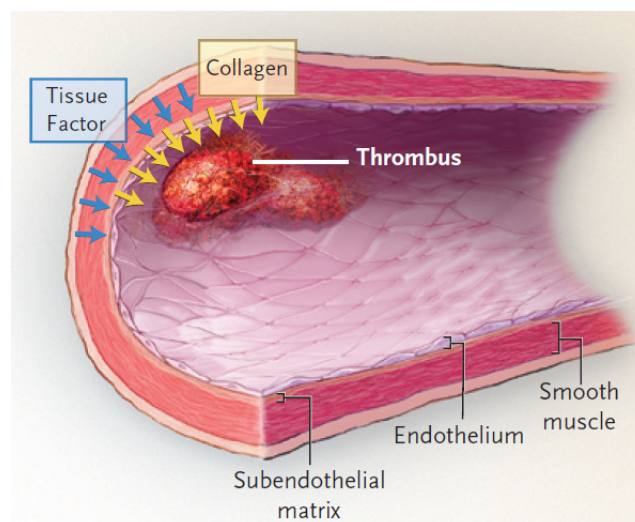


Figure 2.5: Formation of thrombus in vessels response to vascular injury (Furie 2008). The collagen and tissue factor are indicated with yellow and blue arrows, respectively.

2.2.2 Pathology and aetiology of aortic dissection

Direct trauma

The initial event of classic aortic dissection is a sudden tear in the aortic intima, which is rapidly followed by a surge of blood into the aortic media and subsequently separates the intima from the adventitia. The most common site of origin for aortic dissection is the ascending aorta (Hagan et al. 2000). The reason behind this may involve hemodynamic and torsional forces, as well as aortic root motion, that impact upon this section of the aorta which is closest to the heart (Wheat 1983; Beller et al. 2004). The descending aorta just beyond the insertion of the ligamentum arteriosum is the second most common site of origin. This sensitive point, where the mobile aortic arch can move against the fixed descending aorta that is bounded by the spine, is at greatest risk from the shearing forces of sudden deceleration (Eagle & Desanctis 1989). This region is also frequently involved in traumatic aortic rupture due to blunt trauma to the chest and is particularly susceptible to traumatic transverse tears, which may then initiate localized aortic dissection (Hirst 1983). Cardiac surgery is also proposed to be linked with a small risk of aortic dissection occurring at an aortic incision site or the site of aortic cross-clamping (Murphy 1983). Intra-arterial catheterization and the insertion of intra-aortic balloon pumps (Jacobs et al. 1992) both are likely to cause direct trauma to the aortic intima, hence, inducing aortic dissection.

Medial degeneration

The elastic tissue and smooth muscle cells, which are the main supporting elements within the aortic media, provide most of the tensile strength for the aortic wall. Medial degeneration, as evidenced by deterioration of the medial collagen and elastin, is suggested to be the main predisposing factor in most nontraumatic cases of aortic dissection (Coselli et al. 1995). Therefore, any of a variety of processes that lead to the degeneration or destruction of the elastic or muscular components of the media could predispose the aorta to dissection. The three main inherited connective tissue disorders, which are currently known to affect the arterial walls, are Marfan's syndrome, Ehlers-Danlos syndrome and familial forms of thoracic aneurysm and dissection (Nienaber & Eagle 2003). Marfan's and Ehlers-Danlos syndromes are marked by striking degenerative changes in the medial elastic tissue. Patients with the Marfan's syndrome, usually presenting a long and thin habitus, lenticular dislocations, a higharched palate, arachnodactyly, and any of several chest disformities, are indeed at high risk of

developing aortic dissection as Marfan's syndrome accounts for 6 to 44 per cent of all aortic dissection (Spittell et al. 1993; Hagan et al. 2000; Larson & Edwards 1984). Ehlers-Danlos syndrome is a heterogeneous group of hereditary connective tissue disorders, which is characterized by articular hypermobility, skin hyperextensibility, and tissue fragility (Nienaber & Eagle 2003). Histologically classic cystic medial degeneration is also identified in a minority of cases of aortic dissection (Spittell et al. 1993).

Hypertension

The most important disorder predispose to the development of aortic dissection is systemic hypertension. Among 121 cases of aortic dissection which were analysed by Larson and Edwards (1984), 52% had present hypertension with a higher incidence of clinical history of systemic hypertension in type B dissections. According to a new statistical study in IRAD, a coexisting history of hypertension is also found in almost 80% in a series of 452 cases of aortic dissection from IRAD, and is particularly common in patients with type B aortic dissection (Hagan et al. 2000). The arterial wall composition could be affected by chronic hypertension which is associated with intimal thickening, fibrosis, calcification, and extra cellular fatty acid deposition (Nienaber & Eagle 2003). All of the mechanisms may weaken and degrade the arterial wall, and eventually lead to intimal disruption.

Other acquired conditions

A relationship between pregnancy and aortic dissection has also been noticed. About half of all aortic dissection occurs during pregnancy in women under 40 years of age (Mazzucotelli et al. 1993). The increase in blood volume, cardiac output, and blood pressure are thought to be associated with the risk of dissection (Pumphrey et al. 1986). However, the situation is relatively rare, and the relationship is currently unexplained. The risk of suffering acute aortic dissection in women is significant only with concomitant existence of Marfan's syndrome and a dilated aortic during pregnancy. The preliminary data from IRAD also suggests that pregnancy in Marfan's syndrome is not associated with aortic tears unless root size exceeds 40 mm (Hagan et al. 2000).

The peak incidence of aortic dissection is in the sixth and seventh decades of life, with men being affected twice as often as women (Hagan et al. 2000). Certain other congenital cardiovascular abnormalities, including unicuspid aortic valve and possibly coarctation of the aorta, could predispose the aorta to dissection (Larson & Edwards

1984). Bicuspid aortic valve is also a well-established risk factor for proximal aortic dissection. Aortic dissection has also been reported to occur in association with the Noonan and the Turner syndromes (Spittell et al. 1993). In addition, smoking, dyslipidemia, and cocaine abuse are modulating risk factors (Om et al. 1992; Nienaber & Eagle 2003).

2.2.3 Imaging on aorta dissection

Aortic dissection is one of the most dramatic cardiovascular emergencies with extremely high mortality and morbidity if left undiagnosed and untreated. Therefore, once the diagnosis of aortic dissection is suspected on clinical grounds, it is essential to confirm the presence of dissection and to assess the emergent nature of the problem both promptly and accurately to reduce the possibility of death (O’Gara & DeSanctis 1995). Diagnostic imaging techniques are needed to rapidly confirm or refute the initial diagnosis, classify the classification in proximal (type A) or distal (type B) dissection, and identify a number of the anatomical features of the dissection, including its extent, the sites of entry and re-entry, the involvement of the coronary arteries by the intimal flap, branch vessel involvement by the dissection, the presence and extent of pericardial effusion, the presence and severity of aortic regurgitation, false lumen patency, and the presence of thrombus in the false lumen (Khan & Nair 2002). All these diagnostic information is essential and critical for decision making regarding surgical or conservative intervention, as well as the surgery access site. The imaging modalities currently used for the diagnosis of aortic dissection include aortography, contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI) and echocardiography. Each modality has certain advantages and disadvantages with respect to diagnostic accuracy, speed, convenience, risk, and cost. According to the statistics from IRAD, the current use of diagnosis resources is CT in 61%, echocardiography in 33%, MRI in 2%, and aortography in 4% at the initial diagnostic test (Hagan et al. 2000).

Beginning in the 1960s, retrograde aortography was the first accurate diagnostic technique for assessing patients with clinically suspected thoracic aortic dissection. It had long been considered the procedure of choice for the evaluation of aortic dissection for several decades because it was the only accurate method for diagnosing aortic dissection ante modern (Erbel et al. 2001). However, the recent introduction of alternative diagnostic imaging techniques has indicated that the diagnostic accuracy of aortography is not as high as originally thought. According to a prospective study by

Erbel et al. in 1989, the sensitivity and specificity for the diagnosis of aortic dissection were 88% and 95%, respectively. The other disadvantages of the technique include the risk associated with the use of contrast materials and ionized radiation, invasive procedure, long duration and high expense (Erbel et al. 2001). Hence, aortography has been used less frequently over the last two decades, and has been gradually replaced by noninvasive imaging techniques including echocardiography, helical computational tomography, and magnetic resonance imaging. The diagnostic sensitivity and specificity is comparable between the three imaging techniques, and the diagnostic value of each technique is acceptable for confirming or disputing aortic dissection (Shiga et al. 2006). The choice of imaging method is according to patients' presentation, local availability of equipment, and observer experience in interpretation (Golledge & Eagle 2008).

Because echocardiography is usually readily available in most hospitals and larger centres, as well as its accuracy, safety, speed and convenience, it has been considered well suited for the evaluation of patients with suspected aortic dissection. The diagnosis of aortic dissection in echocardiography is the presence of an undulating intimal flap separating true and false lumens (Mohr-Kahaly et al. 1989). Transthoracic echocardiography (TTE) has a relatively low sensitivity and specificity for the diagnosis of aortic dissection, with limitations in visualising the distal ascending, transverse, and descending aortas in patients (Cigarroa et al. 1993). Conversely, the sensitivity of transesophageal echocardiography (TEE) is as high as 98%, and the specificity ranges from 63 to 96% as reported (Khan & Nair 2002). Compared with MRI and helical CT, TEE is advantageous in emergency situations with time constraints as the diagnosis time needed for TEE is the shortest (Shiga et al. 2006). However, the main disadvantages of TEE are its inadequate ability to evaluate the distal part of the ascending aorta and the branches of the aortic arch, as well as its strong dependence on the investigators' experience (Borner et al. 1984). Although TEE is widely used as the first imaging method in diagnosing aortic dissection, it has difficulty in objectively recording the pathologic changes with follow-up studies in chronic dissections (Khan & Nair 2002).

Multi-slice computed tomography (CT)

Currently, conventional CT scanning is probably the most widely used imaging technique in the diagnosis of aortic dissection (Hagan et al. 2000), because it is available in most hospitals; can be rapidly done; and provides important information about the morphological features including the extent of dissection, relation between the true and false lumen, and aortic branch compromise (Golledge & Eagle 2008). In conventional CT

scanning, aortic dissection is diagnosed by the presence of two distinct aortic lumens, but it is associated with an insufficient sensitivity of 83 to 94% and a specificity of 87 to 100% (Erbel et al. 2001; Sommer et al. 1996). The new generation of imaging technology, helical (or spiral) CT, which permits a three-dimensional display of the aorta and its branches, offers many improvements and advantages over conventional CT. It allows diagnosis of aortic dissection with a sensitivity and specificity of nearly 100%, and yields the best value for disputing thoracic aortic dissection when a patient is at low risk for thoracic aortic dissection when compared to other imaging modalities (Shiga et al. 2006). Sebastia et al. (1999) have studied the helical CT features in the diagnosis and follow-up of aortic dissection, and concluded that helical CT is very useful in defining anatomical features, and follow-up procedure by allowing assessment of early and late changes after surgery or medical treatment including post-operative complications, the presence of thrombus in the false lumen, and aneurysmal degeneration of false and true lumen. The disadvantage of helical CT is the need for an intravenous contrast agent (Shiga et al. 2006), and limitations of spatial resolution when longer scan ranges have to be covered.

In 1996, multi-slice CT was first introduced (Hu 1998) and gradually replaced the older helical CT. It has several improvements overcoming past limitations of helical CT that scan length and spatial resolution can be simultaneously optimized, and the evaluation of large anatomic areas and vessels smaller than 1 mm become possible (Prokop 2000). The principle of CT scan is that different tissues of human body are characterised by different levels of attenuation reflecting the tissue density. Each X-ray beam incident on patient body is attenuated by the tissues it goes through, and is subsequently collected by an array of detectors positioned on the opposite side of the X-ray source. During CT scanning, the patient's bed moves within the X-ray tunnel, and the X-ray beam is perpendicular to the patient's axis and is rotating around the patient body, thus, tracing a spiral path relative to the patient. The recorded attenuated X-ray at each angle is constructed mathematically using reconstruction algorithms to form a two-dimensional cross sectional slice of the body. In multi-slice CT, a multiple-row detector array, which is shaped to a cone-beam geometry parallel to the patient bed moving axis, is equipped to simultaneously collect data at different slice locations (see Figure 2.6). The multi-slice CT is able to rapidly scan large longitudinal volume with high axial resolution (Hu 1998). It is reported that the performance of the system is increased by a factor up to 8 over that of a single slice scanner depending on the chosen scan mode, as well as significantly

reduced scan duration time that only up to 50s is needed for the whole arterial system of the chest and abdomen (Prokop 2000).

The application of multi-slice CT in detecting and classifying a suspected aortic dissection has also been widely discussed. As concluded by Prokop in 2000, multi-slice CT is in adventurous for the evaluation of the whole aorta including the side branches, in light of its superior spatial resolution even for long scan ranges. Hence, it is considered as an excellent tool for detecting complications of dissected aorta especially in follow-up period of chronic dissection, planning vascular interventions, and minimally invasively monitoring the effect of therapy. Johnson et al. (2007) investigated the utilization of 64-slice CT with ECG gating in vascular imaging, emphasizing the potential to accurately diagnose coronary atherosclerosis, pulmonary embolism and aortic dissection in one method. Hence, multi-slice CT will remain to be the first choice for diagnostic examination of aortic dissection.

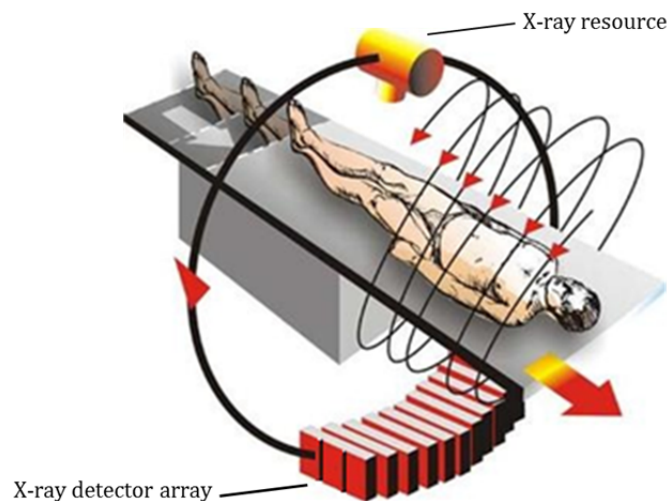


Figure 2.6: The process of helical CT scanner with rotating multi-conductor (adapted from <http://pgmcqs.com/radiology>).

Magnetic resonance imaging (MRI)

As MRI is entirely noninvasive and does not usually need a contrast agent, the use of MRI has a particular appeal for diagnosing aortic dissection. Both the sensitivity and specificity of MRI are in the range of 95 to 100% for detecting all forms of dissection (Stanford type A and B), thus, MRI has been considered the most accurate imaging technique in diagnosing thoracic aortic dissection (Erbel et al. 2001). The remarkably high accuracy of MRI has made it the current gold standard for testing and monitoring the presence and follow-up of aortic dissection. MRI has quite a few functional

assessment abilities including delineating the extent of the dissection, demonstrating the site of the entry tear, identifying the involved arch vessels, and assessing the renal artery involvement (Khan & Nair 2002). Although it is both highly sensitive and specific in diagnosing aortic dissection and powerful in producing high-quality images, MRI is rarely used as an initial diagnostic method for aortic dissection in most centres and hospitals because of its lack of availability on an emergency basis, time delay, incompatibility with implanted metal devices, or monitoring difficulties during examination (Erbel et al. 2001; Shiga et al. 2006). Guidelines recommend the use of MRI in the assessment of chronic dissection, as serial follow-up imaging is very important in patients with aortic dissection and MRI has the advantage of avoiding ionising radiation (Golledge & Eagle 2008).

Clinical MRI is based on the principles of nuclear magnetic resonance (NMR) to image nuclei of atoms inside the body. It utilizes the magnetic properties of nuclei which possess an odd number of protons or neutrons, and their interaction with a strong external magnetic field and radio-frequency pulses to produce highly detailed images of the inner structure of human body. These nuclei are charged particles with a characteristic precession. Hydrogen imaging is the most widely used MRI procedure, as hydrogen nuclei are in high abundance in human body as well as possessing the strongest magnetic moment. The main structure of the MRI scanning system is shown in Figure 2.7.

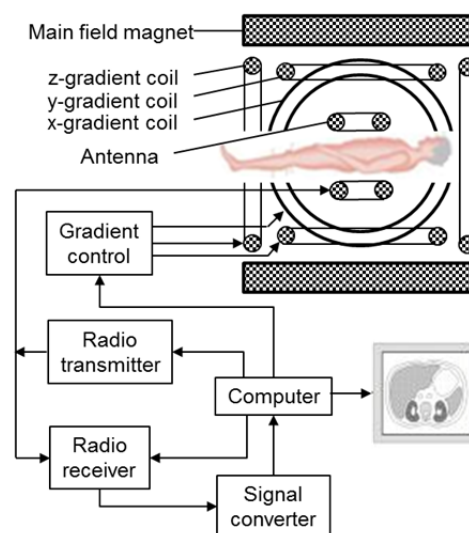


Figure 2.7: Schematic representation of a MRI scanning system.

When a human body is placed in a strong magnetic field, B_0 , most of the free nuclei align themselves in the direction of the magnetic field and simultaneously experience a torque.

This behaviour is termed Larmor precession. The frequency of Larmor precession is proportional to the strength of applied main magnetic field as defined by the Larmor frequency, ω_0 :

$$\omega_0 = \gamma \cdot B_0 \quad (2.1)$$

where γ is the gyromagnetic ratio and B_0 is the strength of main magnetic field. The gyromagnetic ratio is unique for each nucleus. For a hydrogen nucleus, the gyromagnetic ratio is 42.6 Hz/Tesla. In a clinical MRI scanner, the strength of the main magnetic field, B_0 , is usually between 0.5 to 1.5 Tesla.

In a magnetic field, the spin axes are not exactly aligned with the direction of B_0 , they precess around the B_0 axes in a perpendicular plane with a characteristic frequency (shown in Figure 2.8(b)). The spin of the nuclei creates a net magnetic moment, M , parallel to B_0 . The nucleus can spin in one of two orientations with respect to B_0 , parallel (lower energy) state and anti-parallel (higher energy) state. The two states are shown in Figure 2.8(a) marked with the angle, θ , subtended by the orientations and the direction of main magnetic field B_0 . Then, a radio-frequency (RF) pulse, with the same frequency as the Larmor frequency of the nuclei, is applied perpendicular to B_0 , causing the net magnetic moment M to tilt away from B_0 . Once the RF signal is removed, the nuclei enter relaxation period, trying to return to its equilibrium state. During this period, the nuclei lose the energy given to it by the RF pulse by emitting their own RF signal. The signal is measured by the coil placed around the patient body, and is subsequently processed to create 3D MR images.

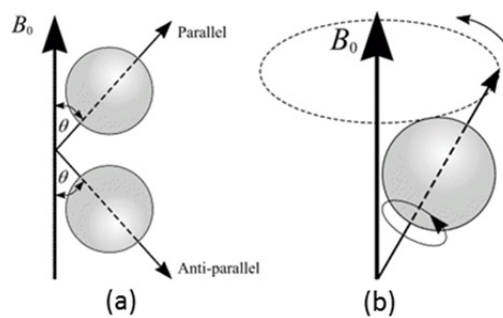


Figure 2.8: (a) Nuclei are constrained to one of two orientations in the external magnetic field, B_0 , forming an angle, θ , between the directions of orientations and B_0 ; (b) A magnetic moment precessing around B_0 .

In order to acquire MR images, the RF pulse needs to be repeated at a predetermined rate. The interval time from the application of one RF pulse to the next one is called the

repetition time, TR . The time from the application of the RF pulse to the peak of the response signal induced in the coil is called the echo delay time, TE . By adjusting TR and TE , the acquired MR images can be created to contrast different tissue types. The contrast of MR images depends on the proton density of the human tissue that higher proton density leads to stronger emitting RF signal from the nuclei. Another two tissue-specific parameters can also affect the MR image contrast: the longitudinal relaxation time, T_1 , and the transverse relaxation time, T_2 . T_1 is the time constant which describes the return of the longitudinal net magnetization to equilibrium, while T_2 constant presents how the transverse magnetization returns to its equilibrium. T_1 and T_2 time are different in fat and water in the human body in that fat has short T_1 and T_2 , while conversely water has long T_1 and T_2 . Hence, according to the interest of objective tissue type, TR and TE are adjusted depends on the specific T_1 and T_2 of tissue. When $TR \leq T_1$, and $TE \ll T_2$, the image contrast is predominantly caused by differences in T_1 of the tissues, called a T_1 - weighted image. Similarly, when $TR \gg T_1$, and $TE \geq T_2$, the MR images are T_2 -weighted image. The proton density weighted images are produced when $TR \gg T_1$, and $TE \ll T_2$.

There are many pulse sequences available for MR imaging. The specific MR examination for the aorta includes black blood imaging, noncontrast white blood imaging, contrast-enhanced MR angiography, and phase-contrast imaging (Hiratzka et al. 2010).

Black Blood Imaging: The black blood imaging, using spin-echo sequences, is utilized to assess anatomical and morphological information of the aorta (such as aortic size and shape), as well as the aortic wall for hematoma or other causes of wall thickening. ECG gating should be applied in the sequence, together with double inversion recovery techniques to null the signal from blood.

Noncontrast White Blood Imaging: Either basic gradient echo sequences or the more advanced balanced steady-state free precession techniques (SSFP) are used in performing the noncontrast white blood imaging. As the signal is generated from blood, the blood region appears white in the images due to the absence of contrast.

Contrast-Enhanced Magnetic Resonance Angiography: The contrast enhanced MR angiography is suitable for patients without a contraindication to receiving contrast agent, as most diagnostic information can be obtained. This technique is usually performed with ECG gating, and could markedly reduce the acquisition time.

Phase Contrast Imaging: These pulse sequences are useful to evaluate velocity gradients across an area of stenosis, an intimal or cardiac valve with ECG triggering. Detailed discussion is presented in the following section.

Phase contrast magnetic resonance (PCMRI)

The utilization of MRI for quantitative flow measurement was first introduced in 1980s. The tissue movement, resulting in alteration of MR signal, has brought advantages for phase contrast (PC) imaging to measure velocities (Bryant et al. 1984). When the magnetic spin moves along a magnetic field gradient (shown in Figure 2.9), it acquires a shift in the phase of rotation as compared to stationary moments. If the field gradient is linear, the amount of the phase shift ϕ is proportional to the velocity of the moving spin. As presented in Figure 2.9, a bipolar magnetic gradient is firstly applied to encode motion for velocity measurement in MR. By repeating an equal but opposite poles of bipolar gradient, the phase shift of static spins are eliminated. The phase difference that remains after subtraction of with and without the applied bipolar gradient can be used to accurately calculate the velocities of each voxel in images (Lotz et al. 2002).

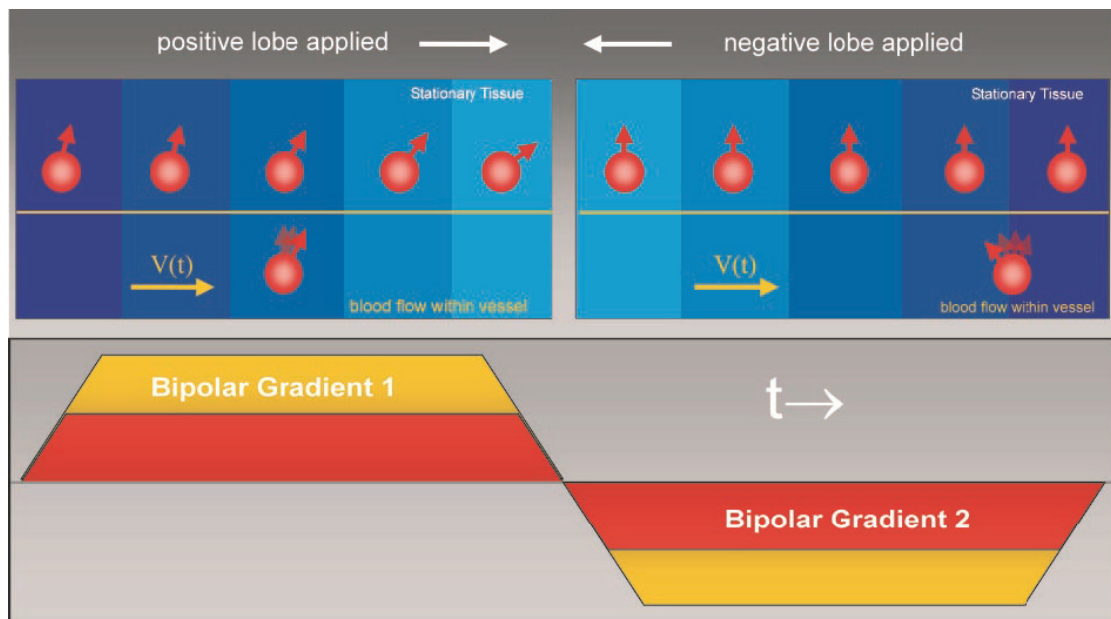


Figure 2.9: Principle of phase-contrast sequences available in clinical MR imaging units. Two equal but inverted bipolar gradients are performed to encode the flow velocity and eliminate the phase shift of static tissue (adapted from Lotz et al. 2002).

The velocity v can be determined by the phase difference $\Delta\phi$ acquired from two interleaved measurements:

$$\Delta\phi = \gamma \cdot \Delta m \cdot v \quad (2.2)$$

where γ is the gyromagnetic ratio of magnetic nuclei and Δm denotes the difference of the first moment of the gradient time curve.

The phase shifts are measured in degree unit within a range of $\pm 180^\circ$. To transfer the phase shift to velocity, the peak velocity of the moving tissue should be estimated before starting the measurement. The threshold value of velocity in the sequence is called velocity encoding, V_{enc} , corresponding to a phase shift of 180° . V_{enc} is a very important parameter which determines the highest and lowest detectable velocity encoded by the phase contrast sequence. Overestimated or insufficient V_{enc} value could affect the accuracy of the imaging results. The better the V_{enc} value matches the real maximum velocity of the region of interest, the more precise the measurement becomes. If the V_{enc} is too high, the sensitivity to lower velocities will be decreased as noise in velocity images increases with larger V_{enc} values. If the V_{enc} value is set below the real velocity, velocities exceeding the value will be aliased or wrapped (Gatehouse et al. 2005). If aliasing happens, repeated flow measurements with modified V_{enc} is needed to correct the aliased data set. Hence, different V_{enc} values have to be adopted according to the target area to acquire accurate velocity measurements.

Another important setting in phase contrast MR scanning is to position the imaging plane properly in the region of interest. Measurements of flow are the most precise if the location of imaging plane is orthogonal to the main direction of flow. However, it is not easy to accurately place the imaging plane during implementation especially when the flow situation is complicated. It has been reported that deviation of $\pm 15^\circ$ from the orthogonal imaging plane is acceptable for flow estimation as the increase of vessel area could be compensated (Tang et al. 1993).

The information from phase contrast measurement yielded from every MR imaging data acquisition includes two sets of images: magnitude image affording information for anatomic orientation and velocity image including phase information for velocity calculation. Figure 2.10 presents an example phase contrast MR images of the ascending and descending aorta. The magnitude image (middle) resembles a normal bright blood image. In the velocity image, the grey value of each pixel presents its phase or velocity magnitude information, as well as the direction of velocity. Black values indicate the flow toward the viewer, whereas white values show the opposite direction.

In order to get the velocity variation during a cardiac cycle, a set of frames, each of which presents the anatomy and velocity information at a different point of time in the cardiac cycle, needs to be obtained from cardiac-gated flow measurement. A technique of k-space segmentation is usually employed in the sequences to acquire data of all frames as quickly as possible. It was suggested that, a number of 30 cardiac frames would be sufficient to represent the time-varying flow with a good compromise between use of disk space, post-processing time, and flow measurement accuracy (Lotz et al. 2002).

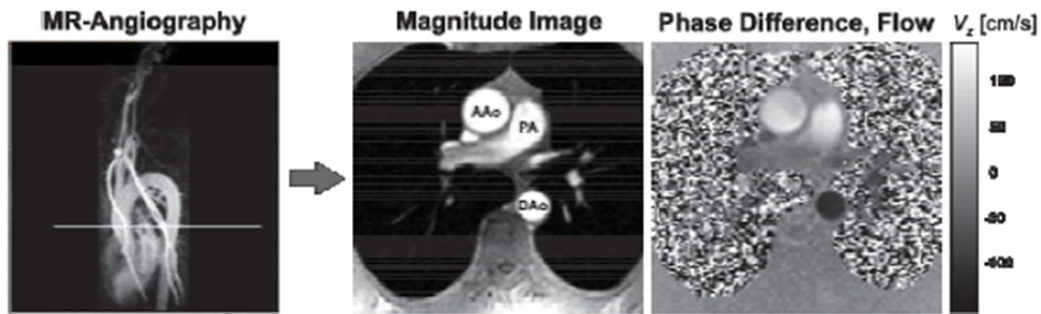


Figure 2.10: Through plane measurement of blood flow in the ascending (AA_0) and descending (DA_0) aorta. From left to right, the images are MR-angiography of the upper part of aorta, the magnitude image and velocity image (adapted from Markl et al. 2003).

Two-dimensional (2D) phase contrast MR imaging has wide applications in assessing cardiac function, heart valves, congenital heart diseases, major blood vessels, coronary arteries and myocardial wall velocity, with the functions of measuring many different aspects of the complicated blood flow in the heart and vessels, including volumetric flow, peak blood velocity, velocity profiles and timings of velocity waveforms and flow distributions within heart chambers and vessels (Gatehouse et al. 2005).

However, 2D phase contrast MR can only provide information about the through plane flow in a prescribed plane with the lack of three-dimensional (3D) flow information. In 3D phase contrast MRI, or four-dimensional (4D) MRI, all three velocity components can be measured at the prescribed plane (as shown in Figure 2.10(a)). True 3D data set of velocities can be created by stacking sequential 2D planes. Over time, data can be acquired in one acquisition without stacking multiple planes of acquired data in time-resolved 3D phase contrast MRI (Markl et al. 2003). This advantage has reduced the acquisition time and improved the image quality, and also overcome the plane alignment issues in 2D phase contrast MRI.

The raw image data of a time-resolved 3D MR velocity imaging can be imported into 3D visualization software programs to present 4D flow data. Vectors, streamlines and

particle traces are usually used to demonstrate the flow patterns in blood vessels. Individual vectors in a plane represent the velocities of each voxels at the level of the plane surface, but are unable to describe complex 3D flow patterns. Streamlines (shown in Figure 2.10(b)) and particle traces are widely used to display complicated helical flow and vortices (Napel et al. 1992; Wigstrom et al. 1999).

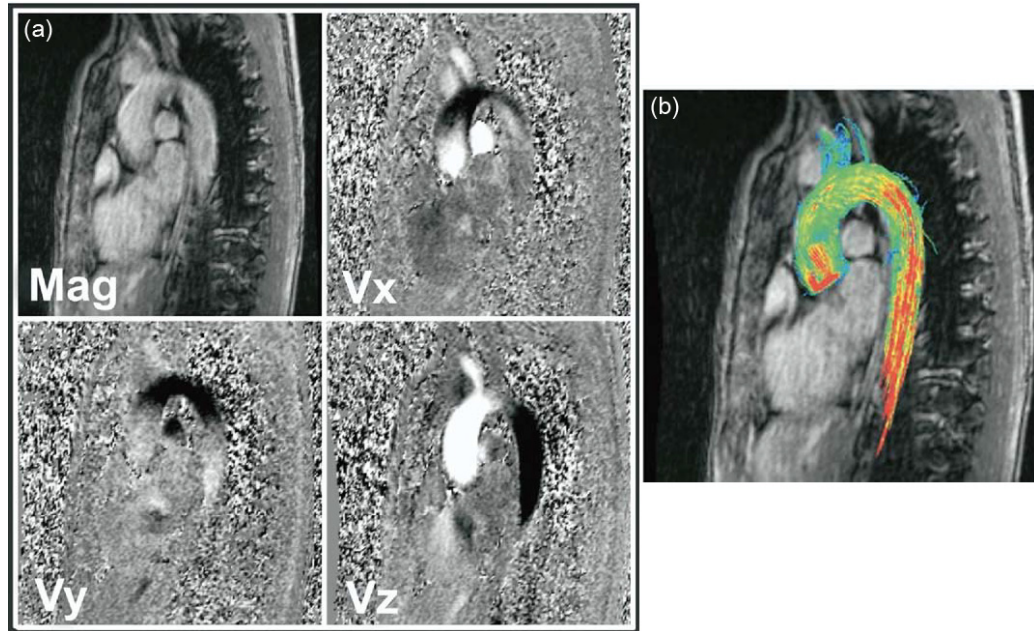


Figure 2.11: (a) The 4D flow data acquired results in a magnitude image (Mag) and three velocity encoded images (Vx, Vy, and Vz). (b) 4D visualization of flow streamlines created from four images on the left (adopted from Hope & Herfkens 2008).

3D phase contrast MRI has been widely applied in investigating the flow patterns in both healthy and diseased vessels. Kilner et al. (1993) were among the first to describe the right hand helical flow pattern in the ascending aorta by using 3D MR velocity mapping. The blood flow was reported to take longer time to enter the descending aorta in older and coronary artery disease patients when compared to younger healthy people (Bogren et al. 2004). The flow patterns in patients with aneurysms have also been investigated (Hope et al. 2007; Markl et al. 2004). The flow pattern in the ascending aorta of healthy people is described in detail by using 4D MRI (Gatehouse et al. 2008) that the jet from the aortic valve could be observed to hit the anterior right wall of the ascending aorta, thus, creating recirculating vortex in the region, and regurgitate flow develops in the diastolic portion of the cardiac cycle. Left-handed helical flow can also be seen in the descending aorta. The common flow pattern in ascending aortic aneurysm revealed considerable differences in local flow patterns compared to healthy individuals that the flow may fold inferiorly along the inner curvature, thus, creating a large region

of retrograde flow (Hope et al. 2007; Weigang et al. 2008). Limited studies have utilized 3D phase contrast MRI to investigate the flow patterns in aortic dissection. Silverman et al. (2000) assessed the accuracy of phase contrast cine MR angiography in the detection of type B aortic dissection with operative correlation on 197 symptomatic patients, and concluded it as a reliable imaging technique for evaluating aortic dissection. The flow pattern in a 54-year-old female dissection patient was presented by Gatehouse et al. (2008) revealing a velocity acceleration in the compressed true lumen, as well as a minimal amount of flow in the false lumen and rich clot in the remainder. Marked flow and abnormal shear stress was also indicated in a small group of dissection patients studied by Pitcher et al. (2011).

2.2.4 Haemodynamics and aortic diseases

Haemodynamics describes the physical aspects of blood circulation, including the dynamic behaviour of blood, forces and physical mechanisms concerned within the circulation. Haemodynamic forces have long been considered as key factors regulating blood vessel structure and influencing development of vascular pathology (Malek et al. 1999). Although no research has been published on the flow environment in aortic dissection before this study, a number of studies have been established to investigate the role of haemodynamic factors in other vascular diseases in the coronary, carotid, abdominal, and femoral arteries (Taylor et al. 1999; Taylor et al. 1998; Fillinger et al. 2002; Chatzizisis et al. 2007; Slager et al. 2005). The most important haemodynamic factors include wall shear stress (WSS), oscillating shear stress, flow disturbances, and pressure gradient. These factors are believed to be associated with the initiation and, perhaps most important, the progression of aortic diseases.

Roles of wall shear stress

The haemodynamic shear stress is the frictional force per unit area on the luminal vessel wall and endothelial surface, engendered by the blood flow by virtue of viscosity (Malek et al. 1999). It can be calculated as a function of time during the cardiac cycle at each location using a least-square fit of velocities measured at three radial positions near the wall as the following equation (Ku et al. 1985):

$$\tau_w = \mu \frac{\Delta V}{\Delta r} \quad (2.3)$$

where τ_w is the wall shear stress, μ is the dynamic viscosity, V is the velocity parallel to the wall, and r is the radial distance from the wall. In pulsatile flow, as the magnitude

and direction of the flow velocity change with time, the absolute shear stress, which is defined as the time-averaged magnitude of wall shear stress is usually adopted. The time-averaged wall shear stress (TAWSS) can be calculated as follows (Taylor et al. 1999):

$$TAWSS = \frac{1}{T} \int_0^T |\tau_w| dt \quad (2.4)$$

where T is the cycle period, and τ_w is the instantaneous wall shear stress. In addition to altering in magnitude, shear stress also changes its direction in pulsatile flow. An oscillatory shear index (OSI) is formulated to account for the cyclic altering of the wall shear stress vector from its predominant axial alignment. The OSI can be defined as (Taylor et al. 1999):

$$OSI = \frac{1}{2} \left(1 - \frac{\tau_{mean}}{TAWSS} \right) \quad (2.5)$$

where τ_{mean} is the magnitude of the time-averaged wall shear stress.

The normal time-averaged level of fluid shear stress was reported at approximately 15 to 20 dyne/cm² in the arterial circulation in human (Moake et al. 1988; Girerd et al. 1996). Abnormal shear stress conditions, including elevated wall shear stress, low magnitude of shear stress, and highly oscillating shear stress, could present in the cardiovascular system, due to abnormal properties of blood, insufficient heart function, and most important and commonly the geometry of artery. Many studies have attempted to investigate the correlation between abnormal shear stress and vascular diseases.

Shear stress can affect endothelial cell functions, such as proliferation, apoptosis, migration, permeability, and remodelling (Lehoux et al. 2006; Li et al. 2005; Tricot et al. 2000). Malek et al. (1999) reviewed the studies which have identified haemodynamic shear stress as an important determinant of endothelial function and phenotype. It was concluded that arterial level shear stress, which is larger than 15 dyne/cm², could induce endothelial quiescence and an atheroprotective gene expression profile, while low shear stress, which is defined as below 4 dyne/cm², may stimulate an atherogenic phenotype (Malek et al. 1999). Wentzel et al. (2003) established an in vivo measuring technique to study the role of shear stress in restenosis. It was demonstrated that shear stress is the main biomechanical factor regulating both neointimal formation and vascular remodelling as up to 50% in-stent neointimal formation could be reduced by high shear stress. Lehoux et al. (2006) emphasised the pulsatile nature of blood flow and

encompassing cyclic mechanical strain on the blood vessel, thus affecting vascular remodelling. Slager et al. (2005) reviewed the varying mechanobiological mechanisms in the surrounding area of plaque, and concluded that high shear stress acting on the endothelium has a regressive effect on the intimal tissue and can disturb the balance, thus determining the stability of the caps of vulnerable plaques at the upstream location of stenosis. As shown in Figure 2. 12, areas of high wall shear stress stimulate the endothelial cells to produce plasmin, transforming growth factor, and probably suppress matrix production by smooth-muscle cells, while low shear stress at the downstream part of the stenosis can stimulate endothelial cells to be apoptotic and dysfunctional (Slager et al. 2005). Increased shear stress was proved to elevate nitric oxide and prostacyclin release, and inhibit atherosclerotic processes (Niebauer & Cooke 1996). Richardson et al. (2002) also noted that mechanical disruption of an endothelial cell layer can promote atherosclerosis in blood vessel as the endothelial cells are sensitive to shear stress, thus altering apoptotic responses under high shear stress. Nakahashi et al. (2002) researched the role of flow loading in abdominal aortic aneurysm. They found that increased flow, wall shear stress, and relative wall strain may attenuate the aortic dilation and aneurysm development. The role of complex haemodynamic insults in cerebral aneurysm initiation was studied by Meng et al. (2007). Strong localization of aneurysm-type remodelling to the region of accelerating flow proposed high wall shear stress and high shear gradient can predispose the apical vessel wall to aneurysm formation. Pritchard et al. (1995) investigated the role of haemodynamic factors in the distribution of monocyte adhesion to the vascular wall with an in vitro flow model. It was noted that the cell rolling velocity changes linearly with wall shear stress, and the adhesion rate tended to decrease with increasing local wall shear stress combined with the effects of radial component of velocity and the dynamics of the recirculation region and flow reattachment.

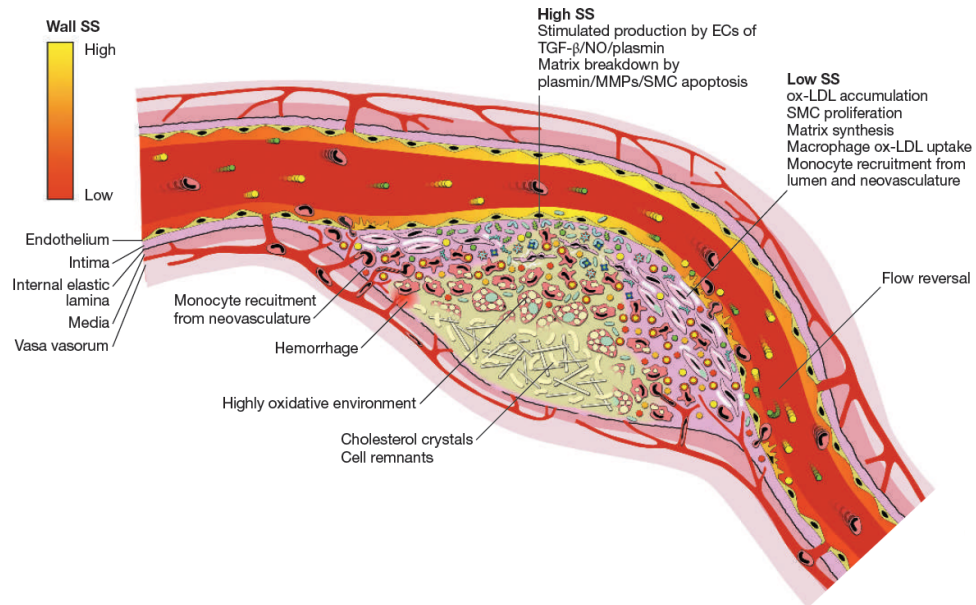


Figure 2.12: Proposed main mechanisms induced by high and low shear stress that affect the stability of the cap of a vulnerable plaque (Slager et al. 2005).

Low shear stress, which is usually combined with oscillatory shear, could lead to human monocytes suspension and binding to the endothelial, and cause plaque formation (Honda et al. 2001; Soulis et al. 2006; Cheng et al. 2006). Chatzizisis et al. (2007) reviewed the role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodelling, and concluded that low shear stress can attenuate nitric oxide-dependent atheroprotection, and promotes low-density lipoprotein cholesterol uptake, synthesis, and permeability. It can also promote oxidative stress, inflammation, vascular smooth muscle cell migration, differentiation, and proliferation. In vascular wall and plaque fibrous cap, low shear stress is proposed to promote extracellular matrix degradation and attenuate extracellular matrix synthesis. Moreover, it plays a potential role in plaque neovascularization and calcification, and increasing plaque thrombogenicity (Chatzizisis et al. 2007). In 1981, Friedman et al. noted that the low wall shear stress located at the lateral walls of the abdominal aortic bifurcation could induce increased intimal thickening. Moreover, a positive correlation between oscillatory shear and intimal thickness was also described by Moore et al. (1994) based on the measurement of the intimal thickness in the distal abdominal aorta. Based on a computational study of Taylor et al. in 1998, low time-averaged wall shear stress and oscillatory shear could lead to a high probability of occurrence of sudanophilic lesions on aorta wall. Low wall shear stress was also suggested to induce aneurysm growth and may trigger the rupture by causing degenerative changes of the aneurysm wall (Boussel et al. 2008; Shojima et al. 2004).

Shear stress has also been found to play an important role in platelet adhesion and aggregation in the process of thrombus formation (Furie 2008; Fuster et al. 1990). Numerical and in vitro models have been utilized to investigate the effect of shear stress magnitude in the platelet deposition and thrombus formation (Wootton & Ku 1999; Berger & Jou 2000). High shear stress in the bulk flow was found to activate platelets which were then more likely to adhere to the wall in underlying recirculation regions (Ramstack et al. 1979; Moake et al. 1988). The same result was also observed via rheological methods that increased fraction of active platelets and elevated tendency to platelet aggregates can be induced by high shear stress in stroke patients (Hellums et al. 1994). Bluestein et al. (1997) examined the blood flow in stenosis numerical model with different Reynolds numbers concluding that high shear stress and long exposure time could enhance platelets activation, while low wall shear stress increase the level of platelets deposition. The blood flow dynamics research from Nesbitt et al. (2009) resealed that platelets prefer to adhere in low-shear zones with stabilization of aggregates dependent on the dynamic restructuring of membrane tethers.

Role of disturbance and turbulent flow

Disturbance and turbulence in the blood flow influence physiological parameters and processes, such as flow resistance, pressure, wall shear stress, wall remodelling, inflammation, and mass transport from the blood to the vessel wall (Giddens et al. 1976). In the case of aneurysms, turbulence has also been suggested to result in wall vibration, with additional stresses on the aneurysmal wall, which can accelerate the progression of the aneurysm, and further increase the rate of wall dilation (Berguer et al. 2006; Khanafer et al. 2007). The time-varying vortices in recirculation region may enhance the delivery of monocytes to the vessel wall (Karino & Goldsmith 1979; Schmid-Schonbein & Wurzinger 1986). Local flow disturbances as a driving force appear to be obligatory in the process of atherosclerotic plaque formation (van der Wal 1999). In arterial regions with disturbed flow and low shear stress, atherosclerotic process could be promoted as the atheroprotective genes are suppressed, while the pro-atherogenic genes are upregulated (Gimbrone et al. 2000; Resnick et al. 2003). Turbulence as a characteristic of blood flow was also identified as a risk factor for the formation of thrombi according to the work in canine models (Stein and Sabbah 1974). Turbulence and recirculation were found to be associated with increased shear stress and exposure time, thus accelerating the process of thrombus formation (Stein and Sabbah 1976; Loree et al. 1991). The unsteady flow development in the recirculation flow region was demonstrated to contribute to platelet deposition by Bluestein et al. (1999).

Geometric factors

Complex geometric configurations determine the shear stress distribution and flow patterns in arteries. Low shear stress typically occurs at the inner bend of curvatures and downstream of stenosis (Ku 1997) and high shear stress can be found in the upstream, while oscillatory wall shear usually occurs primarily downstream of stenosis, at the lateral walls of bifurcations, and in the vicinity of branch points (Chatzizisis et al. 2007). Areas of complex flow in the coronary, carotid, abdominal, and femoral arteries, where plaques are commonly found, often occur due to branching, bifurcations and curvature of the arteries (Taylor et al. 1997). Lee et al. (2008) noted that certain geometric features of carotid bifurcation, including proximal area ratio and bifurcation tortuosity, are significantly related to disturbed flow. The dynamic curvature data and high curvature variations of coronary artery were also demonstrated to have notable effects on the flow patterns and wall shear stress by Prosi et al. (2004). Non-planarity of the aorta was considered as an important factor influencing arterial flows, hence, the pathogenesis of various disorders (Caro et al. 1996). Vorp et al. (1998) investigated the mechanical wall stress in abdominal aortic aneurysm, and found both maximum diameter and the shape factors have substantial influence on the distribution of wall stress within the aneurysm. Hoi et al. (2004) also noted that the curvature of the artery where aneurysms were located could lead to higher haemodynamic stresses, thus implicating the site of aneurysm growth or regrowth of treated lesions. An aneurysm surface index, which is defined as the ratio between the aneurysm area and the artery area, was proposed by Valencia et al. (2007) to predict the wall shear stress distribution in cerebral aneurysms.

Other factors

Elevated blood pressure could affect the ultimate thrombotic occlusion of the vessel (van der Wal et al. 1999). High pressure in arteries was also suggested as a risk for early atherosclerosis and persistent endothelial damage, as well as accelerating the atherosclerotic process via inflammatory mechanisms (Li & Chen 2004). Moreover, pressure oscillations in a flow cycle were believed to cause plaque to fatigue, thus making plaque particles prior to be sheared off by wall shear stress (Stroud et al. 2000). Elevated pressure could induce mechanical stress in the carotid artery bifurcation where atherosclerotic lesions are highly susceptible to occur (Salzar et al. 2000). Stress is a very important parameter determining the rupture and degeneration of diseased vessel wall. Stresses that act on or within the arterial wall could affect the inflammatory

process and the heterogeneous remodelling of vessel structure and composition (Davies 1988). Concentration of circumferential stress in the atherosclerotic plaque was demonstrated to play an important role in plaque rupture and myocardial infarction (Cheng et al. 1993; Richardson et al. 2002; Li et al. 2005). High wall stress in aneurysm has been proved to be more closely correlated with the risk of rupture than the diameter of aneurysm (Fillinger et al. 2003; Venkatasubramaniam et al. 2004).

2.3 Engineering background

2.3.1 Computational fluid dynamics (CFD)

The physical aspects of any fluid flow are governed by three fundamental principles: (1) mass of a fluid is conserved; (2) Newton's second law: the rate of change of momentum in a fluid is equal to the sum of the forces that act on the fluid; and (3) First law of Thermodynamics: energy can neither be created nor destroyed. These fundamental principles can be expressed in terms of mathematical equations, usually in the form of partial differential equations. Computational fluid dynamics (CFD) is, as defined in part, the art of obtaining a final numerical description of the complete flow field of interest via methods of replacing the governing partial differential equations of fluid flow with numbers, and advancing these numbers in space and time (Anderson 2009). It is a very powerful tool in engineering analyses, and is regarded as the third dimension in fluid dynamics, of equal stature and importance to experiment and theory.

The fundamental basis of CFD problems is the Navier-Stokes equations, which describe the motion of fluids. The governing equations are time-dependent and consist of mass, momentum and energy balance giving a system of three equations:

$$\text{Continuity equation:} \quad \frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{u}) = 0 \quad (2.6)$$

$$\text{Momentum equation:} \quad \frac{\partial \mathbf{u}}{\partial t} + (\mathbf{u} \cdot \nabla) \mathbf{u} = -\frac{1}{\rho} \nabla p + F + \frac{\mu}{\rho} \nabla^2 \mathbf{u} \quad (2.7)$$

$$\text{Energy equation:} \quad \rho \left(\frac{\partial \varepsilon}{\partial t} + \mathbf{u} \cdot \nabla \varepsilon \right) - \nabla \cdot (K_H \nabla T) + p \nabla \cdot \mathbf{u} = 0 \quad (2.8)$$

where $\mathbf{u}$ is the instantaneous blood velocity at time t , ε is thermodynamic internal energy, p is the instantaneous static pressure relative to a datum level, T is the temperature of the fluid, ρ and μ are the density and viscosity of the fluid respectively, K_H is the heat conduction coefficient, and F is the external force per unit mass. For an

incompressible, isothermal and Newtonian fluid, the Navier-Stokes equations can be simplified as:

$$\rho \frac{\partial \mathbf{u}}{\partial t} - \mu \nabla^2 \mathbf{u} + \rho (\mathbf{u} \cdot \nabla) \mathbf{u} + \nabla p = 0 \quad (2.9)$$

$$\nabla \cdot \mathbf{u} = 0 \quad (2.10)$$

Being different from analytical solutions of partial differential equations, numerical solutions can only give answers at discrete points in the fluid domain. In CFD modelling, the complex geometry is discretized into a large number of smaller elements. Two types of elements are typically adopted in CFD modelling: tetrahedral element, a polyhedron composed of four triangular faces, and hexahedral element, a uniform brick shape. The numerical calculations are carried out in the single computational space by assuming the shape of the velocity field within these elements. The governing Navier-Stokes equations are solved iteratively at the nodes connecting these elements. The computed flow field is driven by numerical boundary conditions which include the fluid behaviour and properties at the defined boundaries of fluid domain, and dictate the particular solutions to be obtained from the governing equations. Proper and accurate implementation of the boundary conditions is essential for numerical calculations in CFD.

Discretisation of the conservation equations is the process of using a system of linear algebraic equations to replace the partial differential equations. Two different discretisation techniques are commonly used to solve the conservation equations in current commercial CFD software packages: finite element method (FEM) and finite volume method (FVM). The two methods vary in their approximation of flow variables, as well as in the discretisation process. FEM uses simple piecewise polynomial functions on local mesh elements to approximate the variations of flow variables. When the functions are substituted into the governing equations, the concept of a residual is utilized to measure the errors, which will subsequently be minimized by a set of weighting and integrating functions. A set of algebraic equations can be achieved for the unknown terms of the approximating functions, and hence yields the flow solution. FEM is more popular in structural analysis of solids. FVM is the most popular method in current commercial CFD software, especially for fluid mechanics, as it rigorously enforces conservation and is also flexible in terms of both geometry and the variety of fluid phenomena. It employs an integral form of the conservation equations over the finite control volumes of the solution domain which is produced in the meshing. Finite difference type approximations are substituted for the unknown terms of the integrated

equations. This yields a set of algebraic equations which are solved by an iterative method. From the solutions of CFD in haemodynamic research, velocity, WSS, and other important quantities can be extracted straightforward.

2.3.2 CFD studies of blood flow in normal and diseased aorta

In the last 20 years, CFD has been proven to be a practical and reliable tool for cardiovascular research, as it gives researchers full control of geometry and flow data while studying time-varying, three-dimensional blood flow patterns in complex arterial geometries. Since the mid-1990s, the convergence of high-resolution medical imaging, sophisticated image processing techniques, and high-performance desktop workstations have promoted image-based CFD studies of in vivo haemodynamics (Steinman 2002). Now, CFD has almost completely supplanted traditional engineering flow measurement techniques, such as laser Doppler velocimetry (LDV) and particle imaging velocimetry (PIV), in the investigations of artery haemodynamics, and parametric studies of geometric or flow-related factors (Steinman & Taylor 2005). Various image-based CFD studies have been conducted to investigate the flow patterns and haemodynamic factors in both healthy and diseased aortas, as well as their effects on vascular pathophysiology. In this subsection, the development of CFD application in vascular research during the last decade is briefly reviewed.

CFD studies in normal aorta

The aorta, as introduced in chapter 2, has a complex geometry including bending, branching and tapering. Numerous clinical investigations, experimental studies, and numerical simulations using idealized geometries have suggested the presence of skewed and spiral flow patterns in human aorta. Besides these, several CFD studies, usually combined with MRI data, have also been conducted to investigate the flow patterns and haemodynamic factors in normal aorta.

Morris et al. (2005) studied the flow characteristics in realistic models of the aorta created based on CT scans with different arch reconstructions and smoothing methods, by using CFD. They concluded that the radius of arch curvature and the pulsatility of the flow are the main influencing factors in determining aortic flow patterns. Leuprecht et al. (2003) examined the blood flow through the ascending aorta of both healthy and artificial valves planted individuals by using realistic flow simulation enabled by the combination of MRI and CFD. It was demonstrated that flow profiles in the ascending aorta and wall shear stress magnitude and distribution, depended significantly on the

flow rate and profile from the aortic root controlled by the aortic valve. The wall motion resulting from beating heart, and compliance of the aortic wall were found to affect the flow patterns in the ascending aorta based on a MRI-based CFD study (Jin et al. 2003).

CFD models of the aortic arch were also developed with or without the arch branches (Shahcheraghi et al. 2002; Mori & Yamaguchi 2001). Mori & Yamaguchi (2001) noted that the torsion of the aortic arch centreline could lead to a complex localized distribution of wall shear stress at the top of the arch. The flow pattern and shear stress distribution in the aortic arch were also proved highly dynamic by Shahcheraghi et al. (2002). The presence of the arch branches was suggested to affect the structure of secondary flows in the aortic arch. Flow structure and haemodynamic conditions in the descending aorta were studied by Wood et al. (2000) in a MRI-based CFD study. Good agreement of the CFD results and MR velocity mapping was achieved in the study. A detailed analysis of the haemodynamics in the thoracic aorta was implemented based on the integration of flow-sensitive 3D MRI with rapid prototyping technology and CFD (Canstein et al. 2008). Visualization of characteristic 3D flow patterns and quantitative comparisons of *in vitro* experiments with *in vivo* data and CFD simulations in identical vascular geometries were performed, and the accuracy of the vascular model system was evaluated.

CFD studies in diseased artery

Image-based CFD analyses have been widely adopted to elucidate the role of haemodynamic forces in vascular pathophysiology of diseased arteries, especially in the development of atherosclerosis at the carotid and coronary arteries, and in understanding haemodynamics in abdominal aortic aneurysms, owing to their advantageous in providing patient-specific predictions by incorporating medical imaging (Taylor & Steinman 2010).

CFD models of coronary arteries obtained from angiographically guided intravascular ultrasound (IVUS) have been utilized to demonstrate a correlation between low wall shear stress and vessel wall remodelling in a longitudinal study conducted by Stone et al. (2003), as well as the role of haemodynamic factors in interventional cardiology such as balloon angioplasty and stent implantation (Thury et al. 2002; Wentzel et al. 2001). A number of CFD studies have been carried out to elucidate the role of haemodynamic forces in the development of coronary artery plaques, and demonstrated the association between distinct haemodynamic mechanisms and the development and rupture of vulnerable plaques (Slager et al. 2005). Steinman et al. (2002) used MRI to investigate

the association between low and oscillating shear and wall thickening in both normal and mildly diseased carotid bifurcations. A serial MRI-based case study demonstrated an association between the high shear stress and the location of plaque ulceration (Groen et al. 2007). Another IVUS-based CFD study of 31 plaques presented an obvious correlation between high wall shear stress and elevated wall strain within the plaque (Gijssen et al. 2008). A negative correlation between plaque progression, and plaque wall stress and wall shear stress was demonstrated by Tang et al. (2008) in a serial MRI-based study of 21 carotid artery plaques. Lee et al. (2008) studied the relationship between disturbed flow and lumen geometry based on 50 cases of carotid bifurcations in a MRI-based CFD study, and determined certain geometric features as robust surrogate markers of exposure to disturbed flow.

In addition to studies related to atherosclerosis in the carotid and coronary arteries, image-based CFD modelling has been applied in assessing the haemodynamic factors involved in the development and rupture of cerebral aneurysms (Hassan et al. 2004; Jou et al. 2003; Steinman et al. 2003). CFD studies were carried out to relate the complex haemodynamic factors to geometric factors. Shojima et al. (2004) investigated 20 cases of cerebral aneurysm with CFD, and demonstrated that low wall shear stress could accelerate the growth and trigger rupture of a cerebral aneurysm by causing wall degeneration, as well as the role of aneurysm aspect ratio in wall shear distribution. Furthermore, Cebal et al. (2005) found an association between the size and stability of inflow and the risk of aneurysm rupture in a CFD study of 62 cerebral aneurysm cases. Longitudinal studies were also implemented on unruptured aneurysms to examine the effects of haemodynamic forces on long-term aneurysm growth. Low wall shear stress and stagnant flow were demonstrated to play a key role in subsequent aneurysm growth (Boussel et al. 2008), progression (Jou et al. 2005) and thrombosis (Rayz et al. 2008).

Haemodynamics of the human abdominal aorta has been studied by using CFD methods to investigate the progression of abdominal aortic aneurysm (AAA). CFD models of 5 young and healthy abdominal aortas derived from MR images were examined by Tang et al. (2005) with patient-specific flow data extracted from phase contrast MRI as boundary conditions in their simulations. The haemodynamic conditions in the aorta were quantified under both resting and mild exercise pulsatile flow conditions. The results demonstrated that exercise could provide localized benefits to the cardiovascular system through acute mechanical stimuli that trigger long-term biological processes leading to protection against the atherosclerosis development and progression in the abdominal aorta. The role of exercise in slowing the progression of

small abdominal aortic aneurysms was also evaluated by using MR-based CFD modelling techniques combined with MR flow imaging (Dalman et al. 2006). The significantly higher risk of AAA in the abdominal aorta of patients with spinal cord injury than normal control subjects was studied by image-based modelling techniques to identify the differences in haemodynamic conditions (Yeung et al. 2006). The flow patterns in a thoracic aortic aneurysm model reconstructed from MR images were assessed by employing a transitional turbulence model showing a better agreement with the MR data than laminar flow simulation (Tan et al. 2008).

Image-based CFD methods have also been utilized to study the effects of haemodynamic factors on endothelium biology. Realistic CFD models of porcine iliac arteries were established to understand the cellular and genetic responses to abnormal wall shear stress magnitude and gradient, which may cause shear-induced endothelial cell dysfunction (LaMack et al. 2005; Friedman et al. 2006). Low endothelial shear stress was demonstrated to be associated with the localization of high-risk coronary atherosclerotic plaques by an IVUS-based CFD study of cholesterol-fed swine (Chatzizisis et al. 2008), and a CFD-inspired perivascular cuff study of mouse carotid arteries (Cheng et al. 2006). The positive correlation between relatively low wall shear stress and adhesion of molecules on the endothelial layer of aortic wall was examined in an aortic arch model of mouse by Suo et al. (2007). Kadirvel et al. (2007) studied the influence of haemodynamic forces on the expression of biomarkers associated with vascular remodelling in the walls of elastase-induced aneurysms in rabbits. The canine study implemented by Meng et al. (2007) presented that a combination of high wall shear stress and a high gradient in wall shear stress at the apices of arterial bifurcations could favour aneurysm formation.

Fluid-structure interaction modelling

Fluid-structure interaction (FSI) is concerned with dynamic interactions between a movable or deformable structure with the contacting fluid flow. The lack of realistic material properties and boundary conditions has restricted the application of FSI in blood flow simulations. There have been a number of significant advances in FSI simulation of blood flow and vessel wall motion since the middle of last decade, as traditional FSI techniques, which are based on the arbitrary Lagrangian-Eulerian (ALE) method, were improved to meet the requirements of modelling blood flow in arteries (Taylor & Stainman 2010). A number of FSI simulations have been established to solve

patient-specific problems using ALE methods including pulsatile fluid motion and nonlinear continuum of vessel wall.

A robust partitioned, strongly-coupled ALE method was developed to solve the interaction of blood flow and vessel wall dynamics in patient-specific models by Gerbeau and colleagues (Gerbeau et al. 2005; Fernandez et al. 2007). Patient-specific FSI simulations of blood flow in abdominal aortic aneurysm (AAA) models (Wolters et al. 2005; Leung et al. 2006) and thoracic aortic aneurysm (TAA) models (Borghi et al. 2007; Tan et al. 2009) were carried out by using ALE-based methods. Scotti et al. (2005) utilized a set of virtual AAA models with different degrees of asymmetry and wall thickness to study the flow and wall dynamics by means of fully coupled FSI. The parameters of aneurysm asymmetry and wall thickness were found to affect the magnitude and distribution of Von Mises stresses in such a way that varying wall thickness increased the peak Von Mises stress by 4 times its uniform thickness counterpart. Torii and colleagues investigated blood flow in realistic cerebral aneurysms by adopting a stabilized space-time FSI finite element method to assess the effects of blood pressure (2006), and influence of structural modelling (2008). In a more recent FSI study of cerebral aneurysms, 0D peripheral vasculature model was used to compute the outflow through the two branches accurately (Torii et al. 2010). A new isogeometric non-uniform rational B-spline (NURBS)-based FSI formulation, coupling incompressible fluids with nonlinear elastic solids, and allowing for large structural displacements, was developed to solve patient-specific blood flow problems by Bazilevs et al. (2006). The method was applied to realistic models of cerebral aneurysms incorporated with a new approach for the computation of the blood vessel tissue pre-stress (Bazilevs et al. 2010). The coupled momentum method, which embeds the elastodynamics problem for the deformation of the vessel wall within the variational equation of the fluid dynamics problem, was introduced by Figueroa et al. (2006) to solve highly complex blood flow and vessel wall dynamics by simplifying the problems into small deformations and thin-walled vessels.

2.3.3 Biomechanical analysis of diseased aorta

Biomechanical behaviour of diseased aorta wall

The biomechanical behaviour of diseased tissue, especially aneurysm tissue, is different from that of healthy aorta with changes in compliance or wall stiffness. Understanding the tissue constitutive relations which relate the stress (force per unit area) and strain (deformation) in a material, is an important part in wall stress analysis. The

biomechanical behaviour of diseased wall can be examined by means of in vivo measurements and ex vivo tensile testing (Vorp & Van de Geest 2005).

Noninvasive ultrasound or CT imaging techniques have been used to estimate the mechanical behaviour of diseased wall. By using a phase-locked echo-tracking system, a reduced compliance of AAA wall was demonstrated when compared to an age-matched control group (Lanne et al. 1992). The pressure-strain elastic modulus was found to be elevated in patients with AAA by using an M-mode ultrasonography (MacSweeney et al. 1992). The mechanical behaviour of intraluminal thrombus (ILT) in AAA was also estimated in vivo. It was found that ILT could act like a cushion on the AAA wall that the wall compliance was reduced as compared to the luminal surface of aneurysm via non-invasive measurements (Vorp et al. 1996; Wang et al. 2002). Sonesson et al. (1997) investigated wall stiffness of the abdominal aorta in patients with AAA in comparison to healthy subjects, and found an increase in stiffness of AAA wall. A group of 112 patients with non-operated AAA was recruited to determine the relationship between AAA compliance, size, growth, and clinical outcome (Wilson et al. 1998). It was concluded that baseline AAA compliance was significantly associated with rupture and requirement for operative repair, and large size aneurysm tended to be less compliant. The relationship between AAA distensibility and serum markers of elastin and collagen metabolism was investigated by Wilson et al. in 2001, demonstrating the negative effects of serum markers on AAA wall stiffness. The role of AAA wall distensibility in predicting rupture time was estimated in a study of 210 patients (Wilson et al. 2003). The measurement of wall distensibility, blood pressure, and aneurysm diameter were suggested as a more accurate assessment of rupture risk than size alone.

The ex vivo tensile testing studies were mostly carried out by comparing the biomechanical properties of aneurysmal tissue with nonaneurysmal tissue to investigate the effect of extracellular matrix derangements on wall stiffness and strength. A stiffer and less distensible uniaxial response for AAA was demonstrated by He and Roach (1994), as well as a decrease in volume fraction of elastin in the aneurysm wall. Other uniaxial tensile testing studies demonstrated that AAA wall tissue was about 50% weaker than nonaneurysmal abdominal aorta with similar circumferentially-oriented and longitudinally-oriented tissue strength (Raghavan et al. 1996; Vorp et al. 1996b). The observations of spatially varying biomechanical properties of AAA have been reported by several studies (Thubrikar et al. 2001; Vorp et al. 2001; Van de Geest et al. 2006a). The presence of ILT in aneurysm was also suggested to decrease local wall strength as ILT serving as a barrier to oxygen flux from the lumen to the inner layers of

the aortic wall, thus resulting in hypoxic conditions and wall degeneration (Vorp et al. 2001). The local hypoxic environment, which may be important in upsetting the local balance of protein degradation and synthesis in the aneurysm wall, could lead to a decrease in the overall structural integrity of the wall and its eventual rupture (Vorp & Van de Geest 2005). Another ex vivo tensile test was established between AAA subjects prior to surgery and those from electively repaired to investigate the association of wall weakening with aneurysm rupture (Di Martino et al. 2006). Significant differences of wall thickness and tensile strength were presented suggesting severe aneurysm wall weakening could lead to aneurysm rupture. Witkewicz et al. (2005) studied the strength of aneurysm tissue in different tensile direction, concluding that the tissue is stronger in the longitudinal direction than in the circumferential direction. The uniaxial tensile tests were also carried out on the thrombus illustrating the mechanical properties of ILT as a hyperelastic isotropic material (Wang et al. 2001).

Most studies on mechanical properties of diseased aorta wall were conducted based on ex vivo wall tensile testing of abdominal aneurysms. Very limited studies have been performed on other aortic diseases and tissues. Okamoto and colleagues (2002) investigated the mechanical properties of dilated human ascending aorta by implementing opening angle, biaxial elastic, and uniaxial circumferential strength tests on specimens from 54 patients undergoing elective aortic graft replacement surgery. They found greater opening angle and increased wall stress in older patient group, suggesting that age may influence the risk of aortic dissection or rupture of dilated ascending aorta (Okamoto et al. 2002).

Wall stress analysis of diseased aortic wall

Wall stress is not a directly measurable quantity. To acquire accurate wall stress distributions, essential information is required including aortic geometry, wall thickness, applied forces and boundary conditions, governing equations representing the relevant physical laws, constitutive models, material parameters, and a means to solve the resultant system of partial differential equations (Vorp & Van de Geest 2005).

Hypothetical models of aneurysm were initially utilized to perform model evaluation and sensitivity study. Vorp et al. (1998) generated a set of hypothetical computer models of AAA with the purpose to determine the effect of maximum diameter and asymmetric bulge on wall stress. It was concluded that the magnitude of peak stress acting on the aneurysm increased with increasing maximum diameter or increasing asymmetry. As the material parameters specific to each aneurysmal wall and ILT cannot

be determined by destructive mechanical testing prior to surgery, the group mean values of the material parameters obtained for a large number of AAA and ILT specimens (Raghavan & Vorp 2000; Wang et al. 2001) have commonly been used in wall stress analyses. These material parameters were evaluated by repeated finite element stress parametric analyses on a hypothetical asymmetric AAA model (Raghavan & Vorp 2000; Di Martino & Vorp 2003). They suggested that the wall stress was not sensitive to variations in material parameters, and the differences in aneurysm wall stress depended more strongly on the difference in surface geometry.

Wall stress distribution in patient-specific aneurysm models has also been studied. Raghavan et al. (2000) used a continuum-based constitutive model in the finite element analyses of patient-specific aneurysms to investigate the stress distributions in three AAA models. Complex stress distribution with localized regions of high and low stresses was demonstrated, in comparison to more evenly distributed lower peak stress values in a normal aorta. Fillinger et al. (2002) examined 48 patient models of AAA constructed from CT scans to calculate wall stress in vivo for ruptured, symptomatic, and electively repaired AAAs comparing with clinical indices related to rupture risk. Significantly higher peak wall stress was found in AAAs near the time of rupture than those for electively repaired ones. A later study was implemented by Fillinger et al. (2003) to analyse rupture risk over time in patients under observation. Venkatasubramaniam et al. (2004) also found much higher wall stress in ruptured AAAs than those of non-rupture ones. In patients with an identifiable site of rupture on CT scan, the area of peak wall stress was found correlated with the rupture site. Raghavan et al. (2005) developed an automated algorithm to calculate the peak stress in numerous ruptured and nonruptured AAA models, and emphasized the peak stress as a better predictor of rupture. To investigate the influence of thrombus on AAA wall stresses, Wang et al. (2002) incorporated the structure of ILT in the AAA models, and demonstrated that the incorporation of ILT in AAA model could influence the magnitude and distribution of stresses acting on AAA wall. The anisotropic material model determined by experiment was incorporated into the AAA models, which was demonstrated to give an improved prediction of stress distribution in the aneurysm (Van de Geest 2005). Variable wall thickness and patient-specific wall calcifications were also incorporated in some studies, which were believed to improve the estimation of wall stress and the location of rupture (Raghavan et al. 2004; Speelman et al. 2005). Other recent multiple cases studies have continued to focused on patient-specific AAA wall stress analyses in ruptured aneurysm with small size (Truijers et al. 2007), its relationship with certain geometric features

(Speelman et al. 2008), or its role in aneurysm growth and biomarkers (Speelman et al. 2010).

2.4 Experimental studies of blood flow in aortic dissection

Limited experimental studies of blood flow in aortic dissection have been published probably owing to the difficulty of analysing flow results in models of aortic dissection which have highly complicated geometric structure. Idealized aortic dissection models are used in experimental studies to investigate the movement of flap and pressure distribution, and their relationship with anatomic and physiologic factors of the models.

In the experimental study conducted by Chung et al. (2000), phantoms of a Stanford type B aortic dissection model, with an aortic arch, true and false lumen with abdominal branch vessels, and a distal bifurcation, were built to investigate the causative factors in true lumen collapse in the model. The collapse of the true lumen was suggested as an important mechanism for compromised flow in the aortic branch of aortic dissection patients. Figure 2.12 presents the components of the pulsatile mock-flow loop that was filled with water at 28°C to mimic the systemic circuit of human body. The pulsatile pump was a ventricular assist device with controllable rates, hence physiologic pressures and flow velocities could be achieved in the models. The systolic pressure and systolic duration were set to 225 mm Hg and 250 msec, respectively, and the setting for diastolic pressure varied between 5 and 75 mm Hg, which determined the pump output.

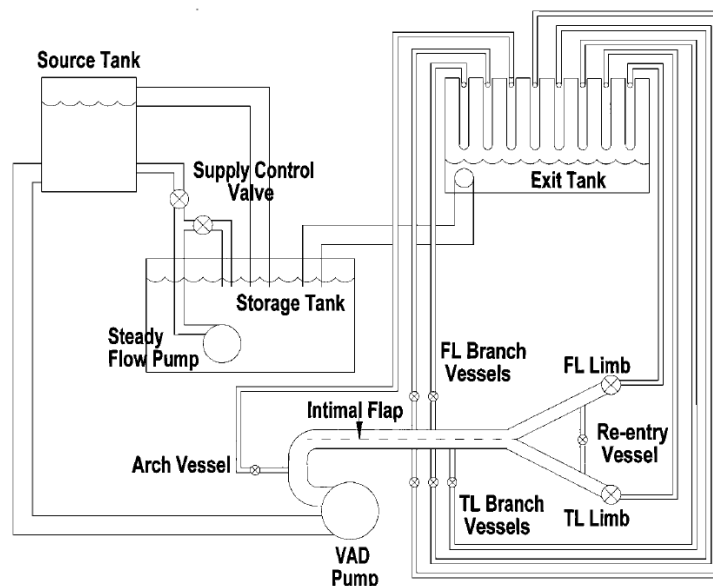


Figure 2.12: The schematic diagram shows the pulsatile flow apparatus. FL = false lumen, TL = true lumen, VAD = Ventricular assist device (Chung et al. 2000).

Two models of type B aortic dissection were placed within the flow loop: one was a compliant and opaque model (Figure 2.13(a)); and the other was rigid and transparent (Figure 2.13(b)) to allow observation of flap movement and to test the effects of the fenestrations. As can be seen in Figure 2.13, both models included an arch to turn the flow as it went to the primary entry tear, a dissected aortic body made of vascular graft material, branch vessels from false and true lumen, and a bifurcation with a re-entry branch to allow communications between the two lumens. In the compliant model, the tube for the aortic body was a 66×5 cm bicycle tire inner tube with a 32 mm internal diameter at 70 mm Hg of pressure and the true lumen was made of 10 mm internal diameter polytetrafluoroethylene (PTFE) dilated to 32 mm diameter. The true lumen extended into the arch bend at the proximal segment with a primary entry tear, and stretched distally through the aortic bifurcation. The flow from each lumen exited through the exit tube of each limb tube below the bifurcation. Being different from the compliant model, the aortic body was an acrylic tube with a length of 40 cm and an internal diameter of 32 mm in the rigid model. Pressure taps were installed in the proximal lumen and distal part to the exit branches to monitor the pressure. Fenestration branch loops were also incorporated into the model to allow the fluid exchange between the true and false lumen mimicking the artificial fenestrations treatment in human body. With the two models, the morphology of the true lumen and the branch-flow compromise situation were observed by Chung et al. based on a large number of pump settings and model configuration. The pump parameters, flow distributions and peripheral resistance in the branch vessels, phantom compliance, entry-tear size, and flow communications between the true and false lumen were investigated in either both models or one of them.

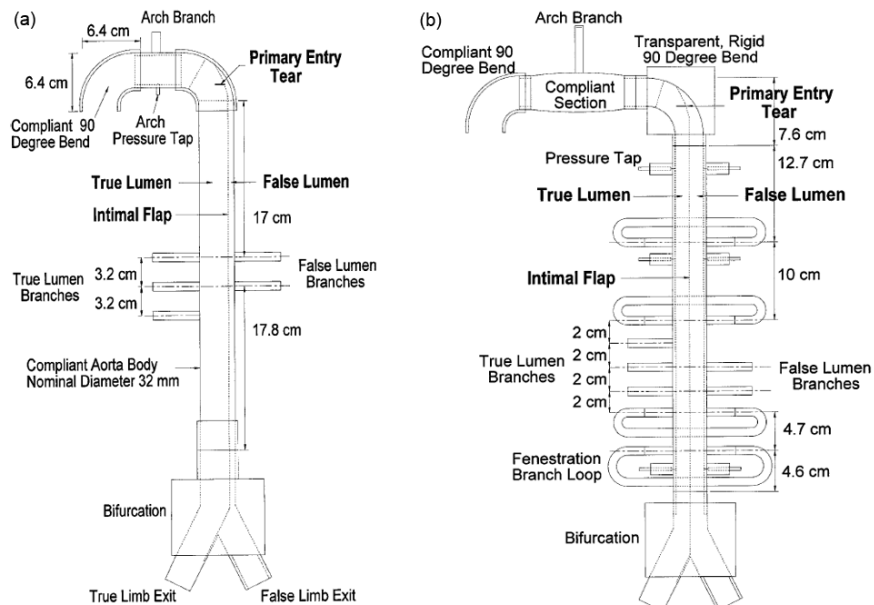


Figure 2.13: The schematic diagram of (a) the compliant, opaque phantom, and (b) the rigid, transparent phantom (Chung et al. 2000).

In the experimental studies, true lumen collapse was demonstrated in the aortic dissection phantoms with pulsatile flow. The situation could be exacerbated by an increase in the size of the proximal entry tear. The difference between the ratios of the inflow and outflow capacity significantly affected the presence or absence of true lumen collapse: a decrease in false lumen outflow and increase in true lumen outflow can cause collapse of true lumen. The collapse also happened with low pump output and low outflow resistance from the true lumen and with converse situation from the false lumen. The distal re-entry communications presented a notable effect in preventing true lumen collapse whereas little impact of fenestrations was demonstrated (Chung et al. 2000). Based on the same flow circuit system, another study was also performed to discover and evaluate the treatment methods for true lumen collapse in models of aortic dissection (Chung et al. 2000 Part II). It was suggested that direct repair of the entry tear to decrease false lumen inflow was the most efficient treatment to prevent true lumen collapse, whereas distal fenestrations and increased false lumen outflow were less effective alternatives.

A more recent experimental study of Stanford type B aortic dissection was implemented by IRAD in 2008. The purpose of the study was to investigate pressure changes within the false lumen, and its relationship with the anatomic changes in tear size, tear number, and tear location in a phantom model of chronic aortic dissection. A flow circuit (shown in Figure 2.14(a)) was built with five main components including a pulsatile pump, and

aortic arch, the compliant dissection model, a compliance chamber with two resistance clamps, and a collecting system. The working fluid in the circuit was Doppler Test Fluid at 37°C to mimic the physical properties of human blood. The stroke volume was maintained at 60 ml/stroke with a fixed diastolic/systolic phase ratio of 60/40 in the system, and the systemic pressure was varied from 93/44 mm Hg to 198/171 mm Hg. The heart beat ranged between 40 and 80 beats per minute, determining the corresponding flow rate and peripheral resistance. As seen in Figure 2.14(b), the glass arch is connected to the dissection part with a proximal “windkessel” latex tube to divert the flow. The dissection part was made of polydimethylsiloxane (PDMS) to mimic the material properties of a human aorta with similar tensile strength. The length of the dissection part was 340 mm, and the aortic diameter was 40 mm. Different thickness of the flap and the wall of true and false lumen were utilized that the dissection flap thickness was 2 mm, false lumen wall was 1 mm and true lumen was 3 mm (Tsai et al. 2008).

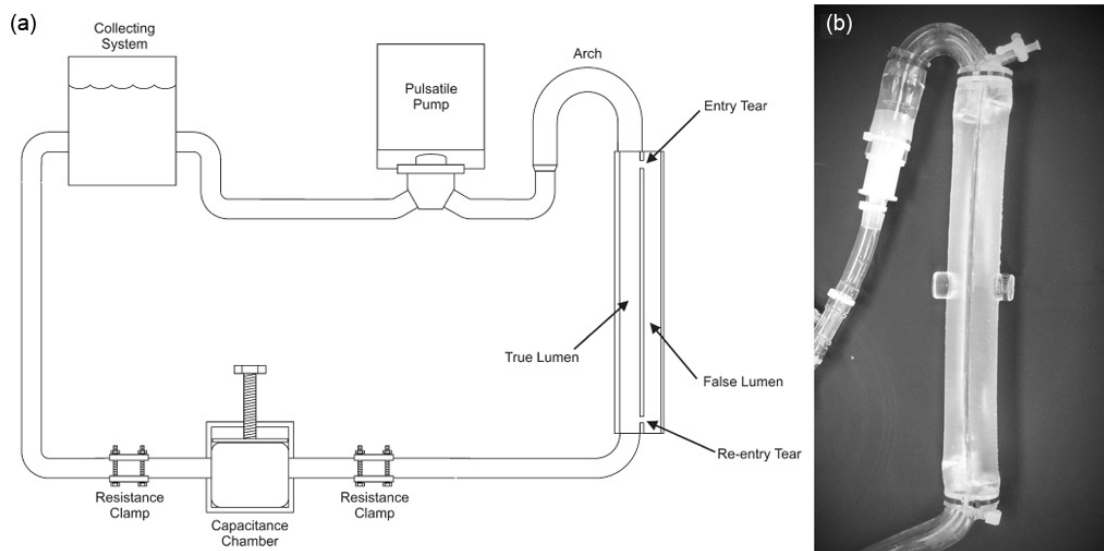


Figure 2.14: (a) The schematic diagram of ex-vivo circulation with a dissection model; and (b) photograph of the dissection model (Tsai et al. 2008).

The dissection flap was located at the middle of the dissection tube to mimic a chronic type B aortic dissection with 50% of the circumference dissected. Holes in the flap were used to mimic the proximal entry tear and distal re-entry tear. A diameter of 6.4 mm or 3.2 mm was regarded as the common size of real human tears. In order to investigate the haemodynamic consequences of tear size, location, and patent false lumen, Tsai et al. conducted three dissection models, based on the configurations (shown in Figure 2.15) presenting the most common situations in type B aortic dissection, with different tear

diameters in the experimental study. Model A presented the most common haemodynamic state in chronic dissection with patent false lumen. Model B and C are relative rare situations simulating partial thrombus in the false lumen and post stent graft state, respectively.

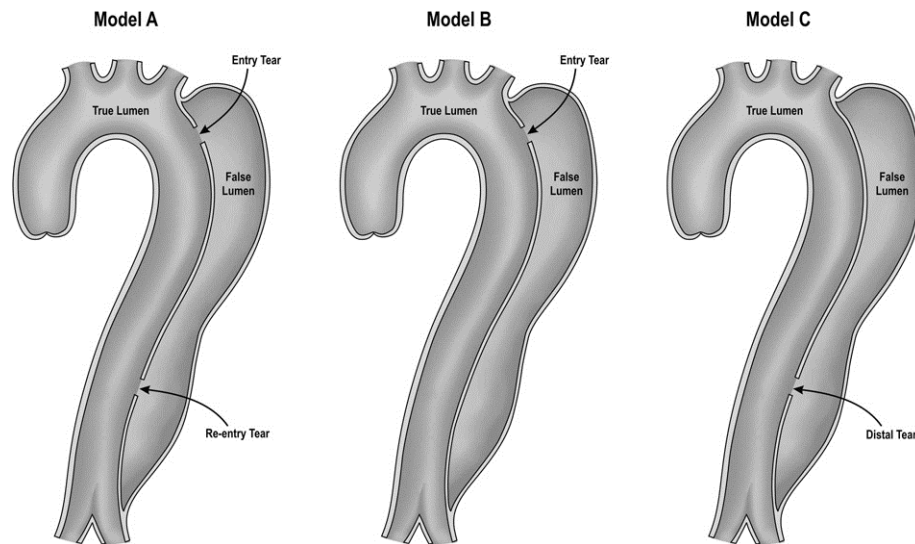


Figure 2.15: Dissection model configurations. From left to right: model A with proximal and distal tear, model B with proximal tear only, and model C with distal tear only (Tsai et al. 2008).

Tsai et al. measured the pressure in both true and false lumen of each model, and found the false lumen had slightly lower systolic pressure and higher diastolic pressure compared with the true lumen in model A. Elevated diastolic pressure was found in the false lumen of both model B and C. The size of tear, as well as the heart rate, was also found to affect the pressure in the false lumen. Smaller proximal tear size and the lack of distal tear could potentially increase the diastolic pressure in false lumen in the chronic type B aortic dissection. These determinants of inflow and outflow were suggested to be possibly associated with false lumen expansion and rupture.

Another experimental study concerning aortic dissection was conducted by Sommer et al. (2008) to investigate the dissection properties of human aortic media. In this study, the direct tension and peeling tests were carried out demonstrating the strength and dissection propagation of the media. Histological images at different peeling stages were analysed to explore the development of irreversible microscopic changes during medial dissection. Extremely higher resisting force/width was demonstrated from the axial peeling tests, indicating the anisotropic dissection propagation of the human aortic media. The axial direction peeling could lead to a significant “rougher” dissection surface

when compared to the surface created by circumferential direction peeling. The histological analysis also revealed that the tissue dissection damage can spread over several elastic laminae which form a pronounced cohesive zone for about 15-18% of the thickness on the dissection surface.

2.5 Summary

Detail review of the human circulatory system as well as the pathology and aetiology of aortic dissection reveal that the development and degeneration of aortic dissection is a complex multifactorial event. The Previous studies demonstrate the correlation between haemodynamic factors, such as wall shear stress, disturbance and geometric factors, and the initiation and development of other aortic diseases. However, no systemic analysis of the effect of haemodynamic factors in aortic dissection has been found so far. Technologies of computational fluid dynamic and biomechanical analysis have been widely adopted in studying the blood flow and haemodynamic environment in normal and diseased aorta. Combined with current medical imaging modalities, the detail analysis of blood flow in dissected aorta could be carried out. The remaining chapters will introduce details of this study.

Chapter 3

Materials and Methodology

3.1 Introduction

In this chapter, a detailed description of the materials and methodology employed in this study is given. Information on medical images including CT and phase contrast MR data is described first. This is followed by the procedure designed to create the patient-specific models: the former are generated from CT images. The details of computational modelling, including the flow models, boundary conditions, and simulation settings, are given in the third section. Finally, analysis procedure of simulation results is described.

3.2 Medical data

Medical data, especially medical images, are essential for clinically relevant flow simulations by providing patient-specific anatomy and/or flow information. Two types of medical images are used in this study for different purposes: contrast-enhanced CT images and phase contrast MR image. High resolution CT images contain detailed morphological information about the dissected aorta, thus, are ideally suited for creating the aorta geometry. Phase contrast MR, on the other hand, can provide flow information in the aorta of individual patient for personalised flow simulations.

3.2.1 CT images

As described in the previous chapter, CT imaging is the most widely used diagnostic technique for aortic dissection because of its high sensitivity and rapid scan process. All of the CT images adopted in this study were acquired over the last six years using the

16-slice Philips Mx8000 IDT CT scanner in the Radiology Department at St. Mary's Hospital, London.

The CT data were carefully selected from a large database according to the requirements for the geometry generation of dissected aorta. For type B aortic dissection, as the dissection can propagate from the aortic arch to the iliac arteries below the bifurcation, a whole body trunk CT scan is required to cover the anatomy of the entire aorta. High in-plane and axial resolutions are also important for the geometry reconstruction, as the anatomic structure of dissected aorta is generally very complicated and the tear size can be quite small in some cases. Four essential anatomic features should be identified from the CT images clearly: the entry tear, the flap, the true and false lumen. Figure 3.1 is a typical cross-sectional CT image of a dissected aorta, which was adopted in the study. From this image, the lumen area, the flap, and the proximal tear site where the blood enters the false lumen from the true lumen can be easily distinguished.

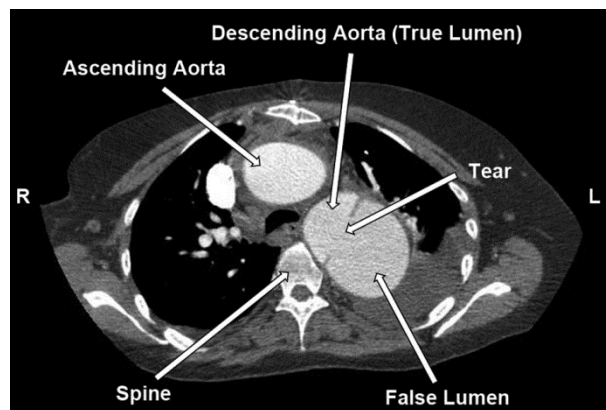


Figure 3.1: A cross-sectional CT image with arrows indicating the tear between true and false lumen, the ascending aorta, and the spine.

Scan parameters of CT images include slice thickness, inter-slice distance, pixel spacing, the volume of investigation, reconstruction matrix, to name only a few. The slice thickness, pixel spacing, and the inter-slice distance are the most important parameters that affect the accuracy of geometry reconstruction. The slice thickness is determined in the centre of the field of view as the full width at half maximum of the sensitivity, and the inter-slice distance is defined as the distance between adjacent cross-sectional images (Chadwick & Lam 2010). It is believed that thinner and more closely approximated cross-sectional CT images can provide more and better information by identifying small objects and increasing the spatial resolution. The pixel spacing is the size of a pixel in the CT images presenting the spatial resolution of the 2D plane. In general, the smaller the pixel spacing, the greater the spatial resolution. Besides, the

volume of investigation is the whole volume of the scan region determining the number of CT images of one CT series, and the reconstruction matrix is defined as the array of rows and columns of pixels in the cross-sectional CT images. For the CT data utilised in this study, the scan parameters of each series of images are not identical. The values and ranges of the key parameters of the CT images are listed in Table 3.1.

Table 3.1: Summary of the scan parameters of CT images used in the study.

Scan parameters	Values or ranges among different series
Slice thickness (mm)	1.5 – 2
Inter-slice distance (mm)	-1 *
Pixel spacing (mm)	0.54 – 0.78
Volume of investigation (slices)	425 – 617
Resolution matrix (pixels)	512 × 512

*-1 for overlapping scan in helical CT meaning the inter-slice distance is 1 mm here.

3.2.2 Phase contrast MR imaging protocol

Phase contrast MRI is able to provide robust images with three-directional velocities at each pixel in the volume. Although it is not practical to use it as an initial diagnostic imaging method due to the relatively long scanning duration and availability, phase contrast MRI is suggested to be an efficient tool for assessment of chronic aortic dissection in follow-up period by monitoring the flow sufficiency and lumen patency of the aortic dissection. In order to obtain patient-specific flow information for the fluid simulations of aortic dissection, 3D phase contrast MR images are adopted. The images were acquired by using a Philips MR system from the MRI department of Hammersmith Hospital.

Due to the complex geometry structure of aortic dissection, three imaging planes, instead of one for general scan, are required in order to acquire a full picture of the flow information in dissected aorta. The locations of the three imaging planes are indicated in Figure 3.2 with blue markers. Each plane was chosen to be perpendicular to the main direction of local flow as accurately as possible. Plane 1 is located in the ascending aorta usually at the level of the pulmonary bifurcation, and above the aortic valve with sufficient distance to avoid the effect of possible valve disease on the flow measurement. Plane 2 is the most difficult plane to be properly placed in the dissected aorta. The purpose of this plane is to measure the flow rate going to the dissection part, as well as the flow profile before the tear site. It is required to locate above the proximal entry tear

but after the left subclavian artery. The proximal entry tear may be very close to the root of the left subclavian artery in some dissection cases, causing difficulties for the prescription of plane 2 in velocity imaging. Plane 3 is preferred in the middle section of the descending aorta where both the true and false lumens are present. This plane is prescribed to acquire the flow distribution in the lumens and the flow direction as well. Usually plane 3 is located at the level of diaphragm for convenience. In addition to the three planes described above, a fourth plane may be required in some cases where the true and false lumens are merged before the iliac bifurcation. This imaging plane needs to be positioned in the downstream part of the descending aorta after the merging site of the two lumens and before the bifurcation.

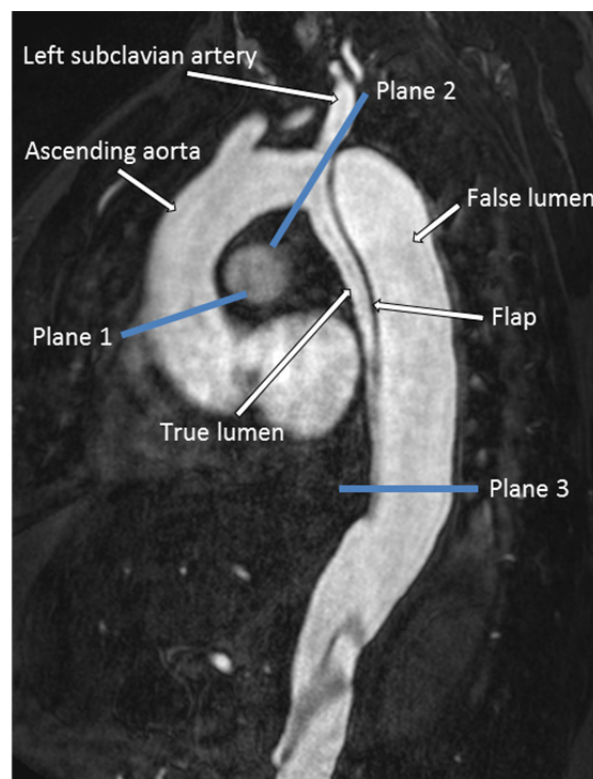


Figure 3.2: The locations of three imaging planes marked with blue lines in a coronal image of type B dissection patient: Plane 1 at the ascending aorta, Plane 2 at the aortic arch after the left subclavian artery and prior to the proximal entry tear, and Plane 3 at the descending aorta where true and false lumen are both present. The ascending aorta, true and false lumen, and the flap are also indicated with arrows.

For 3D phase contrast MR imaging, three velocity components can be obtained at each imaging plane: foot to head (FH) direction, anterior to posterior (AP) direction, and right to left (RL) direction (as shown in Figure 3.3). Each imaging plane has three series of images which include the three directions' velocity encoding images and the correspondent magnitude images. The magnitude images contain the anatomic

information of the aorta from which the region of aorta and other tissues can be identified. To extract flow information from the phase images, the area of interest should be selected from the magnitude images first. Then the position and shape of the area will be projected on to the phase images to guide the extraction of flow information, thus, excluding the noise and signal from the other tissues. The velocity encoding images are acquired at multiple time points in the cardiac cycle. Certain number of time points would be required to ensure the peak and other important phases of flow waveform are not omitted. Through a series of tests on a MR phantom under pulsatile flow mimicking cardiac cycles with different numbers of acquisition time points, 29 points were proved sufficient for this study.

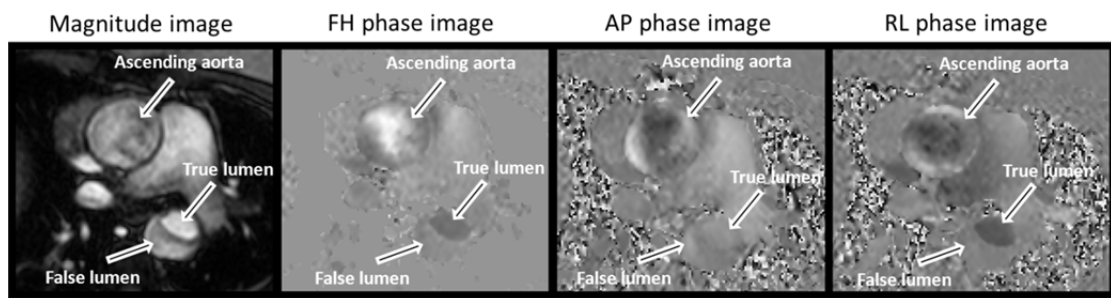


Figure 3.3: The 3D phase contrast MR images including series of magnitude images, and velocity encoding images in three directions. The ascending aorta, true lumen, and false lumen are indicated with arrows.

Besides the location of imaging plane and number of time points, phase contrast MR imaging has a few other important parameters. Velocity encoding V_{enc} , which has been defined in Chapter 2, is one of the most important parameters. As described previously, the closer the V_{enc} to the real peak velocity, the more accurate the velocity measurement results. Hence, for 3D phase contrast MR imaging, different values of V_{enc} are applied to different directions, as the magnitude of velocity varies significantly. For example, in the ascending aorta, the velocity in the FH direction can reach up to or even above 150 cm/s, whereas velocities in the AP and RL directions are usually below 100 cm/s. Also, for different imaging planes, as the main flow direction changes, specific V_{enc} needs to be set carefully for each plane. The FH direction velocity usually dominates in the ascending and descending aorta, whereas the flow velocity in the aortic arch is usually the largest in AP direction. For accurate flow measurements, the sequence may need to be repeated for more than once to adjust the value of V_{enc} . Small values of repetition time (TR) and echo time (TE) can improve the temporal resolution and image quality, and make the measurement less sensitive to motion artifacts and turbulent flow,

but they also reduce the signal-to-noise ratio (SNR) of the measurement. Hence, it is necessary to increase the echo time in some cases to avoid excessive noise in the images. Proper slice thickness should be chosen to balance partial volume effects and good signal-to-noise ratio in the magnitude images. The ranges of TR, TE, and slice thickness are determined by the MR imaging unit. The choice of field of view and matrix is closely related to the anatomy of imaging target. The sequence and all the important parameters used for the phase contrast flow measurement are listed in Table 3.2.

Table 3.2: Sequence and parameters used for phase contrast flow imaging

Parameters	Philips Intera 1.5T*
Reconstructed frames per cardiac cycle	29
Velocity encoding V_{enc} (cm/sec)	100 - 200 [§]
Slice thickness (mm)	8
Repetition time (msec)	4.8 [†]
Echo time (msec)	2.6 [†]
Flip angle (degree)	15
Pixel spacing (mm)	1.3

* Philips Medical Systems with 1.5 T field strength.

§ 200 cm/sec for the main direction velocity, and 100 or 150 cm/sec for the other directions.

† Minimum values are used for all measurements.

3.3 Model generation

Two groups of models are utilized in the study for different purposes: patient-specific models. The patient-specific models are utilized to investigate the flow patterns, morphological factors, and haemodynamic features in real patients' aorta geometry.

3.3.1 Patient-specific models

Patient-specific models are based on CT images which contain the anatomic information of dissected aorta. CT images are regarded as the gold standard for geometry reconstruction of patient-specific models of aortic dissection. Figure 3.4 presents the model generation process from raw CT images to the simulation including two important steps: model geometry reconstruction and mesh generation. CT images were firstly processed by medical imaging processing methods to segment the target area from each of the 2D CT slices. The segmented and smoothed 2D shapes were subsequently stacked up to construct the 3D geometry of the target. After geometry

reconstruction, the surface data of the geometry was exported into the computational mesh generation package ANSYS ICEM CFD where unstructured computational meshing was created. Image processing and geometry reconstruction were mostly accomplished by using a commercial medical image processing package Mimics (Materialise HQ, Leuven, Belgium). The package affords a set of powerful functions including segmentation, measurements, smoothing, and reconstruction. Here, the methods employed in imaging processing and reconstruction are introduced.

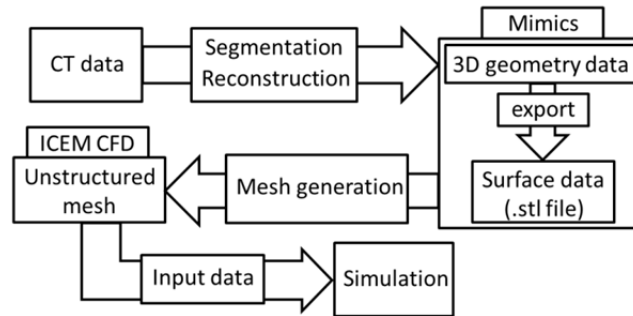


Figure 3.4: Flow chart of the process from raw images to flow simulation.

3.3.1.1 Image segmentation

Threshold: The raw CT data consist of a set of slices with 512×512 pixels in the 16-bit grayscale. All the slices are stored in the format of DICOM (Digital Image and Communication in Medicine) which is a standard format for handling, storing, printing and transmitting information in medical imaging. A single DICOM image consists of two parts: a header file and an image storage part. The header file includes a network communications protocol for images exchanging between different systems, and a file format definition containing the detailed information of the patient, the parameters of image, and the image data storage format. The image storage part stores a series of numbers each of which corresponds to a pixel in the CT image (shown in Figure 3.5(a)). Each number is a grayscale from which the pixel can present a shade of grey colour. The values of grayscale range between 0 and 255 with 0 for pure black and 255 for pure white. For a computer, a digital image is a matrix of these numbers allowing a visual image to be created on the screen. The process of thresholding was accomplished based on grayscale intensities, which were used to create a first definition of the segmentation target. A window of grayscale values was firstly selected based on the grayscale of the target area; then all the pixels whose grayscales were within the selected range were masked in a uniform colour (shown in Fig 3.5(b)). In this study, the lumen of aorta which was the target area is always a bright region. This is because of the principle of

the CT scanning. Different tissues are characterised by different levels of attenuation, hence tissues which have a patently different attenuation from the surrounding tissues can be easily distinguished. In CT images, bone usually has the highest level of attenuation, and displays as the brightest region. The flowing blood also makes the vessel lumen appear bright. When a proper grayscale window was chosen to cover the area of the aorta, it was unavoidable to include other regions which are within the same range as the target area, as well as some floating pixels introduced by noise.

Region Growing: The region growing algorithm was utilized to distinguish the target area from all the regions masked in the threshold step. Firstly, all the masked pixels were regarded as object pixels, and an initial seed pixel was designated in the segmentation object, the lumen area. Then, a set of points within a certain distance from the seed pixel, were searched to see if they were object pixels. For 2D image segmentation, only the closest 8 pixels around the seed pixel were searched for at one time, namely eight-neighbourhood algorithm (Fig 3.5(c)). Each masked pixel in the neighbourhood was regarded as a new seed pixel, and the eight-neighbourhood algorithm was repeated for every new seed pixel until there was no masked pixel within the eight-neighbourhood of all the seed pixels. Others were regarded as scattered pixels and erased from the mask (Fig 3.5(d)). Due to the presence of noise, sometimes manual editing was needed to ensure the accuracy of segmentation.

Morphological Filter: The grayscale of the pixels within the lumen area is not unique, and even vary considerably between pixels. The various grayscale in same tissues may be caused by motion noise and artifacts which occur in CT scanning process. These noise and artifacts could be abated by using filtering algorithms in image post-processing, but cannot be completely eliminated. When we chose a grayscale window to segment the region of interest, a clear contour of the region was the most concerned. Hence, it is unavoidable that the segmented mask was honeycombed with holes as shown in Figure 3.5(d). In order to get rid of the holes, a set of morphological filters were applied on the mask. All morphological filters are based on two basic operations: dilation and erosion. They are defined in the following way. Objects A and B are defined as $A(m, n)$ and $B(p, q)$ for two accidental sets of points in discrete two-dimensional spaces: $\{(m, n)\}$ and $\{(p, q)\}$. The operation dilation is defined as follows:

$$D(A, B)(r, s) = \max_{(j, k) \in B} (A(r - j, s - k) + B(j, k)) \quad (3.1)$$

Operation erosion is defined as:

$$E(A,B)(r,s) = \max_{(j,k) \in B} (A(r+j, s+k) - B(j,k)) \quad (3.2)$$

In this study, A in the above expressions was called the segmented mask, and B the structuring elements. The close filter is utilized here which consists of a dilation action followed by an erosion action and expressed as

$$Close = E(D(A,B), A) \quad (3.3)$$

The radius of the structuring element, which is the number of neighbourhood pixels around each pixel of the mask, varies from 1 to 3 pixels in each direction depending on the size of the holes. The larger the radius, the stronger the effect of the filter.

Smoothing: The Discrete Gaussian filter was applied for mask smoothing, which has become extremely popular in image processing. Its wide application has to do with certain properties of the Gaussian filter, such as the central limit theorem and minimum space-bandwidth product, as well as several application areas such as edge finding and scale space analysis.

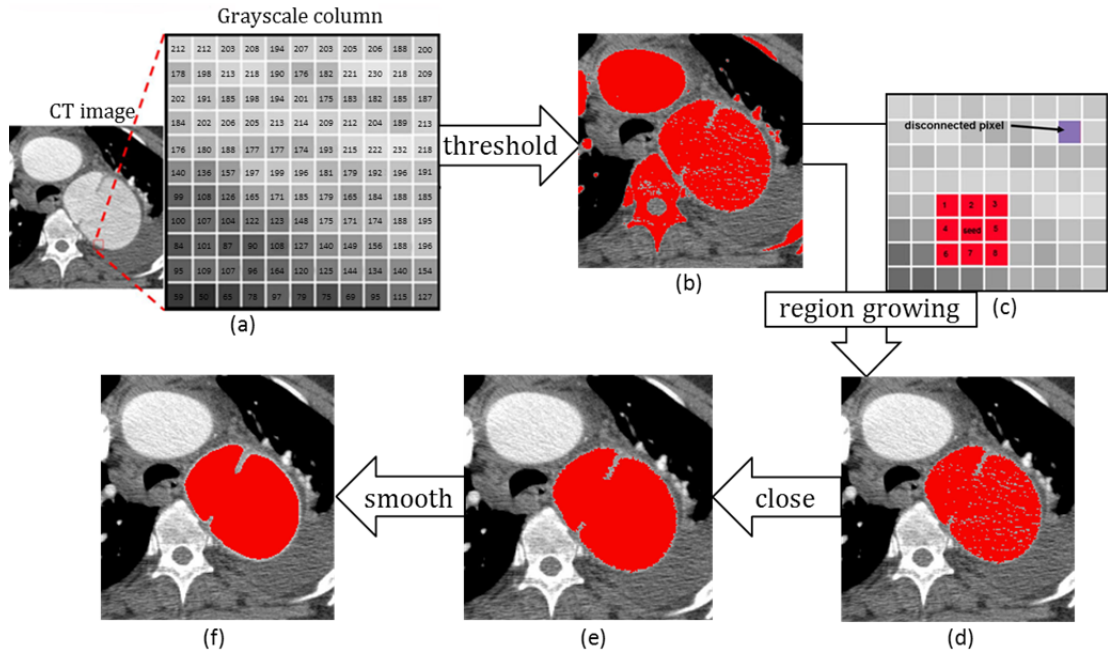


Figure 3.5: Representation of the steps involved in imaging processing with (a) grayscale column picture of the raw CT image, and (b)-(f) the processed pictures after each step.

As the primary focus of this study is the flow behaviour in dissected aorta, especially the thoracic descending aorta including the true and false lumen, the three aortic arch branches and other small branches in the descending aorta were excluded during the

geometry reconstruction process. This was also due to the lack of information on flow through the aortic arch branches. The method adopted to compensate for the flow losses in the branches will be explained in the modelling section.

3.3.1.2 3D geometry reconstruction

Surface Rendering: The surface rendering technology, which is the most common technology in display of medical images, was used in lumen 3D reconstruction. Surface rendering involves outlining the contours of the anatomical structures from the masks of 2D images and forming a 3D surface with triangle grids (see Figure 3.6(a)). Then the surface of these objects could be shown on the screen, and the colour defined in previous steps was applied. It also allowed the lumen and incision surface to be visualized from different angles (Figure 3.6(b)). The advantages of surface rendering are precisely identification of small objects and fast rendering speed. But the surface rendering result cannot provide information about points within the 3D object. In this study, only the geometry of the aortic lumen was concerned, hence the surface rendering method is appropriate for the reconstruction of aortic lumen.

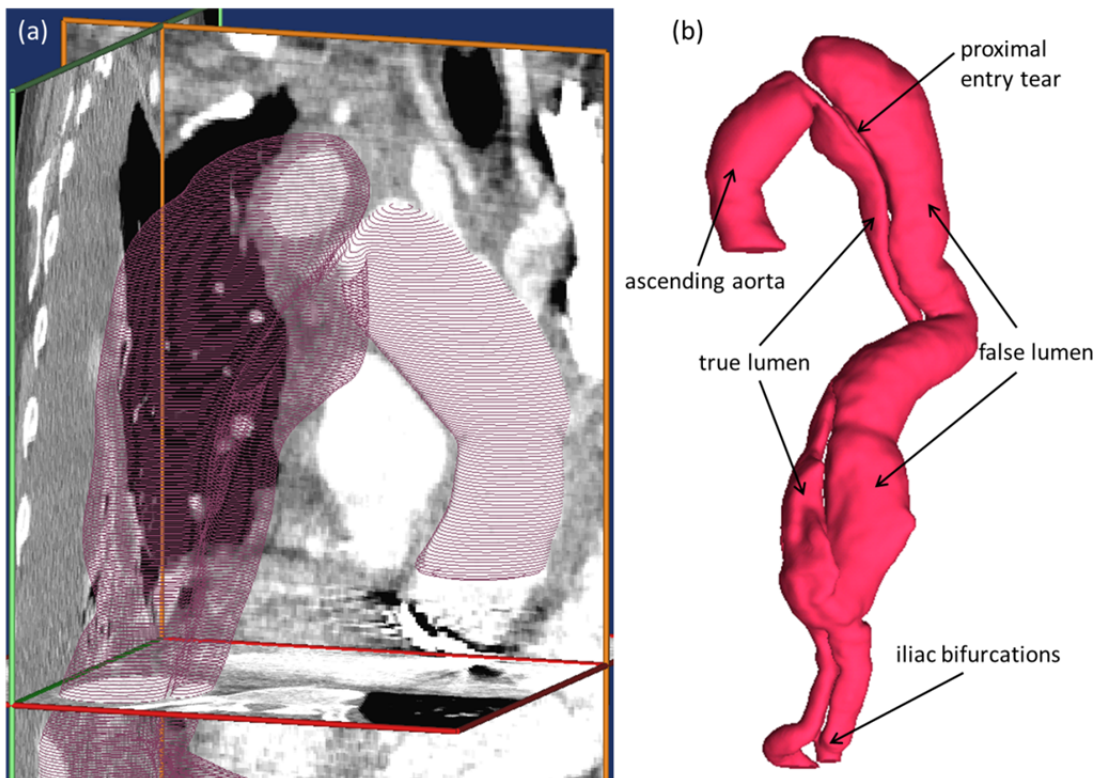


Figure 3.6: (a) The polylines for the aorta lumen area from each CT slice stacked up to form the 3D aorta geometry; (b) The reconstructed geometry of the whole dissected

aorta with arrows indicating the ascending aorta, proximal entry tear, true and false lumen, and iliac bifurcations.

3D Smoothing and Geometry Validation: Although the lumen contours were processed by Gaussian filter, smoothing of the 3D surface reconstructed from CT data is still necessary as the smoothing process on each isolated 2D image is not adequate for good continuity of the 3D geometry reconstruction. A cubic spline algorithm is commonly used to smooth the serial values of segmented areas by expanding or contracting the area while keeping the shape of the contour. Usually, this smoothing procedure is repeated for more than once to obtain a nice smoothed geometry. The more iteration times the smoothing procedure is performed, the smoother the geometry surface becomes. However, a large number of iterations could cause deviation of the smoothed geometry from its original shape. Hence, a balance must be achieved between the smooth factor and geometric authenticity. In this study, cross-sectional contours were calculated at the level of each CT slice, and were then mapped back to the raw CT images to check whether the contours well presented the edges of the aorta lumen.

3.3.2 Mesh generation

The reconstructed aorta geometry was subsequently imported to the computational mesh generation software, ANSYS ICEM CFD, for meshing. Due to the complex geometric structure of the dissected aorta, unstructured mesh was utilized in the patient-specific model of dissection with a combination of several prism layers near the boundary wall and tetrahedral elements in the core region (see Figure 3.7 (a)). The prismatic layer was extruded from the boundary wall by specifying the height of the first layer nearest to the wall, as well as the height ratio and numbers of layers, under the exponential growth law of increasing height. The thin prism layer near the wall ensures a very fine resolution within the boundary layer. The most complex part of the geometry is the region around the tear, which usually has a narrow edge and irregular shape, and also endures velocity acceleration and complex flow pattern. Outcome of the flow simulation can be very sensitive to the mesh in this region. Hence, an entity bound was created in the geometry, wrapping the tear region with a locally refined mesh as compared to the global mesh, to ensure adequate mesh resolution in this region (as shown in Figure 3.7(b)).

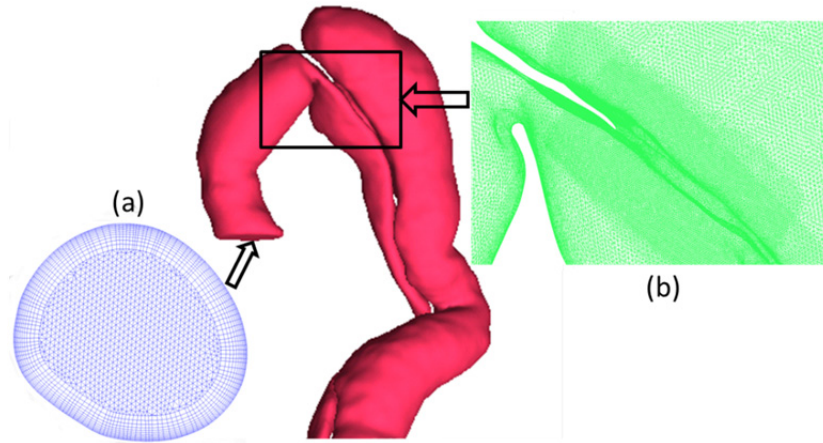


Figure 3.7: (a) A cross sectional view of the inlet of a type B dissection model presenting unstructured mesh with a 12-layer prism mesh and tetrahedral element in the inner blocks, and (b) locally refined mesh near the proximal entry tear.

As the aortic dissection model covers the whole aorta from the ascending aorta to the iliac bifurcations, the large volume of the geometry meant a large mesh size for flow simulations. The number of mesh elements ranged from 2.5 million to more than 5 million according to the volume of the model. Mesh sensitivity test was carried out for each of the dissection models to ensure the simulation results were independent of the mesh. Specific mesh sensitivity test procedures are described in the result chapters.

3.4 Computational modelling

After the geometry of the dissected aorta was meshed, the model was ready for computational flow analysis. All the flow simulations in this study were implemented in ANSYS CFX 12 (ANSYS Inc, Canonsburg, PA). Before starting each simulation, the flow model needs to be specified to define the governing equations for the fluid motion, and the boundary conditions and initial conditions. Numerical methods were subsequently used to solve the equations with defined convergence criteria. After the simulation was finished, the results were analysed and visualized.

3.4.1 Flow models

The geometric structure of the aortic dissection models is extremely complex and tortuous with various geometric features including narrowing, expansion, bending, bifurcation, and especially the presence of tear between two lumens. These geometric features have been proved to induce abnormal haemodynamics and complex flow patterns with secondary motions (Taylor et al. 1998; Caro et al. 1996; Suo et al. 2007; Meng et al. 2007). The convergent-divergent geometries have been found to increase the

likelihood of transition to turbulent flow (Giddens et al. 1976). Blood flow in the ascending aorta, aortic arch, and descending aorta has been demonstrated to be helical and retrograde with local recirculating vortex by phase contrast MR imaging (Kilner et al. 1993; Gatehouse et al. 2008). Some studies have also reported complex flow patterns in dissected aorta from 3D phase contrast MRI (Gate et al. 2008; Pitcher et al. 2011). Moreover, the Reynolds number in dissected aorta is sufficiently high to warrant consideration for possible presence of transition or even turbulence flow. The Reynolds number, which is defined as the ratio of inertial-to-viscous forces in a flow, is the most important dimensionless parameter for flow conditions. It indicates that when the inertial stresses in a flow become sufficiently large compared with the viscous stresses that laminar flow breaks down to a transitional state and even further to a turbulent regime (Wood 1999). The critical Reynolds number, below which the flow remains laminar, was suggested as approximately 2300 (Warhaft 1997). According to the geometry dimension and flow waveform, the Reynolds number varies from 2500 to 3600 at the inlet of the dissection models involved in this study, and could go up to more than 8200 at peak systole in local region of the model domain due to flow acceleration at the tear. Hence, combined with flow pulsation during a cardiac cycle, it is reasonable to assume that flow in type B aortic dissections is likely to be transitional or turbulent, at least during part of a cardiac cycle, leading to our decision to apply a turbulence model in this study.

To account for possible turbulence behaviour, a correlation-based transitional version of Menter's hybrid $k - \varepsilon / k - \omega$ shear stress transport (SST Tran) model (Menter et al. 2006) was adopted in this study. The SST Tran model combines the original $k - \omega$ model of Wilcox in the inner region of the boundary layer and the standard $k - \varepsilon$ model (Wilcox 2006), in the outer region and in free shear flows, together with two additional transport equations, intermittency, and transition momentum thickness Reynolds number (Menter et al. 2004; 2006). The transport equation for the intermittency is used to trigger transition locally, and to turn on the production term of the turbulent kinetic energy downstream of the transition point. The other transport equation, solved in terms of the transition onset momentum-thickness Reynolds number is used to capture the nonlocal influence of the turbulence intensity, which changes according to the decay of the turbulence kinetic energy in the freestream and the changes in the freestream velocity outside the boundary layer (Menter et al. 2006). The additional transport equation is the essential part of the transition model as it ties the empirical correlation to the onset criteria in the intermittency equation and enables the models applicable in

general geometries without interaction from the user (Menter et al. 2006). The proposed transport equations in the model do not attempt to model the physics of the transition process like other turbulence models, but form a framework for the implementation of correlation-based models into general-purpose CFD methods (Menter et al. 2006). This transition model has been proved to be compatible with modern CFD methods using unstructured mesh and massive parallel execution.

This SST Tran model has been evaluated for physiological flows under two different conditions. First, it was applied to an axisymmetric stenosis model, and a good agreement with published experimental data for pulsatile flow in the model was found (Tan et al. 2008). A further investigation was carried out to simulate flow in a patient-specific thoracic aortic aneurysm (Tan et al. 2009). The velocity profiles obtained from the SST Tran model was demonstrated to agree very well with the velocity data acquired in vivo using phase contrast MRI from the same patients. Moreover, the agreement is better than those given by either a laminar simulation or the shear stress transport (SST) model alone. Hence, the SST Tran model was considered as a better flow model for complex flows in aortic dissections as compared to the laminar flow simulation, and was employed in the flow study of all the patient-specific models.

3.4.2 Boundary conditions

The boundary conditions required for the aortic dissection models include velocity or pressure at all boundaries of the model: the inlet, the outlet, and the wall. Different types of boundary conditions are afforded by ANSYS CFX-Pre 12 including velocity, pressure, and mass flow, to name only a few. The choice of boundary conditions depends on available flow information and model design. Proper boundary conditions are essential for achieving physically correct results from flow simulations.

Inlet boundary condition

In this study, the inlet of the patient-specific dissection models was located at the root of the ascending aorta above the aortic valve. Pulsatile velocity waveforms were applied to the inlet boundary of each model based on information derived from phase contrast MR images. A flat through-plane profile was assumed to allow the flow to develop naturally in the ascending aorta before reaching the region of interest. It is assumed that there is no secondary motion at the model inlet, which is at the root of the ascending aorta, due to the lack of patient-specific flow information. This assumption is unlikely to have a

significant effect on flow patterns in the distal aorta where the region of interest is in this study, which has been further justified by the validation case presented in Chapter 6.

The phase contrast MR images cannot give the velocity value directly. Hence, a self-developed programme was utilized to convert the image data to velocity values. The programme was developed by using the Matlab programming language. Figure 3.8 presents the steps followed for flow information extraction from phase contrast MR images. First, the two series of phase contrast MR images, magnitude images and phase images were read and displayed separately. The aortic lumen was segmented from the magnitude image to obtain the contour of the lumen. A manual segmentation process was performed by abstracting landmark pixels at the lumen outline which can be easily identified from the magnitude image. The *cscvn* function was utilized to generate a parametric cubic spline curve based on the selected pixels. The contour was subsequently projected onto the corresponding phase image obtained at the same time point to define the aorta lumen area. Meantime, several important image parameters were extracted from the header file for velocity calculation. The equation, which converts image grayscale to velocity magnitude, depends on the velocity encoding system of the MR scanner. The equation for the phase contrast MR images utilized in this study (generated by Philips Medical Systems) is described as

$$V_{pc} = \frac{V_{enc} \times (I - (I_{max} - I_{min})) \times 10}{I_{max} - I_{min}} \quad (3.4)$$

where V_{pc} is the velocity value at the chosen pixel, V_{enc} is the encoding velocity given in centimetre per second, I is the grayscale of the pixel, I_{max} and I_{min} are the maximum and minimum grayscale values of the phase image, respectively. Based on the velocity value at each pixel, pixel spacing, and the aortic lumen area, the total flow rate and mean velocity at the inlet can be calculated. This self-developed programme was validated by comparing the obtained results with those obtained from the commercial processing package within the Philips MR system. The maximum difference between the two results observed from the test was less than 1%.

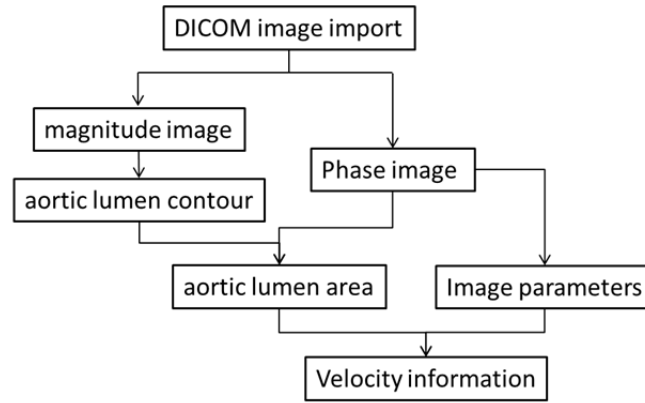


Figure 3.10: The flow chart of the Matlab programme for flow information extraction from phase contrast MR images.

For an easier and quicker implementation of the velocity transferring process, a graphical user interface (GUI) (as shown in Figure 3.9) was designed. The buttons on the interface were encoded with the functions of image importing, region segmentation, velocity calculation, and profile display, as the button name described. The list box (a) and (b) display the name of the imported magnitude and phase images, respectively, in the order of scanning time. List box (c) shows all the parameters of phase contrast image, and those needed for velocity calculation are automatically extracted. The inspector window (e) and (f) display the magnitude and phase images respectively, corresponding to the chosen files in (a) and (b). Lumen segmentation can be directly implemented in window (e), and the created contour is projected to the phase image in window (f) simultaneously. Velocity calculation can be done by pressing one button, and the flow rate and mean velocity would be shown in window (d) and saved for flow waveform construction. The spatial velocity profile is also generated automatically. The designed programme interface can increase the efficiency of image processing, and both the self-developed programme and the GUI worked well with the MR images in this study.

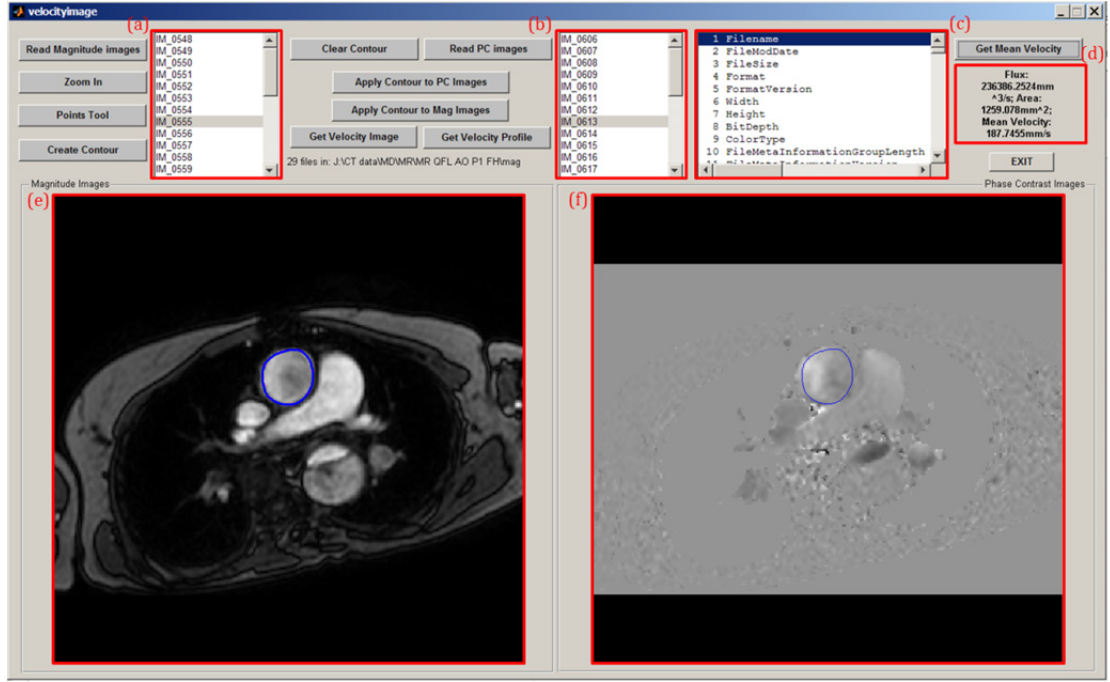


Figure 3.11: The graphical user interface developed for extraction of velocity values from phase-contrast MR images. The toolbox and windows (a)-(f) present the list of imported images, the image parameters, the calculated velocity results, magnitude images, and phase contrast images, respectively.

The velocity waveforms were transferred to a Fourier sum of harmonic components by using the Fast Fourier Transform (FFT) algorithm. The harmonic pulsatile velocity waveforms were applied at the inlet as boundary conditions for flow simulation, expressed as:

$$w(t) = A_0 + \sum_{n=1}^N A_n \cos\left(\frac{2\pi}{T} nt\right) + \sum_{n=1}^N B_n \sin\left(\frac{2\pi}{T} nt\right) \quad (3.5)$$

where A_0 is the mean velocity over a cardiac cycle, A_n and B_n are the Fourier coefficients of the $\cos$ and $\sin$ term respectively, T is one cardiac cycle duration, and N is the degree of the trigonometric polynomials. The two coefficients, A_n and B_n , were determined from the velocity value acquired from phase contrast MR images. In this study, Fourier series of 20 degrees was used, which has been tested and proved to give a good approximation of the velocity waveform.

An inlet turbulence level was required to represent initial disturbances in the flow and allow transition to occur realistically. A low inlet turbulence intensity (defined as the ratio of the root-mean-square of the turbulent velocity fluctuations to the mean velocity) of 1.5% was chosen, since previous in vivo studies of canine aorta showed the presence

of low level laminar disturbances pre-transition (Nerem et al. 1972; Giddens et al. 1976), and the same level was also found to be appropriate for a human thoracic aortic aneurysm (Tan et al. 2008).

Outlet boundary condition

The location of the outlet boundaries in the patient-specific models was determined based on the geometric characteristics of each model. The proximal entry tear of type B aortic dissection usually occurs in the thoracic descending aorta within a small distance from the root of the left subclavian artery, however, the distal re-entry tear which allows the blood in the false lumen to flow back into the true lumen can arise at any location downstream from the proximal entry tear. For those distal re-entry tears occurring before the iliac bifurcation, the model outlets were selected at a location where the true and false lumens were confluent. While for those with a false lumen propagating down below the bifurcation and re-entry tear in the iliac arteries, the outlets were specified at the distal end of the descending aorta just above the iliac bifurcation, which were far away from the proximal tear, thus minimising the effect of outlet boundary conditions on the simulation. For this group of models, two outlets were present with one for each lumen. A sensitivity test of the outlet location was carried out to examine the effect of different outlet locations on flow distribution in two lumens. Five different patient-specific dissection subjects were involved in the test, and each had two models with outlet located in the thoracic aorta and distal descending aorta, respectively. The flow rates in the false lumen were compared between the two models of each subject. Considerable differences were found in some of the subjects as models with a higher outlet location would exclude the influence of downstream descending aorta on the flow, e.g. narrowing and tortuous sections could provide more resistance to blood flow. Hence, the distal outlet boundary was considered as more reasonable and realistic for this study.

The outlet planes were placed perpendicular to the main flow direction. The boundary conditions for the patient-specific models were set as opening with relative static pressure of 0 Pa normal to the outlet plane. While it appears to be unrealistic, it is a reasonable approximation for a rigid wall model provided that the outlet is sufficiently far from the region of interest (see Steinman et al. 2003). The pressures at the outlets of the two lumens were assumed to be the same according to the results of the experimental study from IRAD (Tsai et al. 2007). It was indicated that, in the type B dissection models with a patent false lumen (in the presence of both proximal entry tear

and distal re-entry tear), the pressure values in the true and false lumen were comparable with a very small difference. For scalar quantities like turbulence, zero gradient condition was set at the outlets.

Wall boundary

The wall of the patient-specific model was assumed to be rigid with no displacement. The motion of intimal flap and aortic wall in type B aortic dissection was investigated by using dynamic, ECG-gated CT imaging technique in vivo (Ganten et al. 2009). A remarkable reduction of aortic distensibility in aortic dissection was observed when compared to healthy subjects, which suggested a general loss of vessel wall elasticity in dissected aortic segments. The flap motion, although could cause up to 29% narrowing of the true lumen in some case, was reported with an average narrowing of only 4.4%. A number of reasons have brought difficulties to incorporate wall compliance in the patient-specific models. One is the mechanical properties of the dissected wall: in a dissection aorta, neither the true nor the false lumen is bounded by a complete wall. The intimal tear splits the layers of the aortic wall so that part of the true lumen shares the intima (containing endothelial cells and a subendothelial layer) and media with the inner side of the false lumen, whereas the outer wall of the false lumen comprises mainly of adventitia. The heterogeneous mechanical models required for different parts of the dissected aorta wall are currently unclear. Also, aortic dissection patients may have varying degrees of dissection in the media layer, which could cause different compositions of media tissue in the intimal flap and outbound layer of the false lumen, thus leading to specific mechanical property for each subject. Another difficulty is the identification of intimal flap and aortic wall from general CT images. The similar density of wall, thrombus and other tissue around the aorta makes it impossible to accurately acquire the geometry of the dissected aorta wall. Hence, in this study, the effect of wall compliance was only considered in hypothetical models, rather than patient-specific models, in order to examine the importance of flap motion in flow in aortic dissection. No-slip conditions were applied on the walls, where the fluid has zero velocity relative to the boundary.

Blood properties

The blood was treated as an incompressible and Newtonian fluid with a dynamic viscosity of 4.0 mPa and a density of 1060 kg/m³ in this study. Although blood does not exhibit a constant viscosity at all flow rate, it is widely accepted that blood behaves in a Newtonian fashion in large arteries (Ku 1997). Previous numerical studies have also

indicated that the influences of shear thinning properties of blood are not significant for flow in large arteries (Perktold et al. 1991; Cho & Kensey 1991). In order to examine the effect of non-Newtonian viscosity of blood in aortic dissection, the Quemada model, which calculates the apparent viscosity based on a minimum energy dissipation analysis (Quemada 1978), was incorporated into the transitional flow model on one model. Comparison with the results of the Newtonian simulation showed a very similar wall shear stress and pressure distribution between the two simulations.

3.4.3 Numerical methods and convergence criteria

All the simulations presented in the thesis were implemented in ANSYS CFX-Solver Manager 12 based on the finite volume method (FVM). FVM is suitable for any type of grid. The governing conservation equations are integrated over the finite control volumes, namely the elements in the mesh, as well as to the whole fluid domain. The computational node is at the centre of each element where the variables are calculated. The values for the edges and surface can be reconstructed by interpolation of the element average. The mesh size and quality was ensured to be sufficiently small and fine to meet the requirement of the transitional turbulence flow model introduced in the next section, and allows achieving well convergence and capturing the flow separation and turbulence in the domain. The shape functions used in ANSYS CFX are linear in terms of parametric coordinates. The spatial and temporal discretisation of the Navier-Stokes equations were performed by a high resolution advection scheme and a second order implicit backward Euler scheme, respectively (Barth & Jespersen 1989; Ferziger & Peric 1999). A general multigrid method based on the additive correction strategy was used to obtain the solution (Hutchinson & Raithby 1986). All simulations were carried out for three cardiac cycles to achieve a periodic solution, and results obtained in the last cycle were used for analysis. One cycle was divided into fixed uniform time steps, which can be independent of the Courant number for implicit temporal discretization. A maximum root-mean-square (RMS) residual of 10^{-6} was specified to ensure the convergence of the solution.

3.5 Analysis of results

The simulation results was analysed using ANSYS CFX-Post 12 and CEI ENSIGHT 8 (Shark Ltd., UK). The most interesting parameters from the results are flow velocity, turbulence intensity (Tu), wall shear stress and its time-integrated parameters, such as the time-averaged wall shear stress (TAWSS) over the cardiac cycle and oscillatory shear index (OSI). The velocity, wall shear stress, turbulence kinetic energy and other

parameters can be obtained from the simulation results directly. The TAWSS, OSI and Tu were calculated in the two post-processing packages based on their definition given below.

$$TAWSS = \frac{1}{T} \int_0^T |\tau_w| dt \quad (3.6)$$

where T is the cycle duration and τ_w is the instantaneous wall shear stress.

$$OSI = \frac{1}{2} \left(1 - \frac{\tau_{mean}}{TAWSS} \right) \quad (3.7)$$

where τ_{mean} is the mean shear stress to express the magnitude of the time-averaged surface traction vector, calculated as

$$\tau_{mean} = \left| \frac{1}{T} \int_0^T \tau_w dt \right| \quad (3.8)$$

Turbulence intensity is defined as

$$Tu = \frac{\sqrt{\frac{2}{3}k}}{V} \quad (3.9)$$

where k is the turbulence kinetic energy and V is the instantaneous local velocity.

The TAWSS and OSI were display by plotting the value onto the wall surface as contours. The Tu was presented by iso-surfaces indicating the corresponding turbulence zone of the specified value at chosen time points along the cardiac cycle. The particle pathlines which show the trajectories of blood flow in the dissection model, as well as flow animations, were generated using CEI ENSIGHT.

3.5.1 Effect of image spatial resolution on wall shear stress

The geometries of the dissected aorta were reconstructed based on in vivo images acquired using a standard CT scanner for clinical examinations. The clinical CT scanner has limited spatial resolution that will inevitably affect the accuracy of the reconstructed aortic geometry, thereby introducing uncertainty in the calculated wall shear stress. Given below is an estimation of errors caused by the limited spatial resolution of the images adopted in this study.

The mean spatial resolution of the CT images used here is 0.66 mm, giving an uncertainty of ± 0.66 mm in the measurement of aortic diameter. The mean diameter of

the aorta in this study is approximately 20 mm. If we assume Poiseuille flow in the aorta, the wall shear stress could be calculated as:

$$\tau = \frac{4\mu Q}{\pi R^3} \quad (3.10)$$

where μ is the viscosity of blood, Q is the volumetric flow rate, and R is the radius of aorta. The means uncertainties in the measurement of aortic dimension will be propagated to the calculation of wall shear stress, and in this case, the error will be amplified owing to the inverse cubic relationship described above. Accounting for the measurement error induced by the imaging resolution, and assuming the measured aorta radius being: $R_1 = R + \Delta R$. Hence, the fractional error in wall shear stress, δ , can be estimated as:

$$\delta = \frac{\Delta\tau}{\tau} = \frac{\tau - \tau_1}{\tau} = 1 - \left(\frac{R}{R + \Delta R}\right)^3 = 18\% \quad (3.11)$$

Note that this estimation does not account for uncertainties introduced in the 3D reconstruction process. It has been shown that luminal surface smoothing is an essential step in model reconstruction from magnetic resonance images, and differences in calculated wall shear stress between a smoothed and unsmoothed carotid bifurcation model would be up to 15% (Moore et al. 1999).

Chapter 4

Patient-specific study I: a multiple cases study

4.1 Introduction

This chapter illuminates a multiple cases cross-sectional study which is concerned with computational fluid dynamics (CFD) analyses of patient-specific models of type B aortic dissection. Here, the focus is blood flow through the aortic lumen, with the aortic wall being assumed to be rigid. This study involved a group of ten patients with classic type B aortic dissections to investigate the general characteristics of flow patterns as well as the role of morphological factors in determining haemodynamic parameters.

Aortic dissection patients usually first come to hospital with symptom of severe pain (Spittell et al. 1993; Slater et al.1976). Once the diagnosis of aortic dissection is suspected on clinical grounds, diagnostic imaging, for which contrast-enhanced CT is by far the most commonly used imaging modality (Hagan et al. 2000), is essential to confirm the diagnosis both promptly and accurately. Based on the images acquired, in addition to confirming diagnosis, a number of anatomical features of the dissection, including its extent, the sites of entry and re-entry tear, the presence and severity of aortic regurgitation, can also be identified. Each patient has unique anatomic characteristics and geometry structure. The CT images of ten patients presenting type B aortic dissection were utilized in this part of the study to reconstruct the dissection models, on which flow simulations were carried out.

4.2 Patients information

A total of ten patients with type B aortic dissections on whom CT scans were performed at initial presentation were selected for flow analysis (see Table 4.1). Each patient was numbered with an initial 'M' (meaning Multiple cases study). All patients had patent false lumens at the time of presentation. Three (M1, M2, M4) were females. All patients

had initial CT scans as part of their routine evaluation and interval follow-up scans for those entering surveillance. Ages of the patients ranged from 43 to 80 years, and initial management was based upon clinical presentation. Two of the patients (M3, M5) were diagnosed as acute complicated type B dissection and underwent urgent thoracic endovascular aortic repair (TEVAR) immediately. Two patients (M7, M8) were acute uncomplicated dissections and were medically treated, and six patients (M1, M2, M4, M6, M9, M10) presented with acute complications of a chronic Type B dissection mandating intervention with TEVAR. Clinical details are given in Table 4.1.

Table 4.1: Patient details for the multiple cases study.

Subjects	Gender	Age*	Operative status	Presentation	Complication	Treatment
M1	F	55	Urgent	Chronic dilatation. Acute transient paraplegia.	Dissected Type B aneurysm	TEVAR, abdominal stent, arch + visceral revascularization
M2	F	80	Elective	Chronic dilatation	TA†	TEVAR
M3	M	55	Emergent	Acute Malperfusion	Limb ischemia	Femoro-femoral cross over graft
M4	F	43	Elective	Chronic dilatation	TA†	TEVAR
M5	M	53	Emergent	Acute Malperfusion	Renal failure	TEVAR
M6	M	80	Emergent	Chronic dilatation + rupture	Dissected Type B aneurysm	TEVAR
M7	M	60	Medical	Uncomplicated Type B	N/A	Medical
M8	M	68	Medical	Uncomplicated Type B	N/A	Medical
M9	M	58	Elective	Chronic dilatation	Arch + TA§	TEVAR, Arch revascularization
M10	M	73	Elective	Chronic dilatation	Arch +TA§	TEVAR

* Age at the time of scan

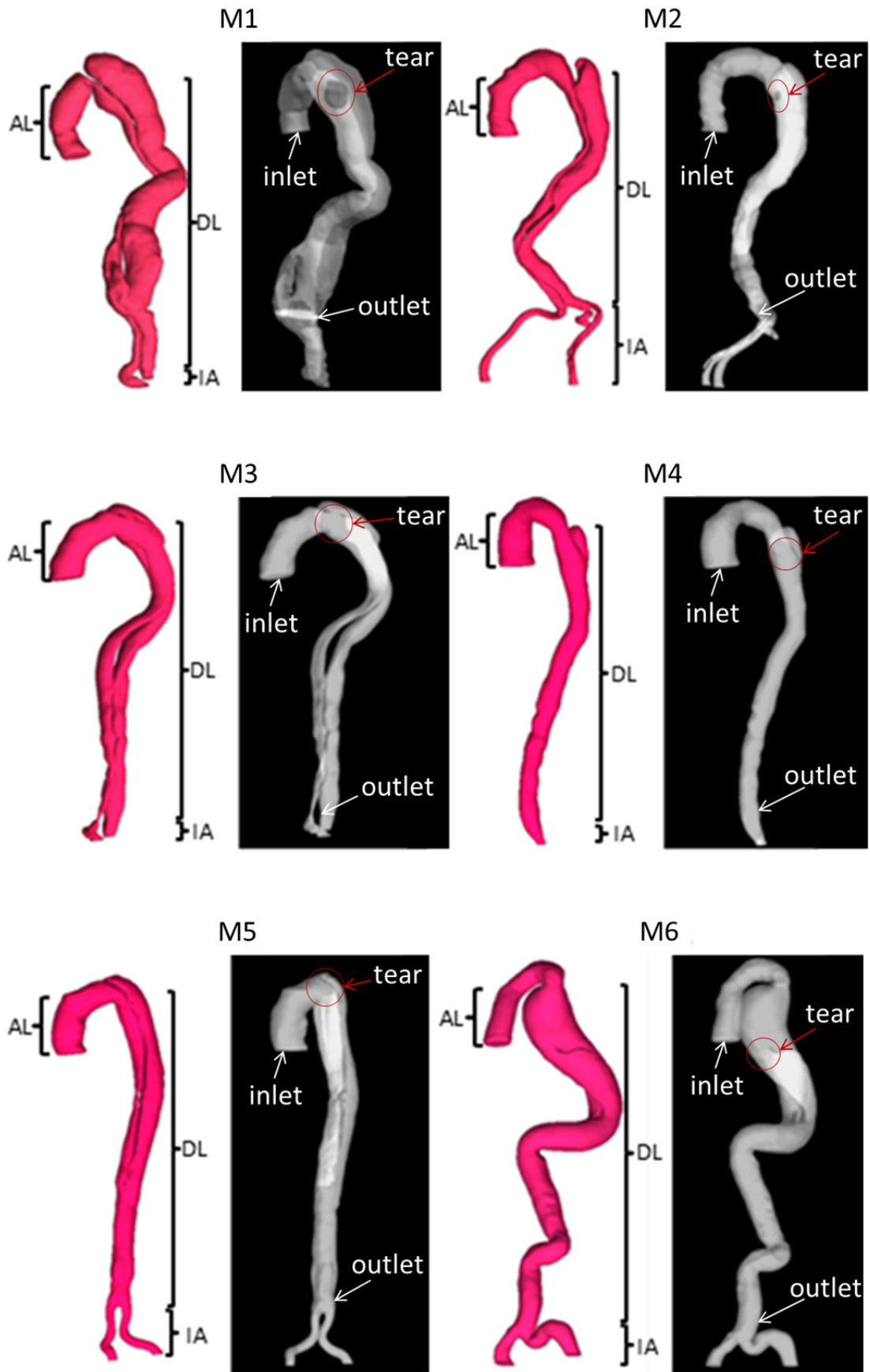
† Stanford type A dissection

§ Stanford type A dissection involving aortic arch

4.3 Patient-specific model generation

The 3D aortic dissection geometries were reconstructed from the initial CT scan images of each patient based on which the patients were firstly diagnosed with type B aortic dissection. The proximal entry tear, the flap between the true and false lumen, as well as the patent false lumen, can be clearly observed from the CT images, thus supporting the diagnosis. In order to examine the extent of the false lumen, all of the CT scans were performed on the whole trunk covering the dissected aorta from ascending to the iliac bifurcation. Contiguous 2-mm-thick slices were used with an interslice distance of 1 mm and an in-plane resolution of less than 1 mm. The segmentation of all images and 3D geometry reconstruction of inner wall surface for each patient was achieved by using an image processing package Mimics (Materialise HQ, Leuven, Belgium). Details of the reconstruction of the aortic lumen are described in Chapter 3.

Figure 4.1 shows the reconstructed aortic dissection geometries of the 10 subjects in both whole-length view and transparent view of the initial tear region. The orientation parameters of whole-length view were defined as right-anterior (R-A). The dissected aorta geometry includes four main sections: the ascending aorta, the aortic arch, the descending aorta, and the iliac arteries. The descending aorta is the most interesting section of the geometry as the type B dissection derives from here. As the primary focus of this study was the flow behavior in the dissected thoracic aortic segment, aortic branches other than the iliac arteries were ignored during the geometry reconstruction process. The transparent view, which is utilized to present the location and shape of the proximal entry tear, is displayed on the right side of the whole-length view of each subject. The locations of inlet, outlet and the proximal entry tear are indicated with arrows in the transparent view. The inlet of the model was located at the ascending aortic root above the aortic valve. The outlet of the model was in the distal descending aorta before the iliac arteries, allowing sufficient length between the outlet and the region of interest. The model was subsequently imported into ANSYS ICEM CFD (ANSYS Inc, Canonsburg, PA) for mesh generation. Unstructured mesh was applied to all of the patient-specific models with a mixture of prismatic and tetrahedral elements.



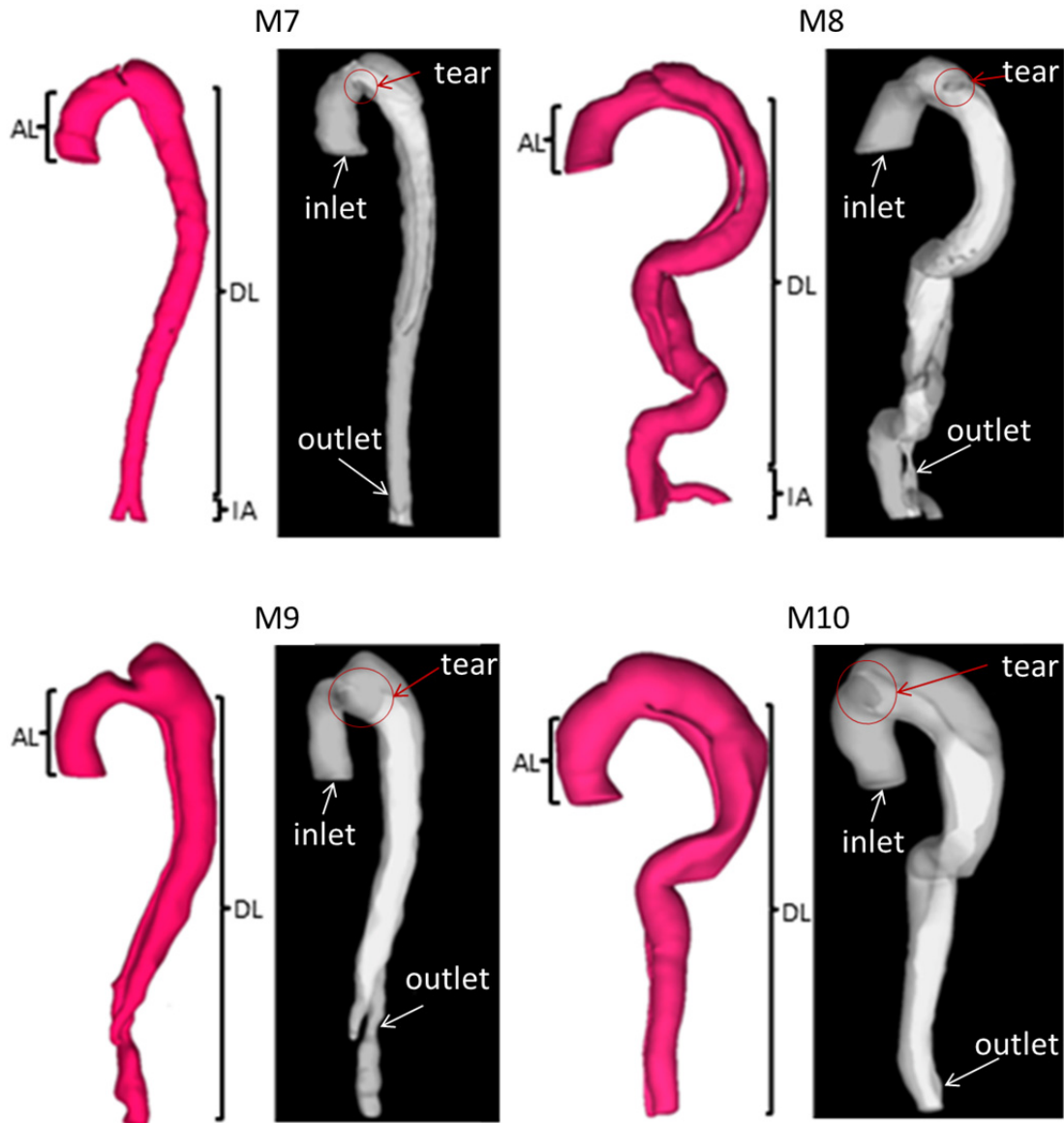


Figure 4.1: Geometrical description of the ten aortic dissection models. Each subject has two pictures: right-anterior view of the reconstructed model (left) and transparent view (right). The ascending aorta lumen (AL), descending aorta lumen (DL) and iliac arteries (IA), as well as the locations of inlet, outlet and primary entry tear, are indicated with arrows. The primary entry tears can be seen clearly from the transparent views.

4.4 Flow simulation

4.4.1 Boundary conditions

With regard to boundary conditions, a flat velocity profile was specified at the model inlet in the ascending aorta, allowing the flow to develop naturally before reaching the region of interest. A time-varying inlet flow rate which is shown in Figure 4.2 was

imposed at the inlet of each subject. The cross-sectional averaged flow rate waveform at the model inlet has a fundamental frequency of 1.25 Hz (pulse period: 0.8 s) and a diastolic/systolic phase ratio of 60:40. The flow rate applied at the inlet of the present model was scaled down about 15% to offset any possible effect caused by removing the branch vessels, by providing a more appropriate flow rate for the descending aorta, since the proportion of the total flow lost through the upper extremities' branches is around 10–15% of the flow in the ascending aorta (Shahcheraghi et al. 2002). The peak flow rate of 345 cm³/s occurred at 0.18 s in a cardiac cycle. Based on different inlet sizes of each subject, flow parameters, such as velocity, Womersley number and Reynolds number, varied from patient to patient. The mean velocity at the inlet varied from 0.1 to 0.204 m/s, Womersley number from 22.2 to 31.9, and Reynolds number from 2500 to 3600 based on the various inlet diameters of the ten subjects. An inlet turbulence level of 1.5% was applied to represent initial disturbances in the flow and allow transition to occur realistically. A constant relative static pressure of 0 Pa was applied to the outlet of each model. The wall boundaries of the models, namely the inner surface of the aortic wall, were assumed as rigid with no-slip condition. The blood was treated as a Newtonian and incompressible fluid with a dynamic viscosity of 4.0 mPa and a density of 1060 kg/m³.

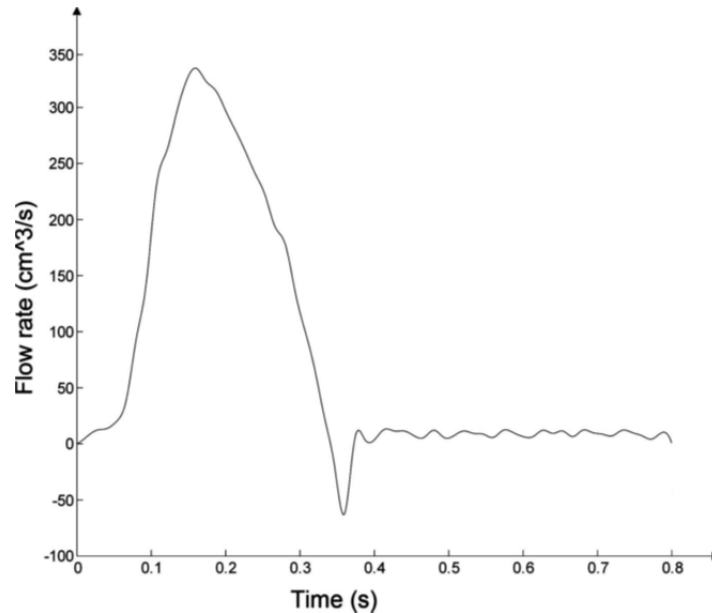


Figure 4.2: Volumetric flow rate used at the inlet of the aortic dissection model.

4.4.2 Mesh sensitivity test

The 3D geometry represented by surface triangles was exported into ICEM CFX for mesh generation. The computational mesh consisted of 3-D tetrahedral cells in the core region

and prismatic cells in the fluid boundary layer at the wall. To satisfy the requirements of the 'low-Reynolds number' turbulence and transition models, a very fine near wall resolution of y^+ (a dimensionless distance perpendicular to the wall, defined by fluid dynamic parameters) of approximately 2 for the prismatic cell adjacent to the wall, and a minimum of 10 grid nodes for the prismatic cells needed to resolve the inner layers of the boundary layer, were ensured. Mesh independence test was carried out on each subject to make sure the results are independent of the element quantity. The initial element size of the mesh for each model started from 1 mm combined with 10 prismatic layers near the boundary wall. Finer mesh was further generated by decreasing the element size and increasing the number of boundary layers. A mesh entity with a maximum element size of 0.5 mm was created at the tear region due to the localized complex geometry structure. The variables including maximum flow velocity, maximum wall shear stress, and turbulence kinetic energy were compared between the meshes, and the differences in each variable were calculated. The mesh was considered as sufficient for the simulation when the differences in the variables were smaller than 5% between the adopted mesh and a much finer mesh. Different mesh sizes were utilized for the dissection models to obtain the final simulation results for analysis. The number of elements varied from 2.8 million to 5.2 million depending on the size and structure of the model geometry.

4.5 Results and discussion

4.5.1 Geometric features

The geometry of aortic dissection models can be very complicated. The false lumen always originates from a tear on the outer curve of the descending aorta and is parallel to the true lumen. It can propagate proximally by extending upward and beyond the top of the arch and distally as far as below the abdominal bifurcation from the primary tear. The propagation of the false lumen oppresses and narrows the true lumen, hence the true lumen is always smaller than the false lumen and localized narrowing commonly occurs. The narrowing of true lumen usually starts from the location of the primary tear and sometimes even before the tear. According to Figure 4.1, the degree of narrowing (shown in Table 4.2) was different from patient to patient. The narrowing scale was calculated as the ratio of the diameter of the narrowed true lumen to the unaffected aorta. It was apparent that the ten subjects presented different patterns of curvature of the dissected aorta. Six subjects (M1, M2, M3, M6, M8 and M10) had highly distorted structure of aorta with an extremely large curvature in the thoracic aorta just after the

primary tear. This large curvature induces a sharp angle at the junction of the thoracic and abdominal aorta, and even more complexities occur in the downstream aorta such as secondary dissection and bending. However, the other four subjects (M4, M5, M7 and M9) have a relatively simple structure as the dissection only caused a mild curvature in the thoracic aorta and doesn't have notable effects on the main trend of the aorta.

Among the ten subjects, M4 and M6 have different geometric patterns from the other eight subjects. Unlike typical shapes of dissected aorta, M4 has an unclear primary tear where the false lumen propagates upward for a short distance and just joins with the true lumen at the tearing site. M6 has the most complicated geometry which has a dilated aorta at the tear site which may propagate from the primary tear. The primary tears in these two subjects are considered to be the cross section of the false lumens.

From the transparent views shown in Figure 4.1, we can see that the shape and dimension of primary tears are quite different among the ten subjects. The shape of the tear is irregular since intimal tear could propagate both longitudinally and circumferentially. The primary tear dimension of the ten subjects ranges from 8 mm to 38.5 mm. The distance of the tear also varies considerably although the primary tears of type B aortic dissection are restricted to the thoracic aorta and after the left subclavian artery. Detailed geometrical parameters are listed in Table 4.2.

Table 4.2: Geometric features of the ten AD models.

Subject	Narrowing Scale †	Primary Tear Dimensions (mm)			Distance of Primary Tear from Arch Top (mm)
		Longitudinal	Circumferential	Ratio *	
M1	16%	37.3	38	0.73	21
M2	50%	13.5	8	0.21	54
M3	57%	33	36	0.93	8
M4	45%	24	20	0.58	45
M5	70%	28.8	19.6	0.82	1.2
M6	51%	15.4	32.4	0.29	99
M7	25%	24	9	0.31	12
M8	55%	18	10.8	0.32	20
M9	66%	38.5	24	0.55	0.6
M10	28%	38.5	35.4	0.88	10

*The ratio of tear diameter to true lumen diameter

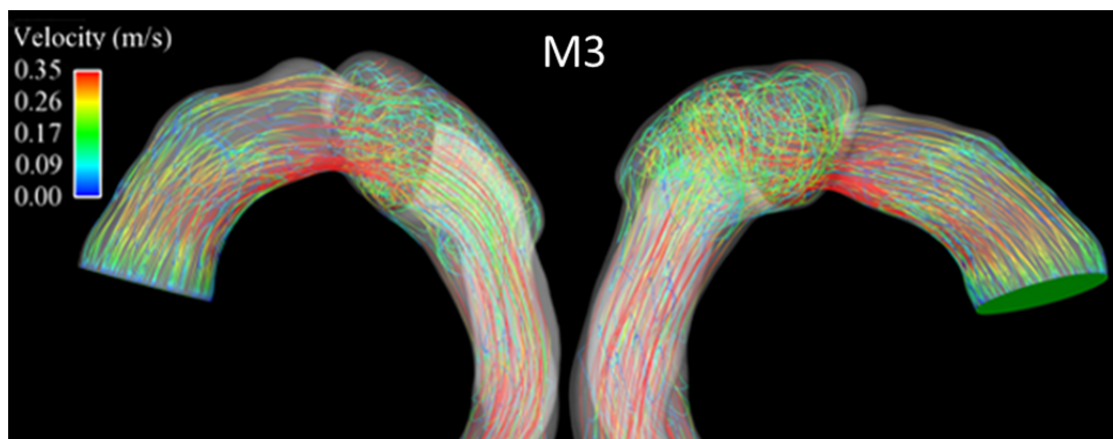
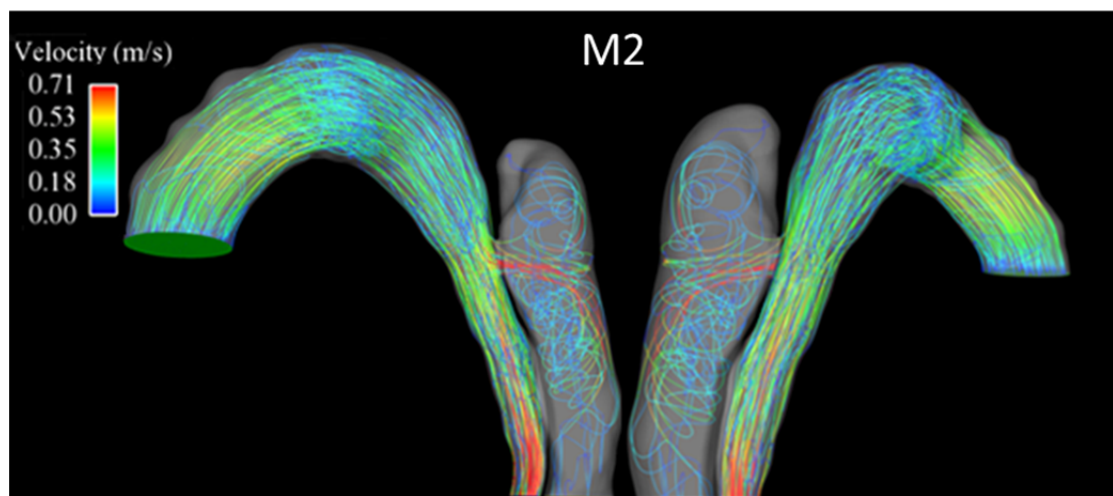
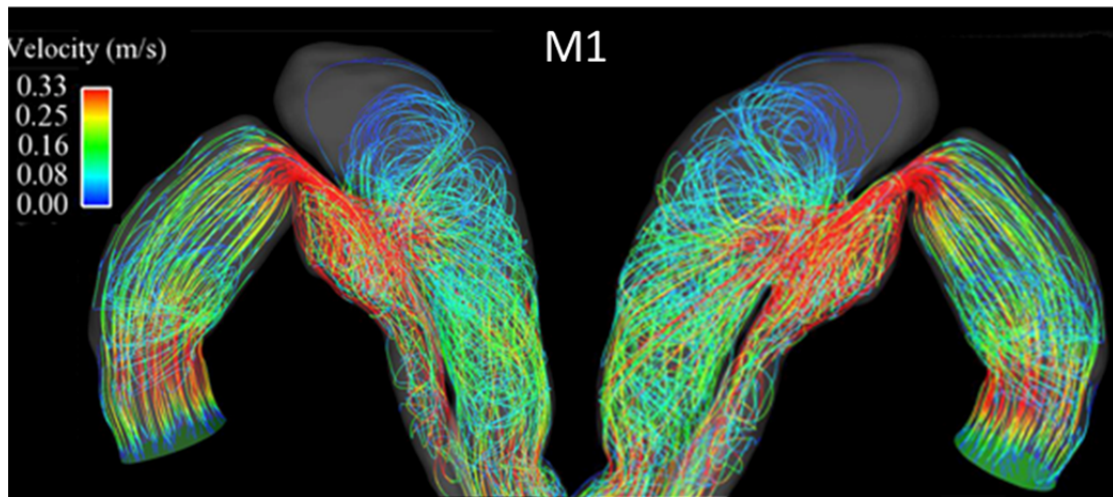
† The ratio of the diameter of the narrowed true lumen to the unaffected aorta

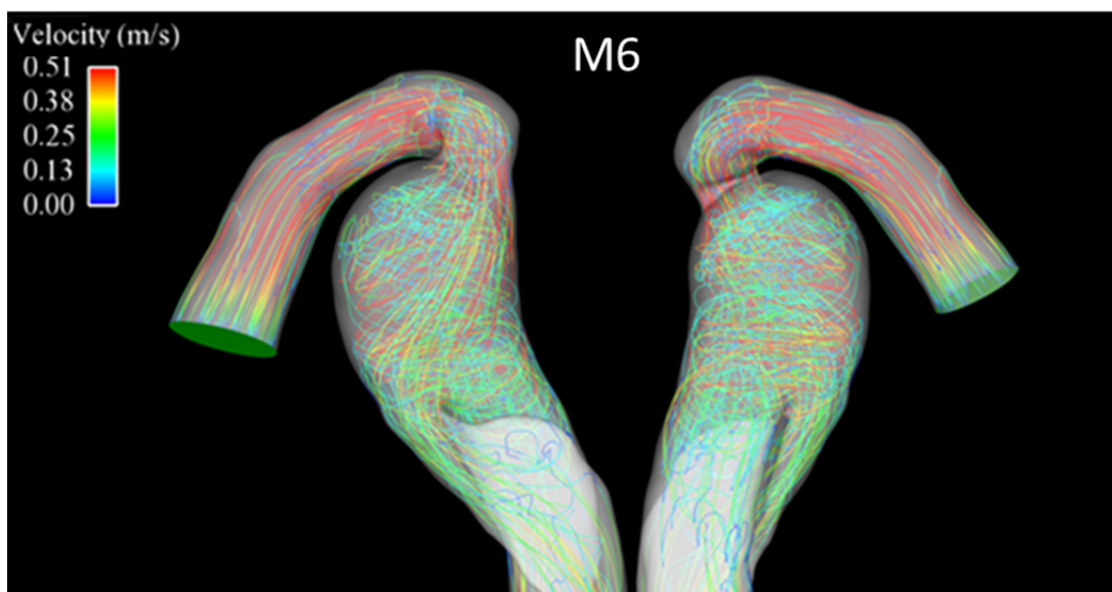
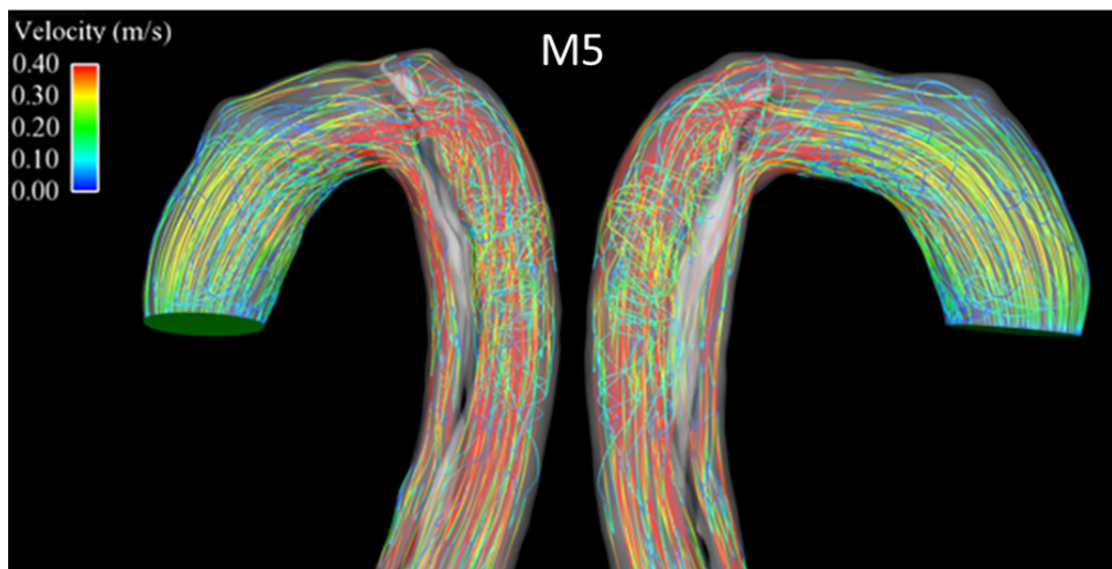
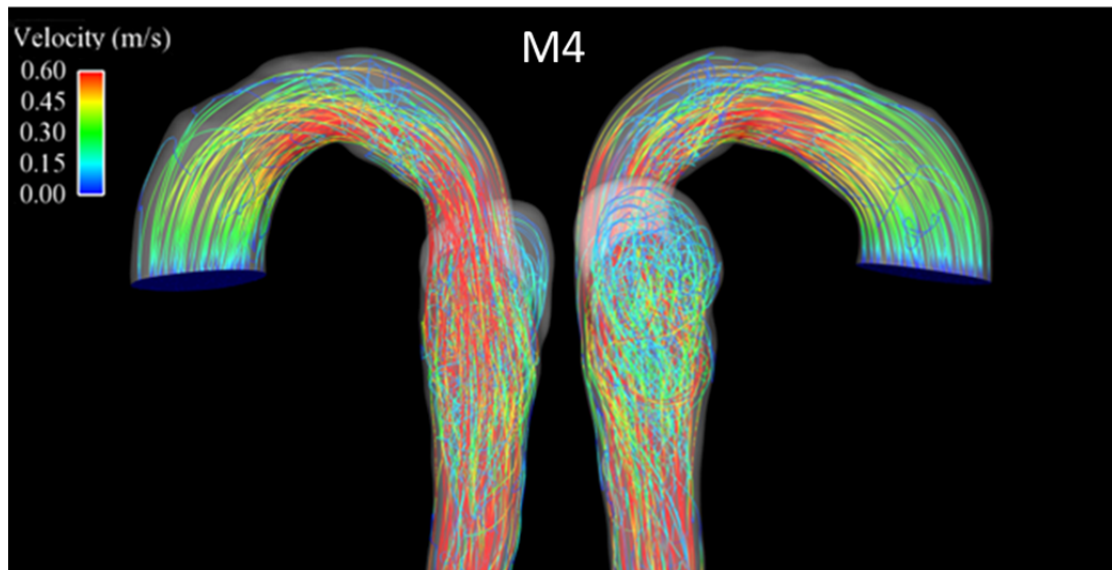
4.5.2 Flow pattern

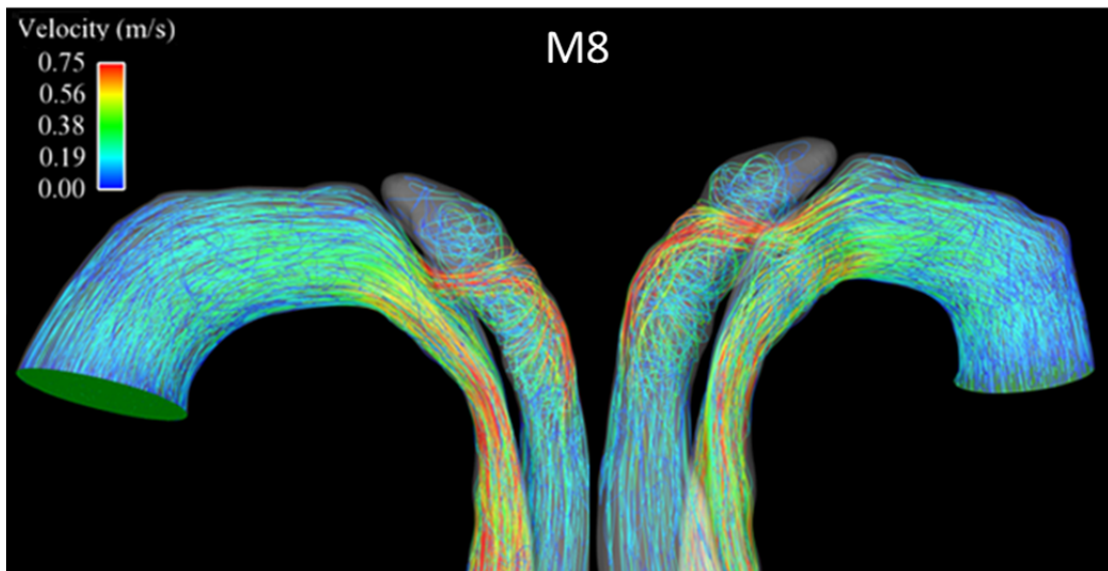
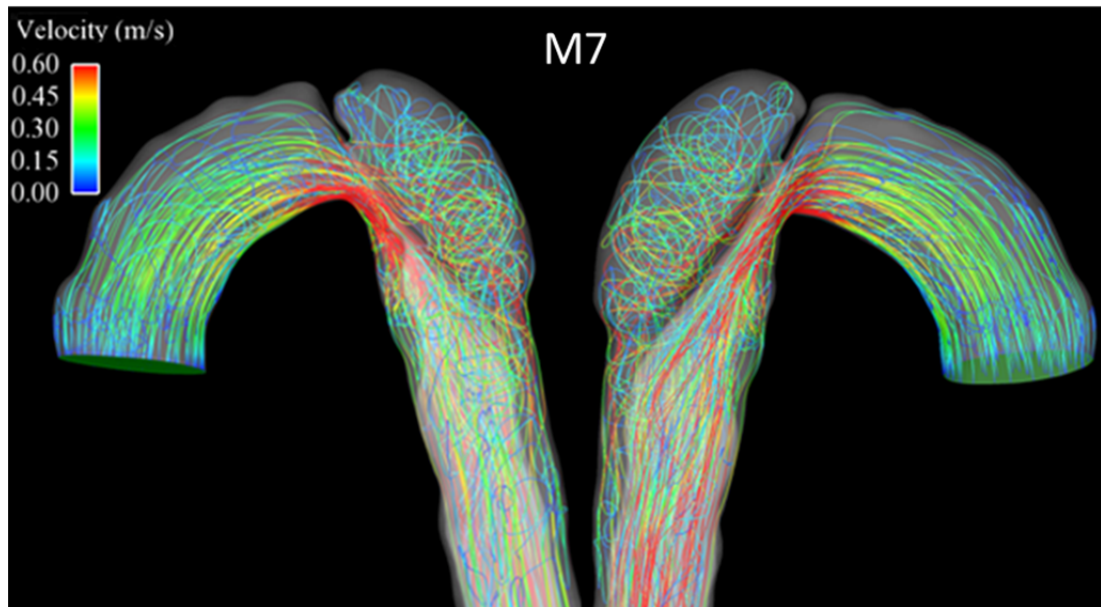
As the region of most interest here is the upper descending aorta, especially the regions surrounding the tear, further analysis of the results in terms of flow patterns, wall shear stress, and turbulence intensity will be focused on this and the neighboring regions, remote from the distal computational boundary.

Geometry plays a key role in determining the nature of hemodynamic patterns. Irregular geometry, including narrowing, bifurcation and dilatation can induce disturbed and turbulent flow, and its effect on arterial flow patterns has been studied by a number of investigators. The blood flow patterns in bends and bifurcations are known to include flow separation and disturbed flow. As seen from Figure 4.1, the geometries of dissected aortas are extremely complicated which always combine various irregular geometric shapes, especially in the upper descending aorta where the primary tear occurs. Figure 4.3 presents the particle pathlines of blood flow in the dissected aortas of the ten subjects over more than 10 cardiac cycles. For each subject, 80 particles were emitted and evenly distributed at the inlet. The color of the paths presents the velocity of blood flow at the corresponding position. Although the flow patterns are not the same among these subjects owing to different geometries, some similar characteristics can be observed. The flow is always fairly organized in the ascending aorta, and accelerates when passing through the narrowed true lumen sections. A certain volume of flow enters the false lumen through the primary tear with high velocity, and impinges on the inner surface of the false lumen opposite to the tear. After that, most of the fluid goes to downstream part of the false lumen. For those subjects (M1, M2, M4, M8 and M10) whose false lumen has propagated upward and forms a cavity above the level of the tear, a small portion of the fluid reaches the superior region of the false lumen with relative low velocities.

Flow in the false lumen is likely to be more complicated with the presence of vortices, retrograde and strong amplification of instability than in the true lumen. Especially for subjects who have relatively large false lumens, the dilated space could result in long residence time of particles in the dissected aorta. For subjects M1, M4, M6, M7 and M9, particles stay in the area of false lumen near the primary tear for more than three cardiac cycles (2.4 s) before continuing along the lumen, while shorter particle residence time is observed in other subjects.







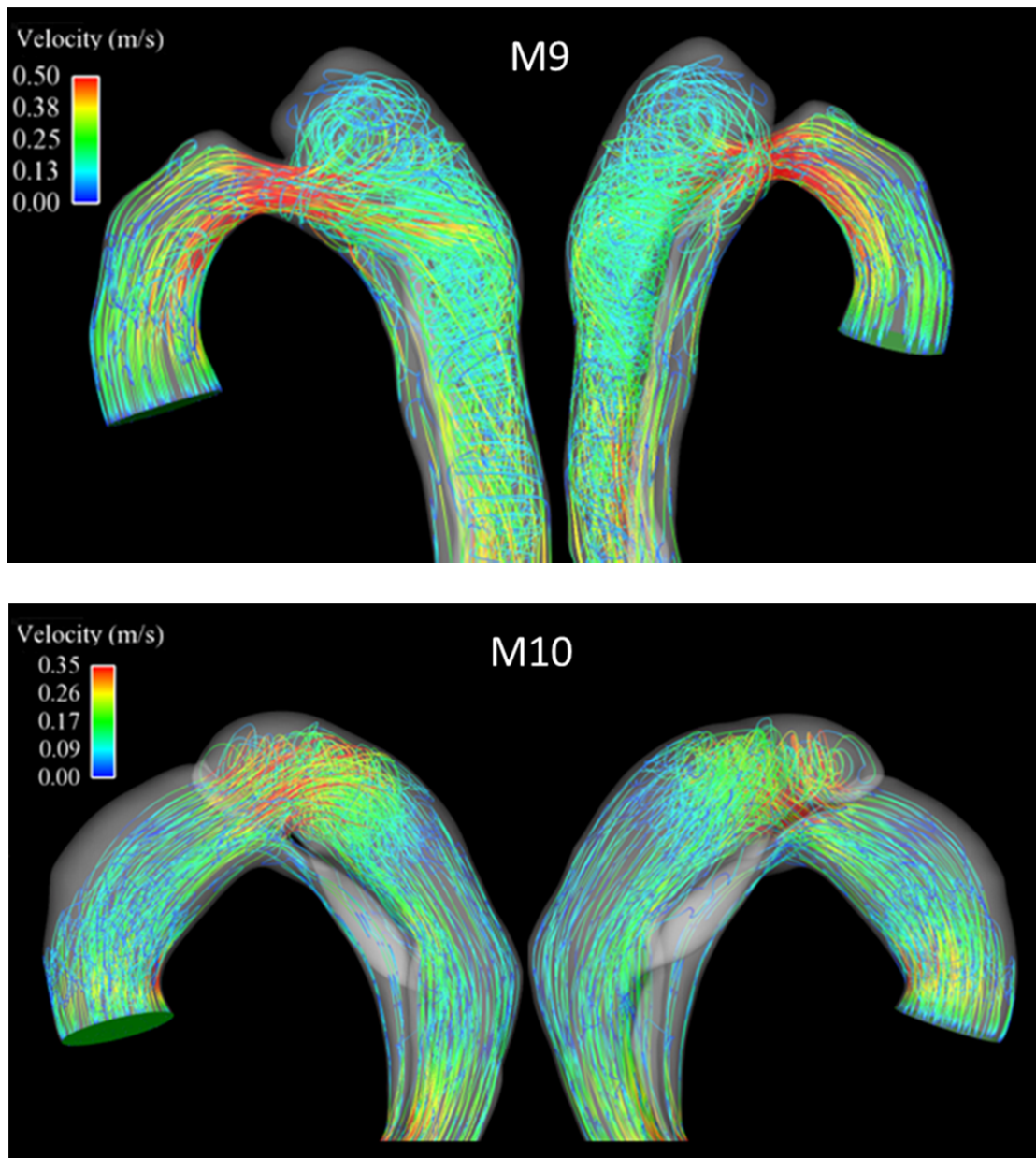


Figure 4.3: Particle paths of blood flow in each of the 10 aortic dissection models (left: right-anterior view, right: left-posterior view)

The flow rate entering the false lumen is an important parameter in characterizing flow in dissected aorta. The amount of blood flowing into the false lumen is associated with false lumen patency which is regarded as a strongest predictor of late outcome of aortic dissection including both short-term and long-term prognosis and mortality. Large quantity of blood in the false lumen will increase the risk of aortic expansion, aneurismal degeneration and late complication in aortic dissection, while limited flow in the false lumen may promote false lumen thrombosis which is desirable for dissection patients.

Table 4.3: Percentage of flow rate into false lumen in AD subjects at peak systole.

Subjects	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
Percentage of Flow rate into false lumen (%)	85.3	25.6	95.5	N/A*	76.7	60.4	51	40.3	78	90.8

* Flow rate into false lumen in subject No. 4 is difficult to calculate due to geometric condition.

Table 4.3 presents the percentage of aortic flow that enters the false lumen in all subjects except M4 whose flow rate into the false lumen is difficult to calculate owing to highly rotating and swirling flow in the tear region and false lumen. All the data recorded here correspond to peak systole when the flow rate is at the maximum. As can be seen from the table, the percentage of flow into false lumen varies significantly from subject to subject. Most of the subjects have more than 50% flow going into the false lumen. M3 has 95.5% flow in the false lumen which indicates that only very limited flow goes into the normal aorta in the dissected section, which may impair blood supply to the organs and branches connected with the main aorta. Around $\frac{1}{4}$ of flow enters the false lumen in M2 which is the smallest amount compared to other subjects. Setting the false lumen flow data against the key geometric parameters, such as the location and size of tear, certain relationships can be found. Figures 4.4, 4.5 and 4.6 present the relationships between the percentage flow rate in false lumen and the size and location of primary tear, respectively. Each subject is colour coded with the patient's category. The red straight lines are regression lines obtained by performing linear regression analysis of the corresponding data.

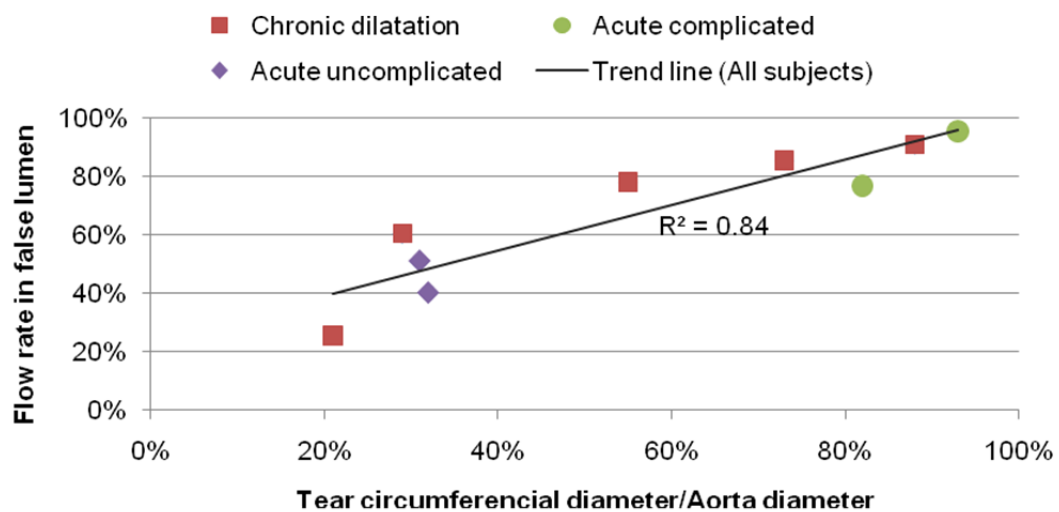


Figure 4.4: The relationship between percentage flow rate in the false lumen and the ratio of tear circumferential diameter to aorta diameter.

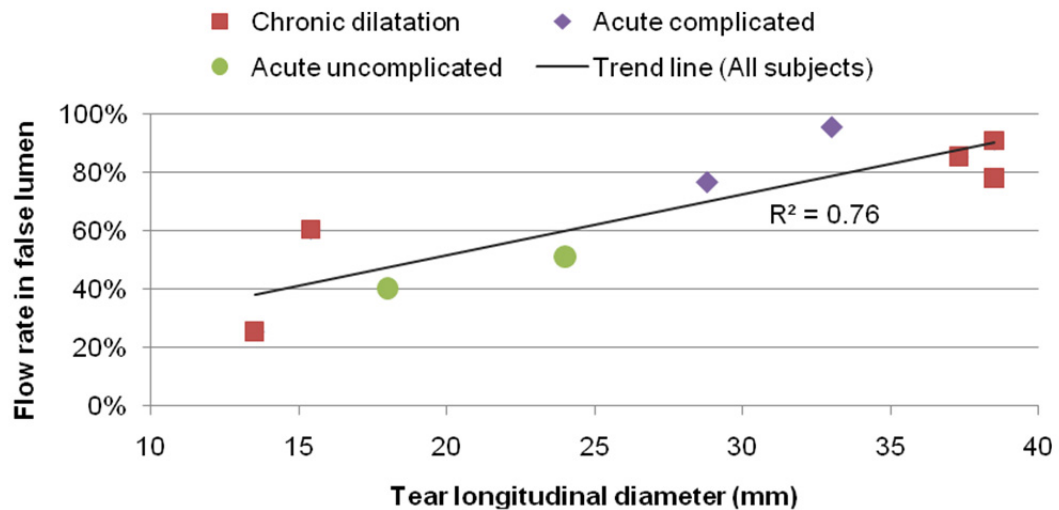


Figure 4.5: The relationship between percentage flow rate in the false lumen and the longitudinal diameter of tear.

Instead of using the tear circumferential diameter directly, its ratio to the diameter of the aorta is used to examine the relationship with flow percentage in false lumen (see Figure 4.4), since the size of the aorta varies considerably among subjects so that tears of the same size may have less impact on a relative larger aorta, but more influence on a smaller aorta. Figure 4.4 shows a strong linear relation, which demonstrates that as the ratio increases, more flow is likely to enter the false lumen. The effect of tear longitudinal diameter on flow rate in false lumen is also analyzed. Since the tear hole is non-circular, the longitudinal diameter of tear is not the same as its circumferential diameter and is usually larger in most of the subjects. It can be seen from Figure 4.5 that larger longitudinal diameter correlates with higher percentage flow in the false lumen. These two figures illustrate that tear diameters in both circumferential and longitudinal directions have a strong influence on the amount of flow going into the false lumen.

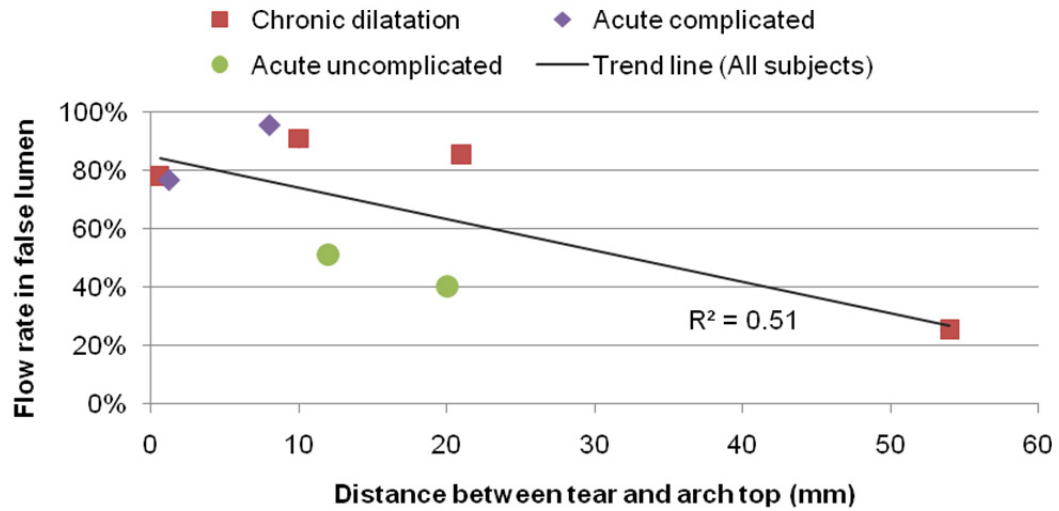


Figure 4.6: The relationship between percentage flow in false lumen and the distance between tear and arch top.

Besides the size, the location of tear may also play an important role in determining the flow distribution in dissected aorta. Although in type B aortic dissection subjects, the primary tears are confined to the descending aorta after the left subclavian artery, some tears occur in the middle section of the thoracic aorta, while others may be very close to the root of the left subclavian artery. In this study, the top of arch is regarded as a reference point, and the vertical distance between the arch top and upper edge of tear is measured to find its relation to percentage of flow rate in false lumen. Figure 4.6 shows an inverse relationship suggesting that there would be more flow in the false lumen if primary tear is closer to the arch. But the correlation is not as strong as that between false lumen flow rate and tear size.

The results demonstrate that each of the three geometric parameters of the tear has a strong influence on the flow division between the true and false lumen. However, the proportion of flow entering the false lumen shown in the results is affected by all the geometric factors at the same time. In order to understand the effect of each individual geometric factor on flow rate in the false lumen, while the other factors are fixed, regression analyses were attempted in an effort to examine the relationship between false lumen flow rate and tear geometric parameters.

The multiple linear regression model with three explanatory variables was adopted. In this model, the dependent variable is a linear combination of the independent variables as described in the equation below:

$$E(Y) = \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \alpha \quad (4.1)$$

where Y is the dependent variable, X_i ($i=1, 3$) is the independent variables, and β_i ($i=1, 3$) is the correspondent parameters, α is the constant parameter. In this study, the false lumen flow rate is the dependent variable Y , and the ratio of tear circumferential diameter to aortic diameter, the tear longitudinal diameter and the distance between the tear and arch top are X_1 , X_2 and X_3 respectively. Values for their corresponding parameters can be calculated and these are given in Table 4.4. The correlation coefficient of the multiple determination, R^2 , which measures the proportion of the total variation in false lumen flow rate that is explained by the predictive power of all the three factors, was calculated (also shown in Table 4.4).

Table 4.4: Parameters and coefficients of the multiple regression analysis

Model variations	Parameters	Unstandardized coefficients		R^2
		Value	Stand. error	
Ratio* X_1	β_1	0.533	0.150	0.947
LONG. Diameter X_2	β_2	0.014	0.005	
Distance§ X_3	β_3	0.003	0.001	
—	α	-0.089	0.117	

* the ratio of tear circumferential diameter to aortic diameter

§ the distance between tear and arch top

According to the calculation results, the prediction equation is $\hat{y} = 0.533x_1 + 0.014x_2 + 0.003x_3 - 0.089$, and the correlation coefficient R^2 is 0.947, which means about 95% of the presented flow rate data can be explained and well predicted by the predictive power of all the variables, through the multiple regression model. The regression equation appears to be very useful for making predictions since the value of R^2 is close to 1.

The partial correlation of each of the geometric factors was also examined. It describes the partial association between the false lumen flow rate and a particular factor by

controlling the other two factors. The partial correlation is based on the ordinary correlations between each pair of variables, and is calculated by the following equation:

$$r_{YX_3 \cdot X_1, X_2}^2 = \frac{R_{Y(X_1, X_2, X_3)}^2 - R_{Y(X_1, X_2)}^2}{1 - R_{Y(X_1, X_2)}^2} \quad (4.2)$$

In this expression, $r_{YX_3 \cdot X_1, X_2}^2$ is the square of the partial correlation between Y and X_3 controlling for X_1 and X_2 , $R_{Y(X_1, X_2, X_3)}^2$ denotes the value of R^2 . $R_{Y(X_1, X_2, X_3)}^2 - R_{Y(X_1, X_2)}^2$ is the increase in the proportion of explained variance from adding X_3 to the model. The denominator $1 - R_{Y(X_1, X_2)}^2$ is the proportion of the variation left unexplained when X_1 and X_2 are the only predictors in the model. The partial correlations of the three tear geometric factors are presented in Table 4.5. The Pearson correlations, which describe the linear dependence between the flow rate data and each of the variables, as well as the significance level, are also given in Table 4.5.

Table 4.5: The Pearson and Partial correlations of the geometric factors.

Model variations	Pearson Correlations	Sig.	Partial Correlations	Sig.
Ratio*	0.915	0.001	0.846	0.016
LONG. Diameter	0.873	0.002	0.804	0.029
Distance §	-0.447	0.228	0.735	0.060

* the ratio of tear circumferential diameter to aortic diameter

§ the distance between tear and arch top

As can be seen, both the ratio of tear circumferential diameter to aortic diameter and the tear longitudinal diameter present significant positive correlations with the false lumen flow rate. The significance level, which is smaller than 5%, demonstrates the correlations are statistically significant. Also, the partial correlations of the two geometric factors are quite close to the Pearson correlation, suggesting that the correlation between each of the two variables and the false lumen flow rate is less influenced by the other geometric factors. What's interesting here is that the partial correlation between the tear location and the flow rate in false lumen is positive, whereas the Pearson correlation is negative. So, the distance between the tear and arch top is negatively correlated with the false lumen flow rate, but the part of the distance that is independent of the tear size is positive. A substantive interpretation of this might be that tears with a large size are located far away from the arch top. This situation can be observed in the geometries of subjects M4 and M6. However, the significance level of

the tear location is larger than 5%. Hence the correlation between the distance and flow rate is not statistically significant.

Finally, it should be stressed that the above regression analyses were based on a small data sample size ($n=10$). Although some interesting correlations were identified, they should be treated with due caution.

4.5.3 Wall Shear Stress

Wall shear stress (WSS) is an important hemodynamic parameter, which still cannot be measured directly, or determined accurately, by current *in vivo* techniques. Determination of WSS via patient-specific CFD analysis remains the best option so far. The distributions of TAWSS contours on the inner surfaces of the ten subjects are presented in Figure 4.7. The color legend is set to range from 0 to 7 Pa as wall shear stress greater than 7 Pa is believed to be abnormally high. All areas where TAWSS exceeds 7 Pa are shown in red color in the figure. As can be seen, high TAWSS is located at the throat of narrowed section if present where blood flow is accelerated and velocity is high, or along the edge of the primary tear. As shown in the last section, the velocity of blood flow through the tear into the false lumen is very high, which could explain the high TAWSS along the edge of tear. Another region of high shear stress is the adventitial bound surface of the false lumen bulge where the jet of fluid from the true lumen impinges on. Depending on the direction of blood flow into the false lumen, moderately elevated TAWSS could be found on the anterior and posterior surface, or the site opposite the primary tear in the false lumen. Some areas of the true lumen also experience high TAWSS owing to narrowing and bending. Nevertheless, most of the dissected aortic wall experiences shear stress below 1.5 Pa especially in the superior region of the false lumen which corresponds to low and stagnant flow. The maximum TAWSS values vary from more than 20 Pa in some subjects to below 10 Pa in others. Although not all of the highest TAWSS are located at the tear edge, the value in this region is greater than 7 Pa for all the subjects.

The OSI map on the inner surface is shown in Figure 4.8. OSI is a measure of the oscillatory character of the shear stress, and can also be related to the residence time of particles near the wall. The OSI distribution presents an opposite trend to TAWSS. Corresponding to extremely high TAWSS values, the throat of coarctation and narrowed sections have low OSI values because of highly accelerated and unidirectional blood flow. On the adventitial bound surface of the false lumen where blood flow through the primary tear impinges on, OSI is also low owing to the persistent flow jets. Regions of

high OSI values of up to 0.5 can be seen at a number of sites in these subjects, indicating that directional changes and/or flow reversal occur frequently during the pulse cycle in the dissected aorta. The ascending aorta presents moderate levels of OSI with localised high OSI regions due to the periods of complete reversal of the flow direction and surface irregularity. The flow reversal in the ascending aorta is most likely determined by the shape of ascending aorta, and the velocity profiles in the proximal ascending aorta, which was dictated by the inlet flow waveform applied. Localized high OSI can be seen in the downstream part of both lumens as disturbed flow dominates in them. Moderate OSI can be found in the superior region of the false lumen, where TAWSS is close to zero. The areas around the primary tear, although experiencing high TAWSS, present moderate OSI values.

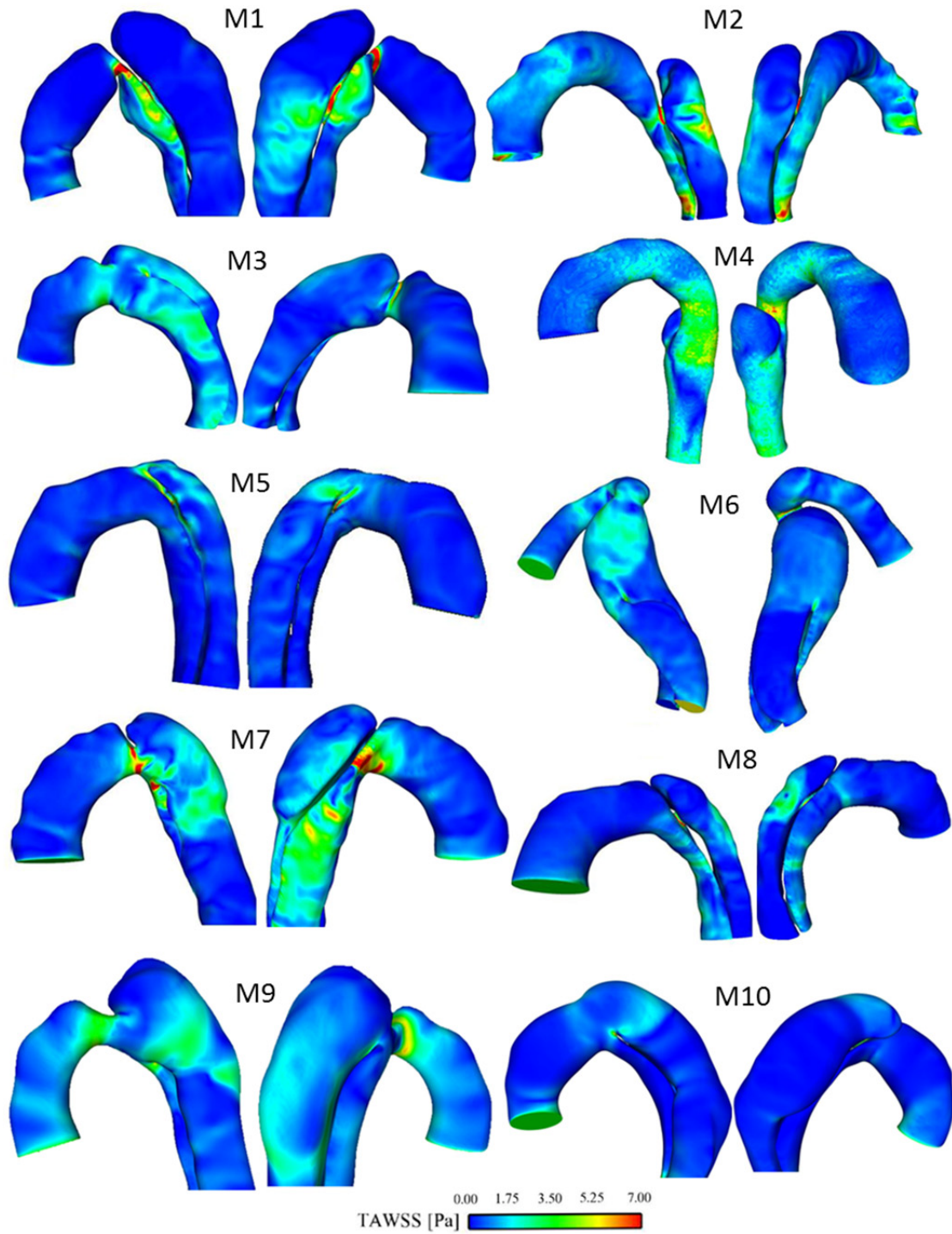


Figure 4.7: TAWSS contours in the aortic dissection models of the ten subjects (left: right-anterior view; right: left-posterior view).

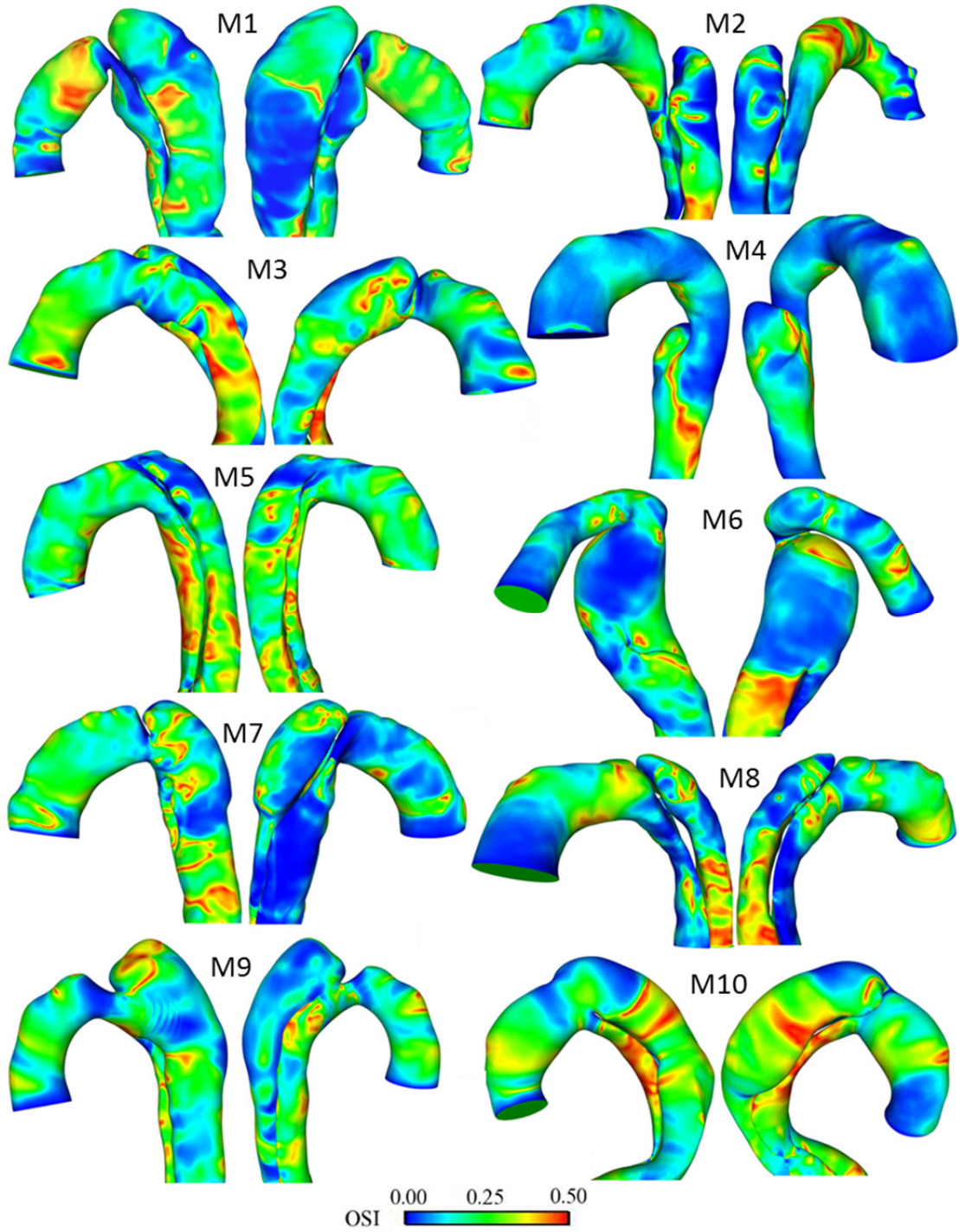


Figure 4.8: OSI contours in the aortic dissection models of the ten subjects (left: right-anterior view; right: left-posterior view).

4.5.4 Turbulence Intensity

The isosurfaces of turbulence intensity (Tu) levels at the midsystolic deceleration phase are presented in Figure 4.9. Instantaneous local velocities were used in the calculation of Tu in order to portray realistic levels. Since the level of turbulence intensity varies

among the ten subjects, the red and blue isosurfaces in each subject represent different values of Tu. Among the ten subjects, subjects M1, M4 and M7 have very high turbulence intensity, which can exceed 40% in the region near the primary tear. However, the other subjects present relatively low turbulence intensities with the highest value being up to 5%. As shown in Figure 4.9, high turbulence intensity tends to be found in the vicinity of the tear where the wall shear stress values are also high, especially in the false lumen. The fluid, flowing from the true lumen, impinges on outbound surfaces of the false lumen, causing flow recirculation induced high Tu levels in the false lumen. High turbulence intensity can also be found in the true lumen in subject M7 where geometric factors, such as the narrowed true lumen and partial primary tear, are likely to amplify the turbulence. Hence the geometry, shape and location of the primary tear could also affect the presence and intensity of turbulent flow.

The reason behind the large differences in Tu level between the subjects is likely associated with the geometric factors of the dissected aortas. Setting the Tu levels against the geometric factors presented in Table 4.2, it can be found that the subjects with narrowing scales of less than 50% have high turbulence intensity. The narrowed true lumen is similar to an arterial stenosis through which blood flow accelerates, resulting in a high velocity jet from the throat; hence the combination of high velocity (i.e. high local Reynolds number) and complicated geometry induces high turbulent flow. Certainly the effects of other geometric factors cannot be neglected, but the narrowing scale of the true lumen is the most obvious factor that can be concluded from the ten subjects.

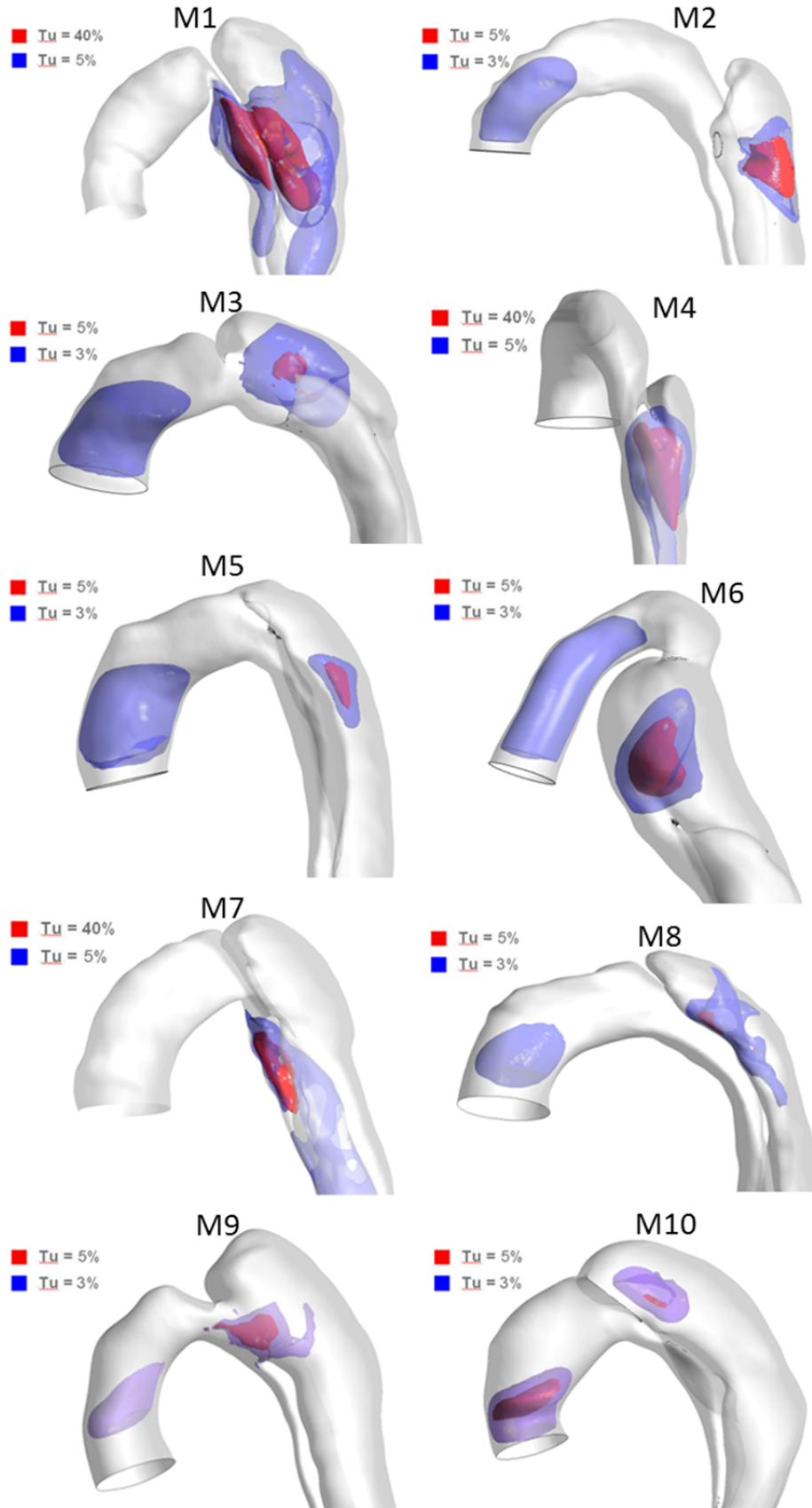


Figure 4.9: Turbulence intensity isosurfaces in the ten subjects of aortic dissection at midsystolic deceleration phase.

4.5.5 Effect of non-Newtonian viscosity

In order to examine the influences of non-Newtonian properties of blood on the simulation results, the Quemada model (Quemada 1978) was adopted and applied to subject M1, which presented the highest value of turbulence intensity with the Newtonian simulation. This model was incorporated into the transitional flow model by calculating the apparent viscosity based on a minimum energy dissipation analysis. Compared with the results of the Newtonian simulation, the non-Newtonian model has a very similar wall shear stress distribution, but a slightly lower maximum WSS value (17.98 Pa versus 16.75 Pa) and similar pressure distribution with a mildly reduced peak (3544 Pa versus 3100 Pa).

Turbulence intensity results were also compared between the Newtonian and non-Newtonian models. The non-Newtonian model seems to have extended the regions of $Tu=40\%$ and 70% in the true lumen, but reduced the region of $Tu=8\%$ in the false lumen. The maximum turbulence intensity is also slightly higher with the non-Newtonian model, reaching 82% in midsystolic acceleration (shown in Figure 4.10).

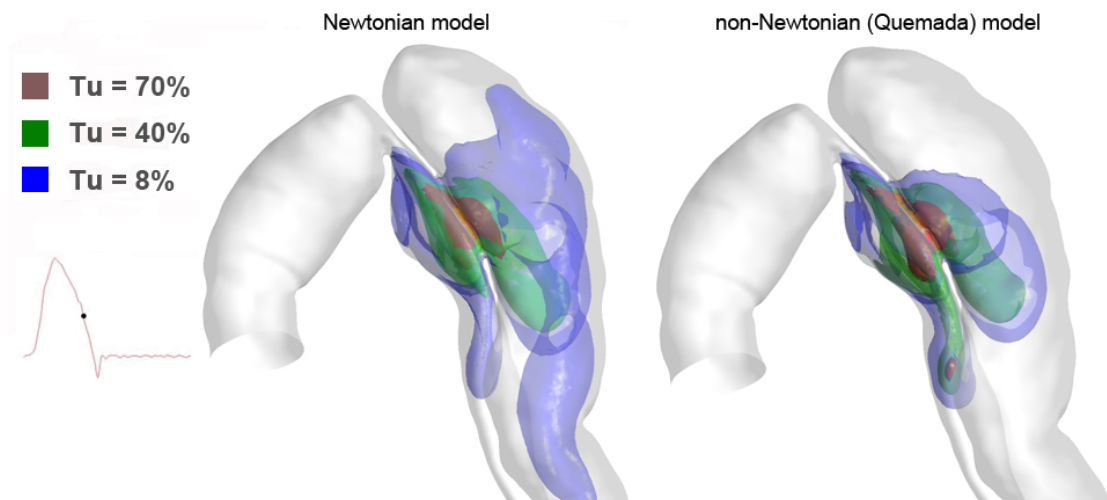


Figure 4.10: Turbulence intensity isosurfaces of Newtonian model (left) and non-Newtonian model (right) in aortic dissection subject M1 at midsystolic deceleration.

4.5.6 Effect of Turbulent Flow

According to the turbulence intensity results presented in the previous section, although not all of the subjects showed elevated turbulence intensity, high value of turbulence intensity could happen in some subjects. For example, in the model of subject M1, up to 70% (Newtonian) and 82% (non-Newtonian) turbulence intensity can be observed in

the flow near the tear in both the true and false lumen during the mid-deceleration phase. A laminar flow simulation was also performed to compare the results with those from the transitional turbulence model in the model of subject M1. From Figure 4.11, it can be observed that the TAWSS of the laminar flow simulation was quantitatively different from that of the transitional model (maximum values of 12.6 Pa versus 17.98 Pa), although similar in qualitative terms. A much higher maximum value of TAWSS was found in the transitional model. This finding is consistent with the previous suggestion that the turbulent flow could increase WSS on the inner surface of arteries (Khanafer et al. 2007).

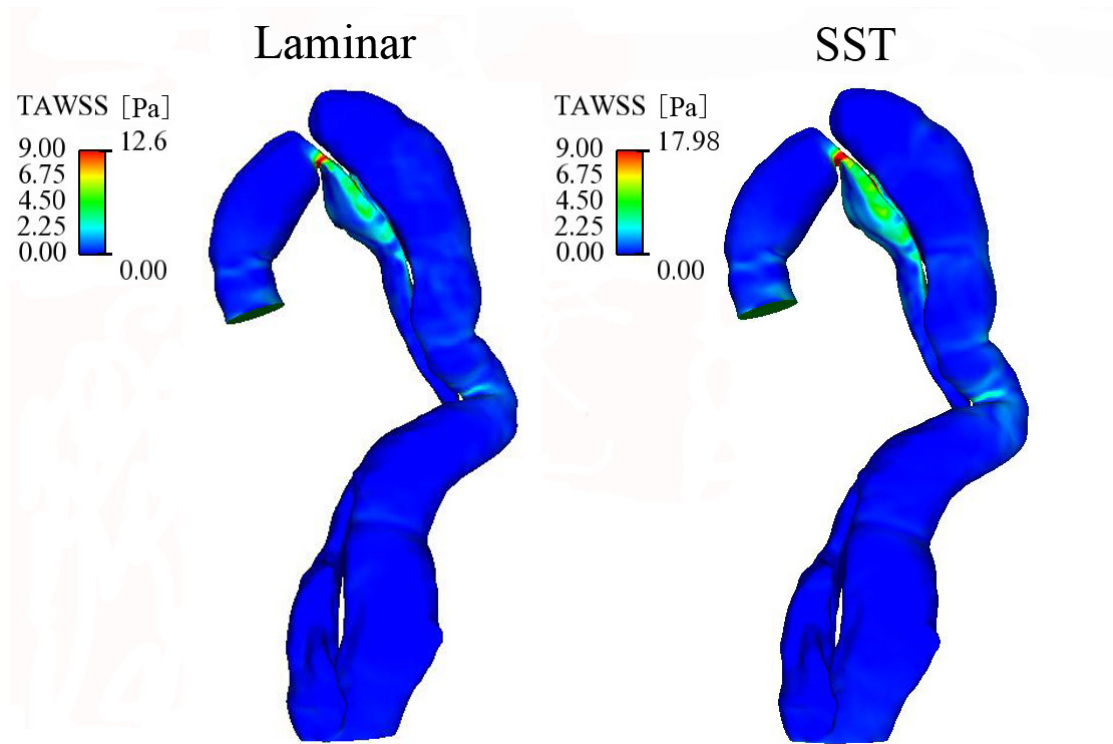


Figure 4.11: TAWSS contours of the laminar flow model (left) and transitional model (right). The scales have been chosen to show direct comparison between laminar and transitional flows, but the differing peak levels have been highlighted.

4.5.7 Pressure Distribution

Pressure values presented here are relative to the outlet pressure and correspond to the difference in instantaneous pressure between the aortic wall and the outlet of the computational model resulting solely from the velocity variations. Pressure distributions of the ten subjects show different patterns. Figure 4.12 presents the pressure distributions in three subjects: M1, M7 and M10, at the peak velocity phase. High pressure values can be found in the ascending aortas of all of the subjects due to

coarctation of the arch. Different levels of narrowing scale of the true lumen result in different pressure values in the subjects. The narrower the arch or the true lumen is, the higher the pressure becomes in the ascending aorta. The pressure at the edge of the primary tears is very low, owing to the high velocities of blood entering into the false lumen. Another important common pattern found in all the ten subjects is that pressure in the true lumen is generally higher than in the false lumen in the upper part of the aortic segment, but the opposite is true in the lower segment, owing to different directions of blood flow communicating between the two lumens. The relative pressures predicted here are much higher than that in the abdominal aortic aneurysm model of Khanafer et al. (2007) owing to the presence of large false lumens. Rather than the pressure difference between the true lumen and false lumen, the shunting of flow to the false lumen, combined with a concomitant reduction of the real lumen induced by shear dependant remodelling, may contribute to the large compression of the true lumen.

Each subject has a typical pattern of pressure distribution according to his/her specific geometric characteristics. The pressure distribution is highly non-uniform in subject M1 due to the highly narrowed true lumen sections and tortuous aorta. Subject M7, which has a straight and relative simple geometry, has more uniform pressure gradient in the lower section of both lumens, while disturbed and turbulent flow in the upper part of the two lumens cause non-uniform pressure distributions in that area. A more uniform pressure distribution is seen in subject M10 where although the geometry of the dissected aorta is quite tortuous, the flow in both lumens is less disturbed as discussed previously due to the high location and large size of the primary tear. Hence flow patterns may have a strong influence on pressure distributions in the AD models.

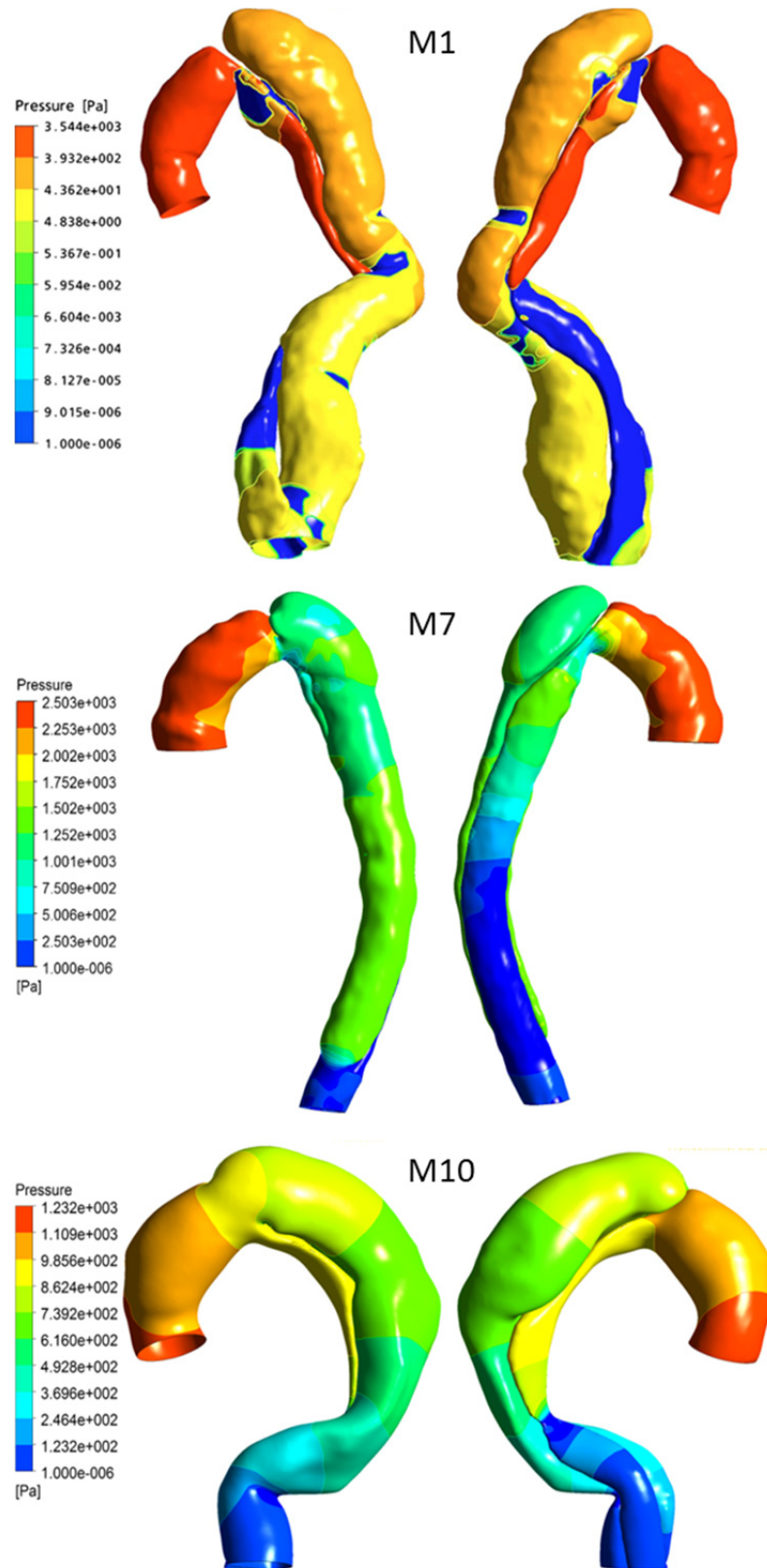


Figure 4.12: Pressure contours in the aortic dissection models of M1, M7 and M10. (left: right anterior view; right: left-posterior view)

4.5.8 Effects of middle tears

Aortic dissection begins with an intimal tear that allows the blood to enter the aortic wall, splitting the middle and outer layers of the media until blood finds its way back into the true lumen through a re-entry tear on the intima-media layer (Demos et al. 1986; Khan & Nair 2002). The primary entry tear and re-entry tear make blood circulate through the false lumen and maintain its patency. The identification of primary entry tear is important for understanding the original site of dissection and surgical decision making. The location of the entry tear is fundamental to the successful performance of the stent-graft repair (Marvin et al. 2006). However, in addition to these two tears, it is typical that several middle tears between the primary and final re-entry tears in the intimal layer are also present, allowing multi-channel communications between the two lumens. The size of these middle tears is usually small compared to that of the primary tear, and the identification of them strongly depends on the resolution of CT scans and diagnosis of radiologists. Although the impact of middle tears on late development and degeneration of aortic dissection is still unclear, the flow patterns and related parameters in an aortic dissection model incorporating middle tears have been examined as part of this study.

The location and size of the middle tears in the ten subjects are identified by a professional radiologist from CT images which were used for geometry reconstruction. The longitudinal and in-plane resolutions of the CT images are approximately 1 mm, hence tears smaller than 1 mm could be missed out. Based on the radiologist's examination, middle tears are distributed in the intimal flap either longitudinally or circumferentially, and the number ranges from two to eight among the ten subjects. The sizes of middle tears also vary, with the largest being up to 3 mm. A detailed fluid dynamics analysis was carried out on subject M1 who has the most and largest middle tears.

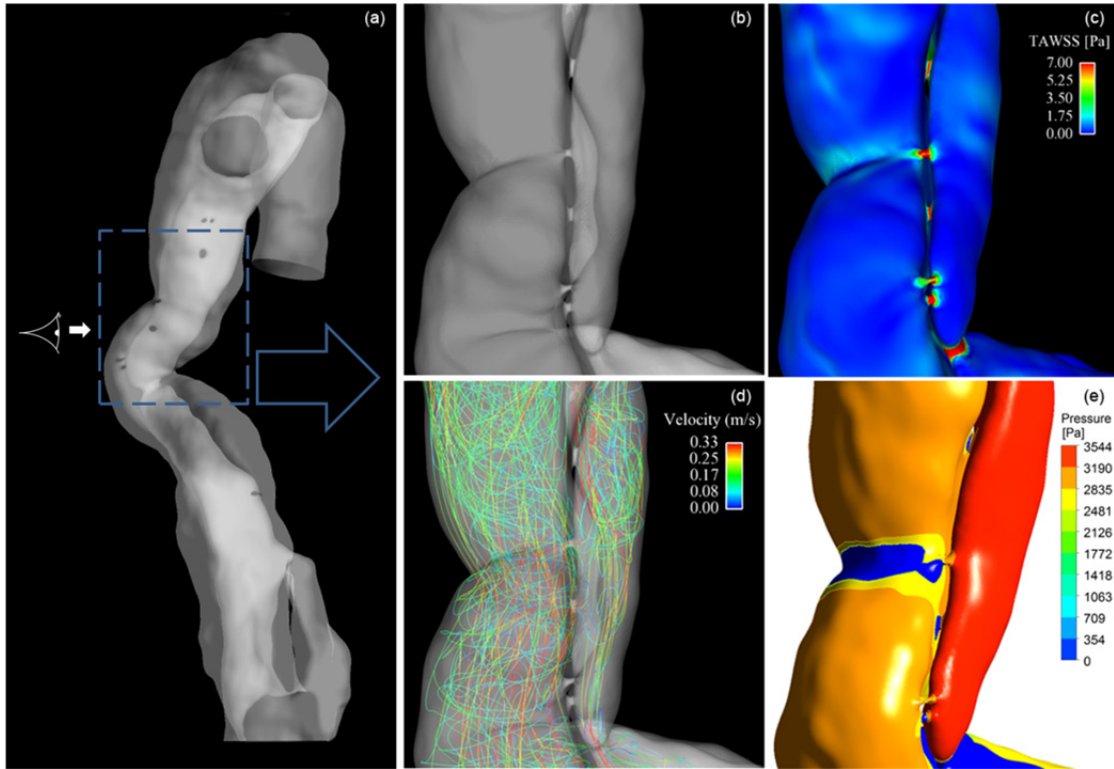


Figure 4.13: Geometric description and CFD analysis results of subject M1 with middle tears. (a) the reconstructed model viewed from the right, (b) a zoomed in section showing middle tears from the left-posterior view angle, and (c)-(e) the TAWSS, particle paths and pressure distributions of the section with middle tears respectively.

The geometric description and flow simulation results are shown in Figure 4.13. Eight middle tears are clearly displayed in Figure 4.13(a), and Figure 4.13(b) shows the section where middle tears are the most concentrated. Compared to the results in the model without middle tears, the TAWSS, pressure distributions and flow pattern in both lumens are not affected by the presence of middle tears from a qualitative point of view, but local quantitative changes are observed. Figure 4.13(d) shows the particle path lines of 100 particles emitted evenly from the inlet during a total time of 18 cardiac cycles. Although the flow is quite disturbed in the two lumens, only very limited path lines can be seen through two of the middle tears (3 out of 100 path lines in all), and all of them are from the true lumen to false lumen because of the pressure gradient. The small proportion of flow is still sufficient to cause high TAWSS around the edge of the middle tears as shown in Figure 4.13(c), but the pressure difference between the two lumens is not affected. These small tears, which form several bridges allowing communications between the two lumens, only have minor effects on small areas near the tears (presented in Figure 4.13(e)).

It seems that the presence of middle tears in dissected aorta have no obvious impact on the flow condition and haemodynamics parameters. Localized flow communication and pressure changes are quite limited and inconspicuous. However, the high wall shear stress acting on the edge of the tears, which have been associated with matrix degradation and disease progression, may play a role in weakening the intimal flap and enlarging the size of the tears.

4.5.9 Discussion

Current management of acute Type B aortic dissection is hampered by the lack of approach to predict the clinical sequelae of the dissection process in individual patients. Treatment options currently fall into three categories: those patients who spontaneously develop false lumen thrombosis who would benefit from best medical management alone; those patients who rapidly develop acute complications requiring urgent intervention and those who have persistent false lumen patency and subsequently develop aortic dilatation. Confident prediction of which category an individual patient will fall into will facilitate optimal management. TEVAR is not without complications (Rodd et al. 2007), and intervention should only be undertaken in those patients in whom a demonstrable benefit accrues. The results of the multiple cases study demonstrate that the aortic geometry of individual dissections varies significantly. As a consequence blood flow patterns and wall shear stress also vary. The key question is whether these differences alter clinical progression of the dissecting process.

Current literature shows that false lumen size and patency are the most important predictors of adverse early and later outcomes (Eggebrecht et al. 2005), but the reasons for continued false lumen patency are yet to be elucidated. The data obtained in this study suggest that tear size (both circumference and length) and position significantly alter the flow rate into the false lumen, which in turn is associated with false lumen patency. Figure 4.6 shows the relationship between the position of the tear and the flow rate into the false lumen, with a sharp decrease in the flow rate the further the tear is from the aortic arch. Figures 4.4 and 4.5 demonstrate that the greater the size of the tear, the greater the flow rate into the false lumen. Clinical correlation is also revealing. In terms of acute presentation, subjects M3 and M5 were both complicated by acute malperfusion, whilst subjects M7 and M8 were acute uncomplicated presentations. The two subjects complicated by malperfusion had larger dimension tears than the uncomplicated cases with significantly larger tear to true lumen diameter ratio (93% and 82% compared to 32% and 55% respectively). Table 4.3 shows the resultant flow

rate into the false lumen was much higher in the patients with malperfusion (95% and 76.7% vs. 51% and 40.3% of total aortic flow respectively).

The remaining cases were chronic dissections, and all had patent false lumens with associated aortic dilatation. The treatment of chronic aneurysmal degeneration secondary to Type B dissection is predicated on size alone in order to prevent rupture. Endovascular stent graft placement is used to treat these aneurysms, and a key question is whether early placement of these grafts before dilatation occurs will prevent aneurysm formation. As the aorta dilates it also elongates, introducing tortuosity into the process. Proximal and distal landing zones are reduced or lost, rendering any endovascular procedure more difficult or impossible at a later stage in the evolution of the aneurysmal process. Early intervention would hypothetically confer significant advantage, but a recent randomized trial failed to demonstrate survival advantage in aorta related deaths in patients randomized to TEVAR vs. medical treatment alone in uncomplicated Type B dissection (Nienaber et al. 2010), and complications occurred due to the intervention. The trial did however demonstrate aortic remodeling (with true-lumen recovery and thoracic false-lumen thrombosis) occurring in 91.3% with endovascular repair vs. 19.4% with medical treatment. Accurate prediction of the group of uncomplicated Type B survivors that go on to develop dilatation would mean the associated risk of intervention would be justified. It is noteworthy that in this study all chronic dilatation cases with patent false lumens had greater than 60% of blood flow into the false lumen with the exception of subject M2. The inference is that failure of the false lumen to thrombose is driven by high flow rates into the false lumen due to entry tear size and position. Both entry tear dimensions and position in relation to the arch peak are features that can be detected on CT scanning, and as such may prove to be reliable indicators of both acute complications and future false lumen patency.

A number of common characteristics of the flow pattern and hemodynamic parameters can also be deduced from the results. The flow pattern in the dissected aortas was found to be complex with recirculating and disturbed flow dominating especially in the false lumen and the region close to the tear experienced the highest levels of turbulent flow. Relative stenoses of the true lumen were found to have significant influence in determining flow patterns. High WSS can be found on the edge of the tear in all of the dissection models, while low WSS was normally located in the superior region of the false lumen which had extended upward. The helical and recirculating flow in the dissected aorta also induced high OSI values in localized regions on the lumen surface.

Previous studies have suggested that abnormal hemodynamic stresses and recirculating and turbulent flow within the diseased aorta are an important influence in the formation, degeneration and ultimate rupture of aortic aneurysms (Malek et al. 1999; Thubrikar et al. 2001; Fillinger et al. 2002; Slager et al. 2005). Shear stress can affect endothelial cell functions, such as proliferation, apoptosis, migration, permeability and remodeling (Lehoux et al. 2006; Li et al. 2005). Low shear stress may increase monocyte adhesion due to flow reattachment, and recirculating flow would enhance the delivery of monocytes to the vessel wall (Pritchard et al. 1995). Disturbed flow and turbulence in blood flow influence flow resistance, pressure, wall shear stress, wall remodeling, inflammation and mass transport from the blood to the vessel wall (Giddens et al. 1976). The subjects with a highly compressed true lumen at the tear site were more likely to have an increased rate of wall dilatation. High WSS has been found around the edge of primary tear point which may erode already weakened dissected aortic wall and lead to further degeneration (Chatzizisis et al. 2007; Khanafer et al. 2007).

One point needs to be mentioned is that the ten subjects included in this multiple case study were from three different classifications. Two of them are acute complicated, two are acute uncomplicated, and the rest are chronic dissection. Flap thickness and movement may be different between the acute and chronic categories. For acute dissections, the intimal flap is relatively thin and elastic; hence flap motion is more often observed in this group of patients. With the development of dissection, the flap becomes thicker and more fragile, even with calcification. Hence, the motion of intimal flap can be significantly restrained in chronic dissection patients. By applying the same computational model to both the acute and chronic groups, the rigid wall assumption may have different impacts on the simulation results for these patients.

4.6 Summary

This multiple case study found that the location and size of the primary tear determine the amount of flow circulating in the false lumen; larger primary tear diameter or shorter distance from the top of aortic arch can lead to increased flow rate into the false lumen. Because large amount of blood flow would keep false lumen patent and less likely to be thrombosed, aortic dissection patients who have a large primary tear with proximal location may be at higher risk of developing aneurysm or late degeneration. General characteristics of flow patterns in dissected aortas have been found, these include extremely complex flow with recirculating and disturbed flow dominating in the descending aorta especially in the false lumen. The flow is most likely to be turbulent,

and the region surrounding the tear experiences the highest levels of disturbed or turbulent flow. High wall shear stress has been found around the edge of the primary tear in all cases, while shear stress in the proximal part of the false lumen is very low. These hemodynamic factors have been suggested to be involved in the initiation, growth and progression of aortic diseases, hence are suspected to play an important role in the development and long term outcome of type B aortic dissection. This strong correlations between morphological and hemodynamic factors reported in this chapter are promising, and may lead to a better understanding of the morphological factors that can be used to predict the likelihood of subsequent aneurismal degeneration and rupture in the dissection patients.

Chapter 5

Patient-specific Study II: a single case with multiple follow-ups

5.1 Introduction

Generally, patients who have Stanford type B aortic dissection without complications are treated medically, and are under surveillance after hospital discharge. Although the in-hospital outcomes in this group of patients are generally acceptable (Hagan et al., 2000), the short- and long-term outcomes are variable among patients. Some of the affected aortas may progress to late degenerations requiring surgical intervention during the chronic phase, while others may manage to survive without further complications. Previous study of IRAD has shown that three-year survival for patients who were treated medically was 77.6% (Tsai et al., 2006), demonstrating the high follow-up mortality in patients after hospital discharge. The reason behind the long-term stabilization or late degenerations of type B aortic dissection remains unclear. In this chapter, detailed analyses are presented of a patient with uncomplicated type B aortic dissection who has been under surveillance for three years with a specific aim to better understand the role of hemodynamics in stabilized dissected aorta.

5.2 Patient information

A male patient who was treated medically for more than three years after the initial diagnosis was studied. Sequential CT scans of the patient were available, which allowed the progression of the dissected aorta to be examined and computational models corresponding to different stages of the development to be generated. This patient was admitted to St. Mary's Hospital with an acute type B aortic dissection in February 2007 when he was 40 years old. He was diagnosed with hypertension in 1995. The diagnosis of type B aortic dissection was established with CT angiogram of the aorta on admission.

Based on the CT images, there was a dissection originating just distal to the left subclavian artery origin, extending down into the common iliac arteries bilaterally and into the right external iliac artery. The dissection had not extended more proximally, and the coeliac axis, superior mesenteric artery (SMA) and left renal artery were patent and arose from the true lumen. The maximum size of the thoracic aorta was estimated at 3.1 cm. As the etiological factor would appear to be his malignant hypertension secondary to Conn's syndrome, the patient was initially treated conservatively with intravenous anti-hypertensive drug to control his blood pressure. A follow-up scan five days later with maximum contrast density in the aortic arch again demonstrated the presence of type B dissection, and excluded the possibility of type A aortic dissection. Compared to the first scan, no significant interval change was seen since the previous scan despite a little more thrombus within the false lumen posterior to the arch extending towards the right innominate artery. As his symptoms settled down and there was no further progression of the dissection, this patient was discharged from hospital. After the discharge, he has been under a CT surveillance program until present. According to the latest clinical report, the patient remains fairly well, and his blood pressure has been very stable. Although the size of the dissected thoracic aorta has increased slightly over the time, it is still well under control with no intervening consideration.

5.3 Patient-specific model generation

Since the first CT scan, the patient has taken eight follow-up scans. The scans were initially taken at weekly intervals to keep a close watch on the patient's situation at the beginning after hospital discharge. As the patient's condition has remained stable, the intervals between scans were gradually increased. Now, the patient is under an annual surveillance program. All the eight series of CT scans are utilized in this study to observe the anatomical changes of the dissected aorta. In order to get detailed geometrical information, contrast enhanced CT slices of the chest, abdomen and pelvis were acquired for each scan. The resolution of the CT images was kept at an in-plane pixel size of less than 1 mm and an interslice distance of 1 mm. From the CT images, the initial tear between the true and false lumen, and the thrombus between the lumens and aortic wall can be seen clearly. Figure 5.1 shows the time series of the images acquired at the cross-section where the initial tear occurred. Each series of CT images is numbered according to the sequence of scan time with an initial 'S' (stands for Single case study). The time interval between each scan is also shown in the figure. The initial tear is located near the edge of the flap. The size of true lumen has not changed very much during the follow-up

period. However the false lumen has gradually shrank due to the formation of thrombus along the outer curvature of the descending aorta and the false lumen side of the flap.

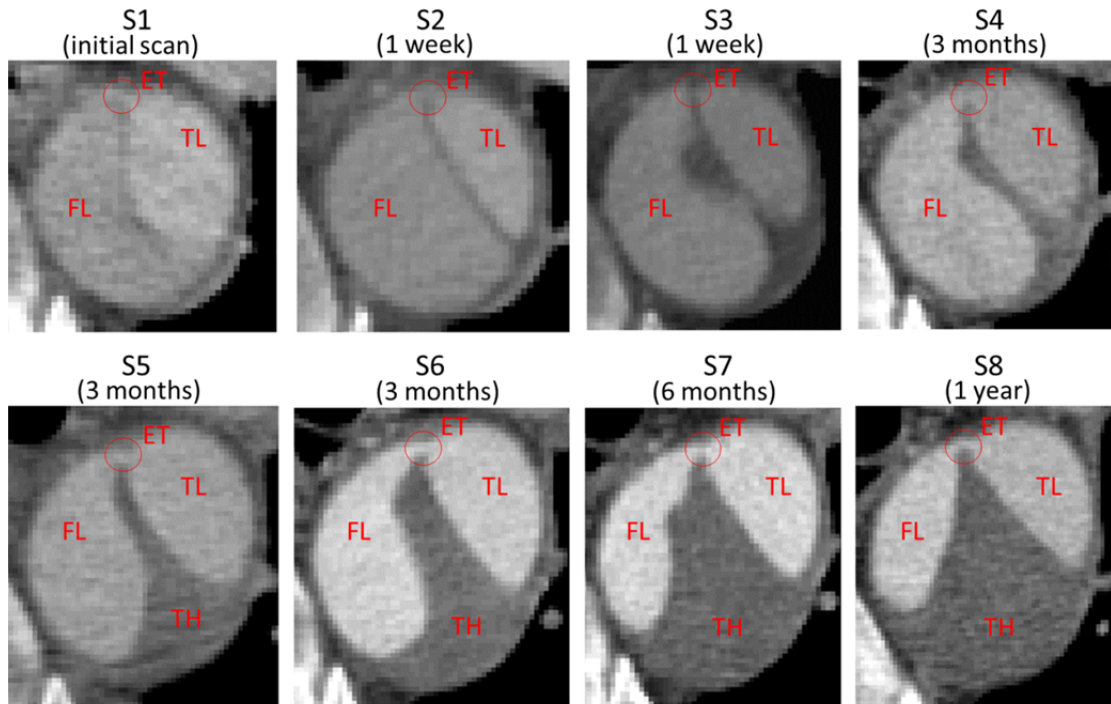


Figure 5.1: Cross-sectional CT images of the descending aorta at the section where initial tear occurred with annotations for the primary entry tear (circled with 'ET'), true lumen (TL), false lumen (FL), and thrombus (TH). The time presented is the time interval between two sequential scans.

The CT images were imported into a medical image processing software Mimics (Materialise, Leuven, Belgium). The segmentation of all images and 3D geometry reconstruction were accomplished to obtain the region of aortic lumens from each slice. Smoothing factor of the reconstruction was adjusted by registration of 2D contours on the corresponding CT images. The complete geometry of the aorta from the ascending aorta to iliac arteries was created. Figure 5.2 shows the reconstructed aortic dissection geometries for each follow-up scan. Closer views of the thoracic descending aorta are also shown to show the tear region more clearly.

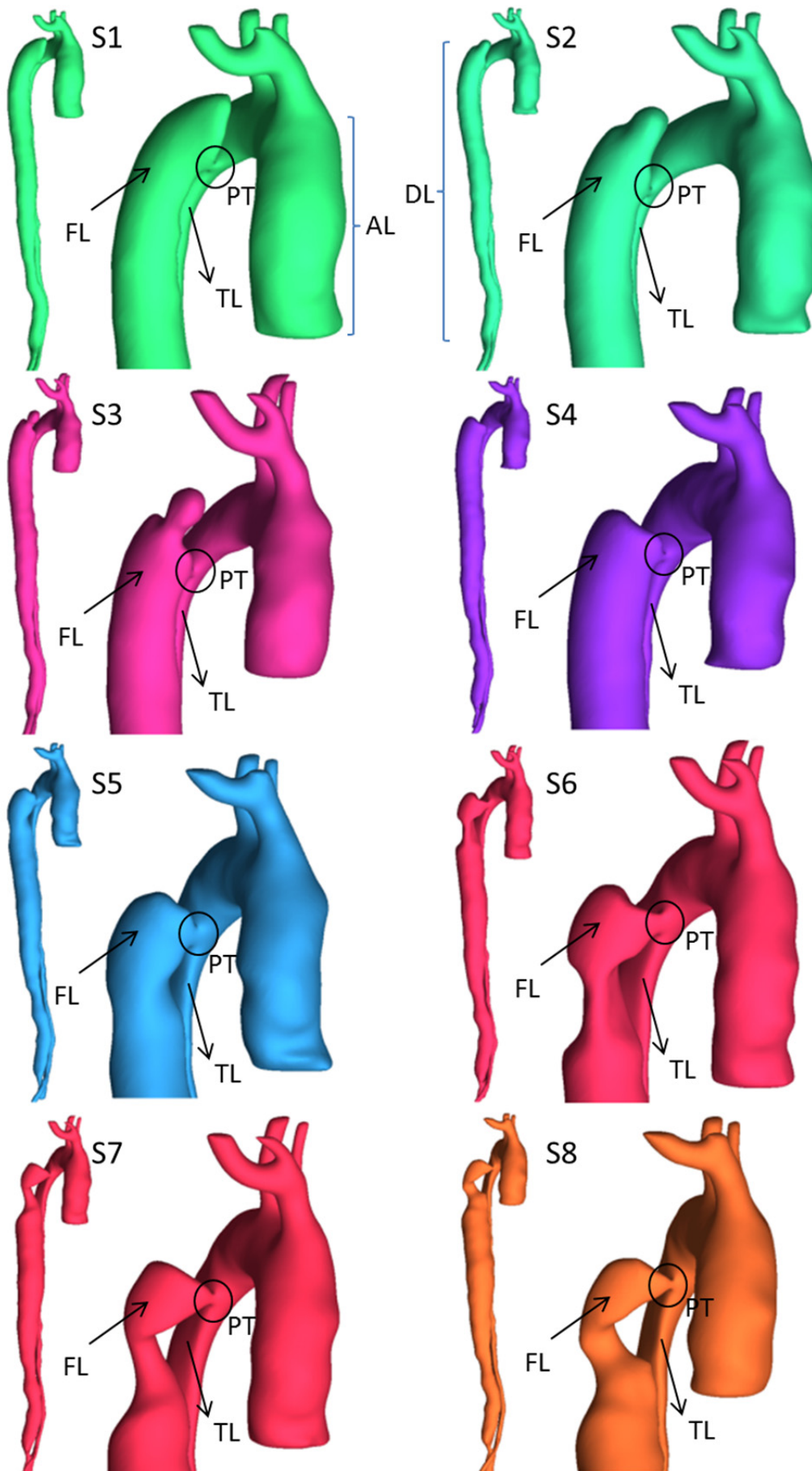


Figure 5.2: Geometrical descriptions of the aortic dissection at eight follow-up stages. The primary entry tear (PT), true lumen (TL), false lumen (FL), ascending aorta lumen (AL) and descending aorta lumen (DL) are indicated.

Figure 5.2 presents the changes of the aorta geometry from the initial scan to the latest follow-up scan. The most significant changes are the thrombosis of the false lumen and the arising of a second entry tear. Based on the geometric changes observed, the progression of the dissection over the follow-up period can be divided into two stages: Stage I is from the initial scan S1 to S4 with thrombosis of the top part of the false lumen; Stage II is from S5 onwards, which presents the formation of the second entry tear in the middle of thoracic aorta, and continuous thrombosis in the false lumen between the two tears. In order to examine the role of flow related parameters in the observed changes, initial models for each of the stages, S1 and S5, were analyzed. The small aortic branches on the models were excluded, as the primary focus here is the flow behavior in the dissected descending aorta, especially in the false lumen. The inlet of the model was located in the ascending aorta just above the aortic root, and the outlet was at the end of the descending aorta before the iliac arteries. As the true and false lumen converged below the abdominal bifurcation, each model has two outlets corresponding to the two lumens respectively. Figure 5.3 is the transparent images of the two models, which shows the primary and secondary entry tears, inlets and outlets.

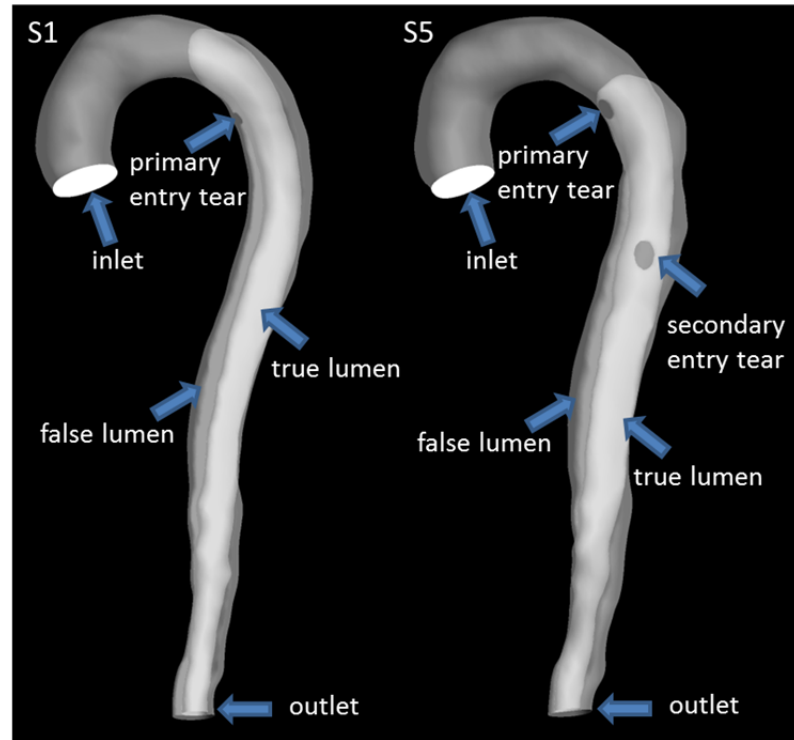


Figure 5.3: Transparent view of models S1 and S5 with arrows indicating the location of the tears, the inlet and outlet planes.

5.4 Flow simulation

Similar to the multi-case study described in Chapter 4, a correlation-based transitional version of Menter's hybrid shear stress transport (SST Tran) model (Menter et al., 2004) was employed to simulate flow in the dissected aorta. The Navier-Stokes equations for transient flows, together with the SST Tran model were solved using a finite-volume based CFD solver, ANSYS CFX 12. The blood was treated as a Newtonian and incompressible fluid with a dynamic viscosity of $4.0 \text{ mPa} \cdot \text{s}$ and a density of 1060 kg/m^3 . The aortic walls were assumed to be rigid with no-slip condition.

5.4.1 Boundary conditions

A flat velocity profile was specified at the model inlet in the ascending aorta, allowing the flow to develop naturally before reaching the dissection region. The realistic aorta flow rate waveform extracted from phase contrast MRI data of another typical type B aortic dissection patient was imposed. As the upper extremities' vessels were excluded in the models, the original velocity waveform was scaled down by 15% to account for the flow lost through the branches (Shahcheraghi et al., 2002). The flow rate waveform at the model inlet is shown in Figure 5.4, which was obtained by fitting through velocity

data at twenty-nine time points during a cardiac cycle. The cycle duration was 1.054 s, and the length of the systolic and diastolic periods was 0.413 s and 0.641 s respectively. As the anatomy of the ascending aorta did not change from S1 to S5, the two models had comparable flow parameters at the inlet. The mean and maximum Reynolds numbers were 770 and 3498 respectively, and the Womersley number was 20.8. A low inlet turbulence level of 1.5% was chosen to represent initial disturbances in the flow and allow transition to occur realistically. At the model outlets, a relative static pressure of 0 Pa was applied to both surfaces. All simulations were carried out for three cardiac cycles to achieve a periodic solution (Cebal et al. 2002), and the results of the last cycle were extracted for further analysis. A uniform time step of 0.001 s was used and the same convergence criteria as applied to the multi-case study was adopted.

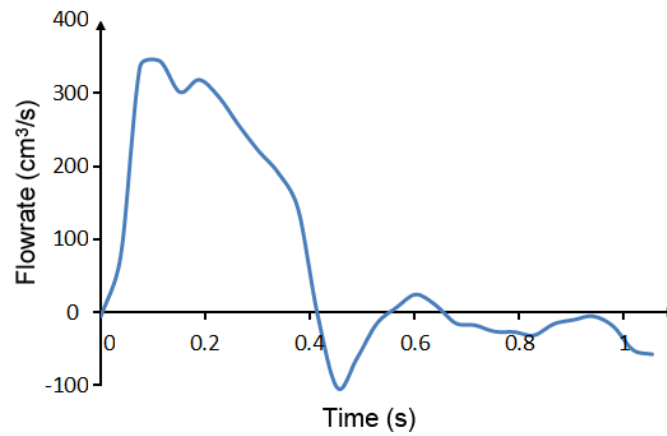


Figure 5.4: Flow rate waveform applied at the inlet of models S1 and S5.

5.4.2 Mesh sensitivity test

The 3D geometries of models S1 and S5 were imported into ANSYS ICEM CFX for mesh generation. 3D tetrahedral cells combined with prismatic cells in the fluid boundary layer at the wall were generated for both models. A very fine near wall resolution and a minimum of ten layers of prismatic elements were ensured to satisfy the requirements of the turbulence and transition model. Enhanced mesh density and local refinement were also applied to the tear region due to the small size and narrow edge of the tear. Mesh independence tests were carried out on both models. The initial mesh contained 1,800,000 elements. This was further refined and the results in terms of maximum wall shear stress (WSS) and turbulence kinetic energy were compared between different meshes. The mesh consisting of 2,400,000 elements for S1 and 2,200,000 elements for S5 was believed to be sufficient for mesh independent simulation results. The results of mesh sensitivity tests are summarized in Table 5.1.

Table 5.1: Results for mesh independence test results showing difference in maximum WSS and turbulence kinetic energy values between meshes.

Model S1			Model S5		
Elements number	Difference (%)		Elements number	Difference (%)	
	Max. WSS	TKE*		Max. WSS	TKE*
1,900,000	4.5	3.5	1,800,000	3.8	3.3
2,400,000	3.9	3.0	2,200,000	3.1	2.5
3,500,000			3,000,000		

*Turbulence kinetic energy

5.5 Results and discussion

The geometric features and anatomy changes of the dissection models, as well as the flow pattern and other time-integrated parameters in terms of time-averaged wall shear stress (TAWSS), oscillatory shear index (OSI) and relative residence time (RRT), were derived from flow simulations.

5.5.1 Geometric features

As can be seen from Figure 5.2, models S1 and S5 have less complicated geometries compared to the other cases described in the multiple cases study. The ascending aorta, abdominal aorta and aortic arch have been normal without visible changes over time. The descending aorta is quite straight without any abnormal tortuous sections, and no obvious narrowing of the true lumen can be found. The false lumen is on the posterior side and parallel to the true lumen along the entire descending aorta. It extends upward beyond the primary tear and with its top being close to the left subclavian artery at the initial scan. The two lumens are not merged before the iliac bifurcation as the false lumen extends down into the common iliac arteries bilaterally and into the right external iliac artery.

The most significant change happened in the false lumen. During Stage I, from S1 to S4, the top part of the false lumen gradually vanished due to the formation of thrombus in this region. Thrombus began to form on the inner side at the top of the false lumen first, which extended to the entire region above the tear in less than 3 months. The process of

thrombosis in the false lumen continued in Stage II. The region distal to the primary entry tear became partially occluded from S5 to S8, while the area opposite the tear remained patent over time. The downstream part of the false lumen had no sign of narrowing and thrombus accumulation.

Another noteworthy change is about the tears. In this case, the primary entry tear occurred at the inner curvature of the distal aortic arch, 32 mm below the arch top. The size of the tear was only 1.9 mm at the initial scan. And then, the size increased rapidly during Stage I and reached 2.93 mm at scan S4. From S4 onwards, although the primary tear was slightly enlarged during Stage II, it has stabilised with a maximum value of 3.24 mm. The variations of the primary tear diameter are shown in Figure 5.5.

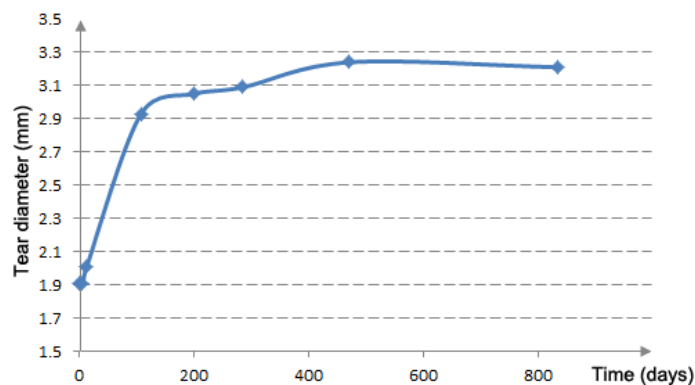


Figure 5.5: Variation of primary entry tear diameter over time.

A secondary entry tear was noticed from scan S5. The diameter of the secondary tear was 4.5 mm, which was larger than the primary tear, but no further enlargement was found in subsequent surveillance. The location of the secondary tear is about 90 mm distal to the primary tear in the middle of the thoracic descending aorta. The thrombosis process in Stage II mainly occurred between the primary and secondary entry tears in the false lumen.

5.5.2 Flow pattern

The flow patterns in the dissection models are displayed by particle path lines which track the motion of passive particles in the fluid domain over several cardiac cycles. About 200 uniformly distributed particles were emitted from the inlet at the beginning, and the paths of these particles were tracked for 18 cardiac cycles to allow enough time for some particles to enter into the false lumen and reach the downstream part of the descending aorta. Figures 5.6 and 5.7 present the particle paths of blood flow in models S1 and S5 respectively with color indicating velocity values.

From Figure 5.6, it can be seen that the flow is fairly organized in the ascending aorta and true lumen. The flow begins to accelerate from the distal aortic arch where the true lumen is partly compressed by the false lumen, and keeps at a relatively high velocity throughout the true lumen. About 6.1% of the blood enters the false lumen through the primary tear. The flow jets into the false lumen along its posterior side of the wall imposing a zone of disturbance and recirculation in the thoracic section of the false lumen. A small quantity of fluid goes up to the superior region of the false lumen along the left side of the wall, while most of flow keeps swirling until reaching further downstream. After 18 cardiac cycles, the particles going to the true lumen have all flown out of the domain through the outlets rapidly, but only a few particles enter the abdominal false lumen and at very low velocity. The final positions of particles in the false lumen are mostly in the thoracic section, indicating a prolonged residence time in this area. Helical and recirculating flow dominates in the false lumen.



Figure 5.6: Particle paths of blood flow in aortic dissection model S1 from different view angles.

As shown in Figure 5.7, the flow pattern in the ascending aorta and true lumen of model S5 is also well organized with no abnormal features. Flow in the false lumen is highly helical with strong secondary motion. The enlarged primary tear allows an increased amount of flow, which is about 11% into the false lumen. This jet of flow, being accelerated when passing through the primary, impinges on the posterior surface of the false lumen and swirls down along the wall. Hence the top part of the false lumen is filled with clock-wise helical flow. The presence of a secondary tear causes an additional 20% of the aortic flow to enter the false lumen after the primary tear. Again, the blood jets through the secondary tear and hits the opposite wall, inducing disturbance in the middle section of the false lumen. Part of the flow goes upwards, whereas the rest moves

down along the posterior wall. In the middle section between the primary and secondary tears, only a small quantity of flow goes to the region near the left and anterior side of the false lumen wall.

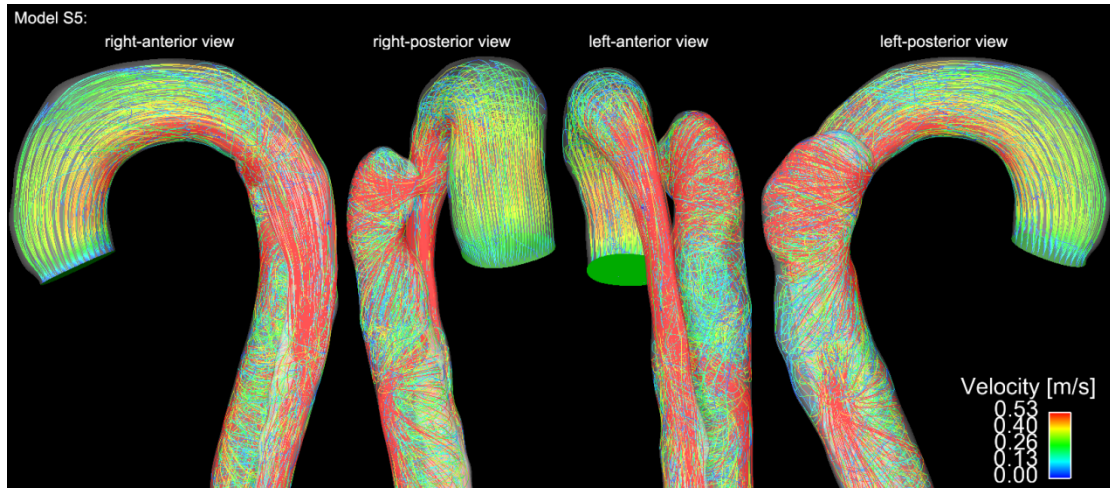


Figure 5.7: Particle paths of blood flow in aortic dissection model S5 from different view angles.

5.5.3 Wall shear stress analysis

The wall shear stress and oscillatory shear index (OSI) in models S1 and S5 are analyzed in correspondence to the geometries reconstructed from their subsequent scan: models S2 and S6, with an aim to examine whether there is any association between wall shear stress derived parameters and observed geometry changes.

Figure 5.8 presents the TAWSS and OSI distribution on the lumen surface of model S1. The edge of the primary tear experiences extremely high TAWSS with an average value of 22 Pa where persistent flow scours through with high velocity. The highest TAWSS value in the model is 50 Pa located on the top surface of the tear. A jet of fluid from the tear surges into the false lumen, impinging on the inner surface of false lumen and inducing an area of high TAWSS (>15 Pa) on the right and posterior wall opposite the tear. Around this area, the recirculating flow in the false lumen section near the tear, caused by the fluid jet, generates a moderately high TAWSS region which spreads to the left side of the surface. The accelerated flow in the partially compressed true lumen also results in moderately high TAWSS on the true lumen especially in the area around the tear. Low (nearly 0 Pa) and less variable TAWSS is found in the superior region of the false lumen due to sluggish flow.

The OSI map shows moderate values on most of the ascending aorta with localized high values due to flow reversal caused by the vessel curvature. The left posterior surface of the false lumen, where TAWSS is high, has very low OSI of nearly 0. A localized high OSI area can be seen on the left surface of the superior region of the false lumen due to low and stagnant flow in the area. The low velocity flow in the downstream section of the false lumen also leads to regions of moderately high OSI on the surface.

Comparing the geometry between S1 and S2, the most noticeable change is the much reduced false lumen in the top section as a result of thrombus formation (indicated by arrows in Figure 5.8). At the same location, extremely low TAWSS and high OSI can also be found. Scan at S2 was taken seven days after S1. During this short period, the abnormal wall shear stress condition in the top section of the false lumen might have contributed to the formation and growth of thrombus in this region.

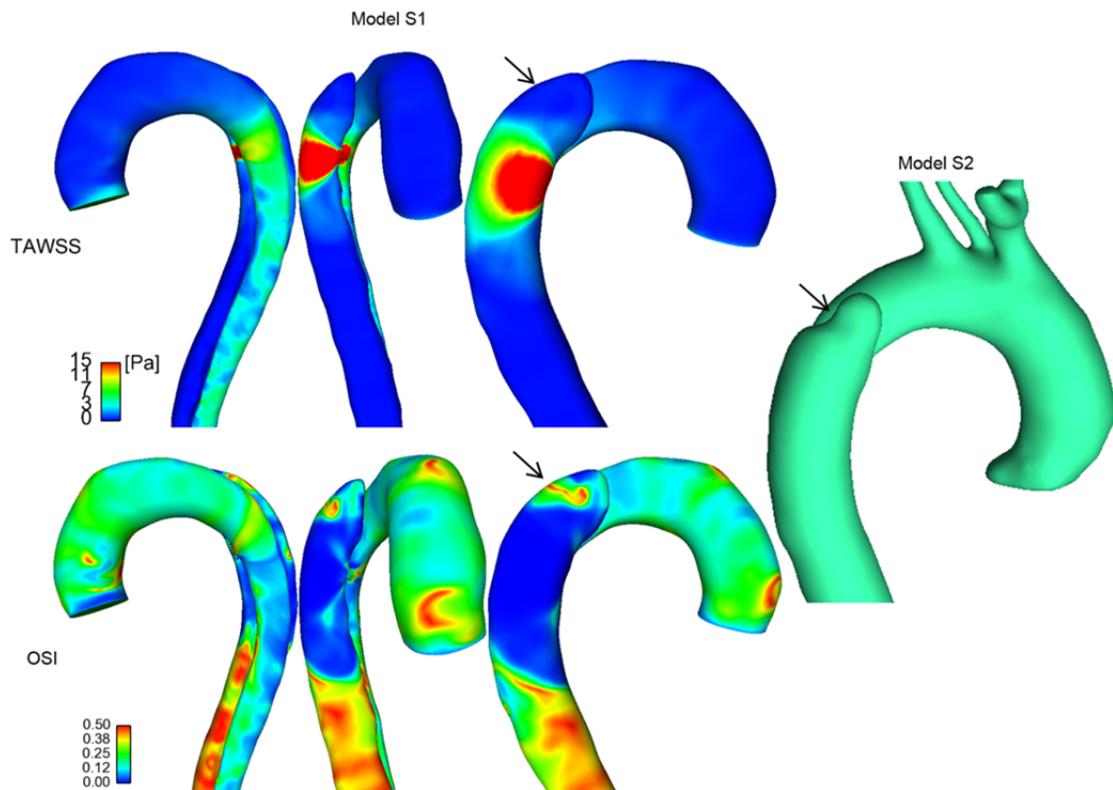


Figure 5.8: Left: TAWSS (top) and OSI (bottom) contours in model S1 from three different views. Right: aortic lumen geometry of model S2. The arrows indicate the thrombosed region in model S2 and the corresponding area in S1.

The distribution of TAWSS and OSI in model S5 is also examined (Figure 5.9). At this stage, the top part of the false lumen has almost completely thrombosed. The highest TAWSS of 18 Pa is also found on the edge of the primary tear, and the mean TAWSS

along the tear surface is around 12 Pa. The fluid flowing into the false lumen produces moderately high TAWSS (around 10 Pa) on the posterior surface. The flow swirling down along the surface in clockwise direction induces TAWSS of 3 Pa on the left anterior surface of the superior section of the false lumen, but leaves the downstream region at the left side, which is not on the path of flow surge, a very low TAWSS (<1 Pa). The other jet of flow entering the false lumen through the secondary tear results in a moderately high TAWSS (7 Pa) on the posterior surface opposite the secondary tear. The ascending aorta in model S5 experiences a similar level of TAWSS as in model S1, and localized areas of moderately high TAWSS appear in the true lumen due to accelerated flow caused by its compressed size.

Retrograde flow in the ascending aorta and aortic arch owing to the geometric curvature and the nature of flow waveform introduces more spatial variation in OSI. The rather frequent change in flow direction as shown in the waveform (see Figure 5.4) indicates that OSI in the ascending aorta cannot be low. The isolated regions of high OSI spots in this area, which can be observed in Figures 5.8 and 5.9, may also be related to surface irregularity. Corresponding to the high and moderately high TAWSS regions, very low OSI values can be found on the posterior surface of the false lumen. Between the primary and secondary tears, an area of high OSI up to 0.5 is present at the right side surface indicating unsteady flow reattachment in this region. The top region of the false lumen also experiences very high OSI value, where the TAWSS is low.

Comparing models S5 and S6, it is clear that the top region of the false lumen above the primary tear observed in S5 has completely disappeared in S6. The formation of thrombus also happened on the right side of the false lumen just above the secondary tear, thereby narrowing the false lumen. Compared with the TAWSS and OSI distributions in model S5, these two regions also endure very low TAWSS and significant OSI. This finding is consistent with that drawn from the analysis of models S1 and S2.

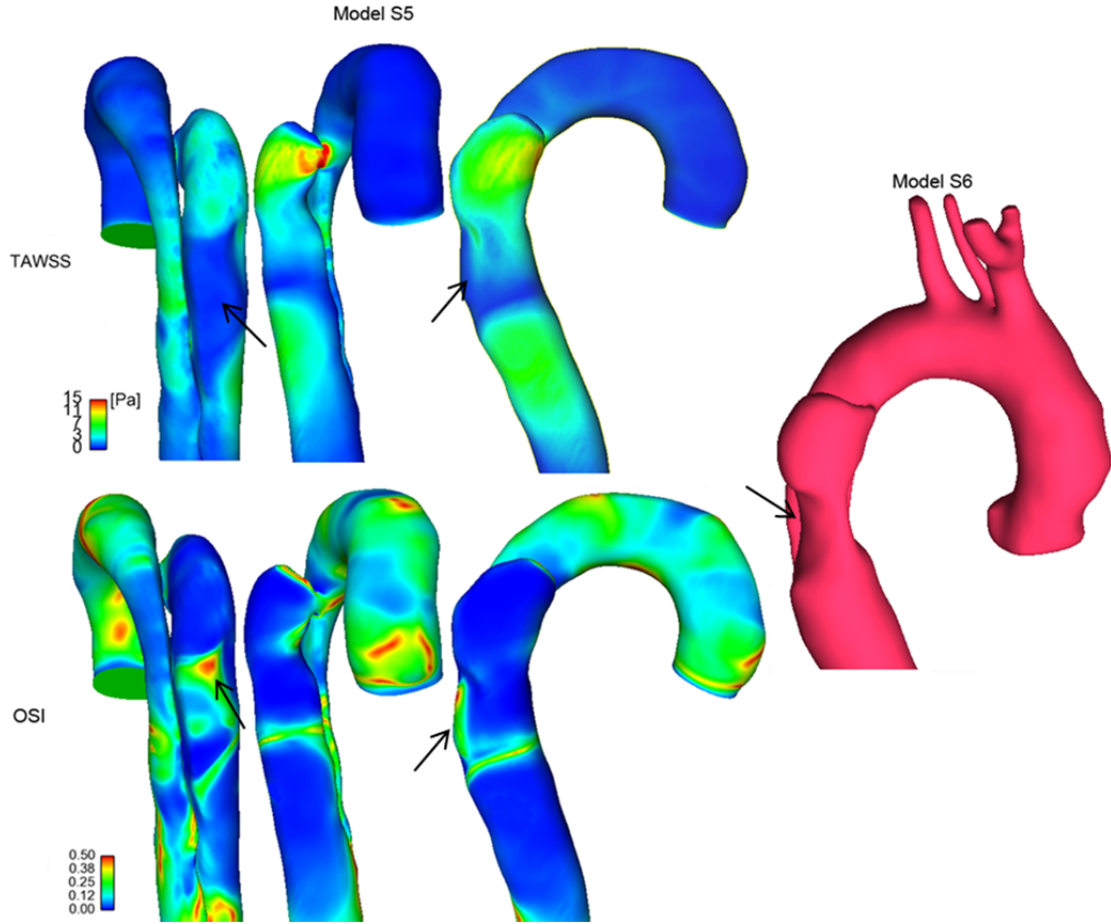


Figure 5.9: Left: TAWSS (top) and OSI (bottom) contours in model S5 from three different views. Right: aortic lumen geometry of model S6. The arrows indicate the thrombosed region in model S6 and the corresponding area in model S5.

Another geometric change observed by comparing models S1 and S5 is the enlargement of the primary tear from 1.9 mm to 3.1 mm. Referring to the variation of tear diameter with time as previously shown in Figure 5.5, the rate of increase in tear size is much slower and more stable in the second stage than stage I. On the other hand, comparison of TAWSS in both models revealed a much higher TAWSS in model S1 (50 Pa) than in S5 (15 Pa). High wall shear stress could affect endothelial cell functions, wall remodeling, and matrix degradation (Lehoux et al. 2006; Li et al. 2005). It is speculated that the excessively high TAWSS in S1 might lead to degeneration of the wall around the tear, thereby enlarging the tear size.

5.5.4 Relative particle residence time

Residence time of solutes and formed elements of the blood in the neighborhood of vascular endothelium has been shown to be important in the polymerization of fibrin,

clot formation under flow conditions and vascular permeability modulation (Reininger et al. 1995; Tozer et al. 1997; Himburg et al. 2004). Therefore, it is believed to be important to also evaluate the residence time of particles near the inner surface of the aorta in the dissection models.

Residence time, referring to the duration that a particle spends at a particular site, is a relative concept, as all non-adherent particles in the flow are moving and, thus, have zero “residence time” at any location (Himburg et al. 2004). As illustrated in Himburg et al.’s paper, the residence time can be expressed in terms of the Cartesian distance, $\delta(y)$, the travel distance of a fully entrained particle locating at a small distance y from the wall during a cardiac cycle. Thus the residence time, t_r , of such a particle is proportional to δ^{-1} . When near the wall, the excursion of the particle is small enough that the spatial variation in shear can be neglected (Himburg et al. 2004). Incorporating the equation for TAWSS and OSI, described in Chapter 3, the $\delta(y)$ can be expressed as

$$\delta(y) = \left| \int_0^T u(y) dt \right| = \frac{y}{\mu} \left| \int_0^T \tau_w dt \right| = \left(\frac{Ty}{\mu} \right) (1 - 2 \times OSI) \cdot TAWSS \quad (5.1)$$

where T is the cycle duration, μ is the dynamic viscosity. For any arbitrarily small value of y , the term $\frac{Ty}{\mu}$ is a constant, hence

$$t_r \sim \frac{1}{\delta} \sim [(1 - 2 \times OSI) \cdot TAWSS]^{-1} \quad (5.2)$$

Himburg and co-workers (2004) proposed $t'_r = [(1 - 2 \times OSI) \cdot TAWSS]^{-1}$ as relative residence time that combines the OSI and TAWSS variables. It should be noted that t'_r is not the exact residence time as it is calculated based on $TAWSS$ and OSI . This variable could be a useful measure of the shear environment for correlative purposes regarding the level of the shear and its oscillatory character. Figures 5.10 and 5.11 show the relative residence time (RRT) contours mapped onto the lumen surface of model S1 and S5 respectively.

Regions of curvature in the ascending aorta and aortic arch may experience flow reversal and possible flow separation, thus causing longer RRT at the right side of the ascending aorta just above the aortic root and the aortic arch top in both models S1 and S5. The true lumens in both models have very low RRT values as the flow follows a fairly straight path without any recirculation. The distribution of RRT shows different patterns in models S1 and S5. Markedly longer RRT on the right superior side at the top of the false lumen is observed in model S1, where a large area of long RRT can also be seen in the downstream segment of the false lumen. In model S5, most of the false lumen surface presents a very small RRT close to 0, except a narrow area on the false lumen top and an

area of moderate RRT with spots of focally long residence time at the left side and the posterior side in the middle of the thoracic false lumen.

Geometries of models S2 and S6 are also shown for comparison. The areas which are thrombosed in models S2 and S6 (indicated in Figure 5.10 and 5.11), have longer RRT which might have contributed to the deposition of platelets leading to thrombus formation in these locations.

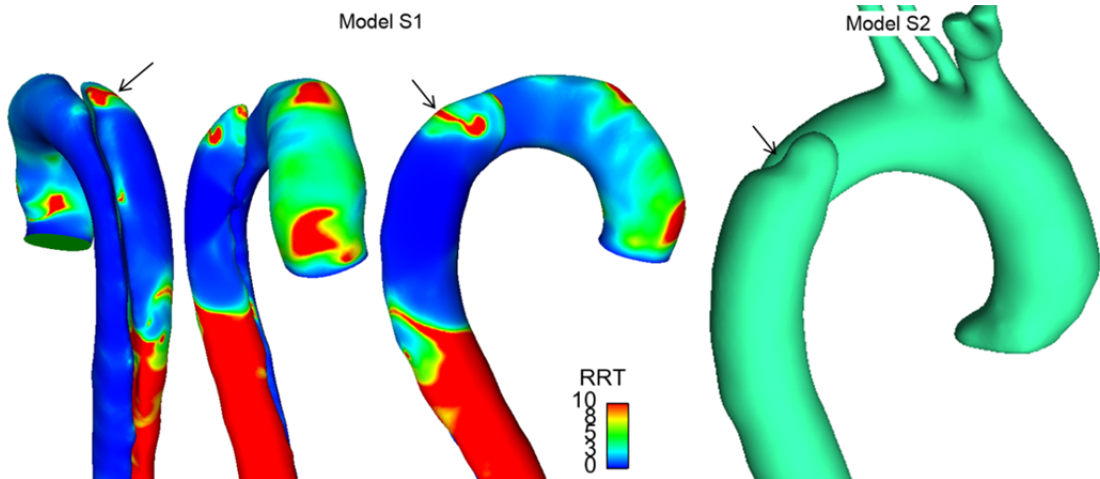


Figure 5.10: Left: Relative residence time (RRT) contours in model S1 from three different views. Right: aortic lumen geometry of model S2. The arrows indicate the thrombosed region in model S2 and the corresponding area in model S1.

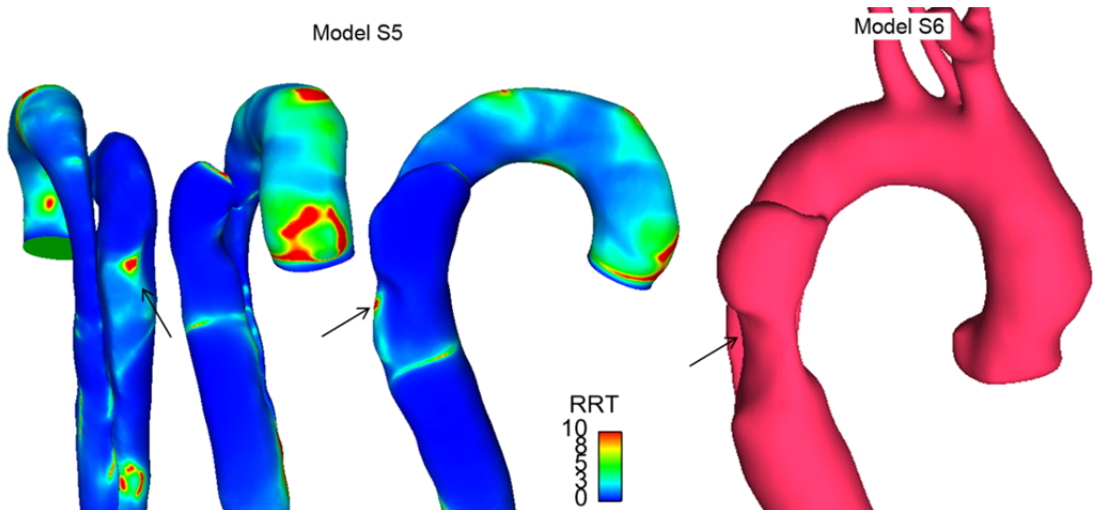


Figure 5.11: Left: Relative residence time (RRT) contours in model S5 from three different views. Right: aortic lumen geometry of model S6. The arrows indicate the thrombosed region in model S6 and the corresponding area in model S5.

5.5.5 Turbulence intensity

The isosurfaces of turbulence intensity (Tu) levels at the peak systole and mid-systolic deceleration phase in model S1 are presented in Figure 5.12. At peak systole (0.1 s), the jet of fluid from the tear impinges on the right-posterior surface of the false lumen, causing flow recirculation and separations induced high Tu levels. The Tu levels are approximately 8% near the primary tear in the left-posterior region of the false lumen. At the mid-systolic deceleration phase (0.3 s), partly because of the lower instantaneous time-mean velocity used in calculating Tu, the Tu level of 8% is observed in the entire segment of the false lumen from the top until the middle of the thoracic segment. The turbulence intensity can reach 60% at both peak systole and mid-systolic deceleration phases distributing a local area of high turbulence intensity near the posterior surface. About 8% turbulence intensity is also found in the downstream segment of the true lumen at mid-systolic deceleration phase. The turbulence intensity in other regions of the dissection lumen is low.

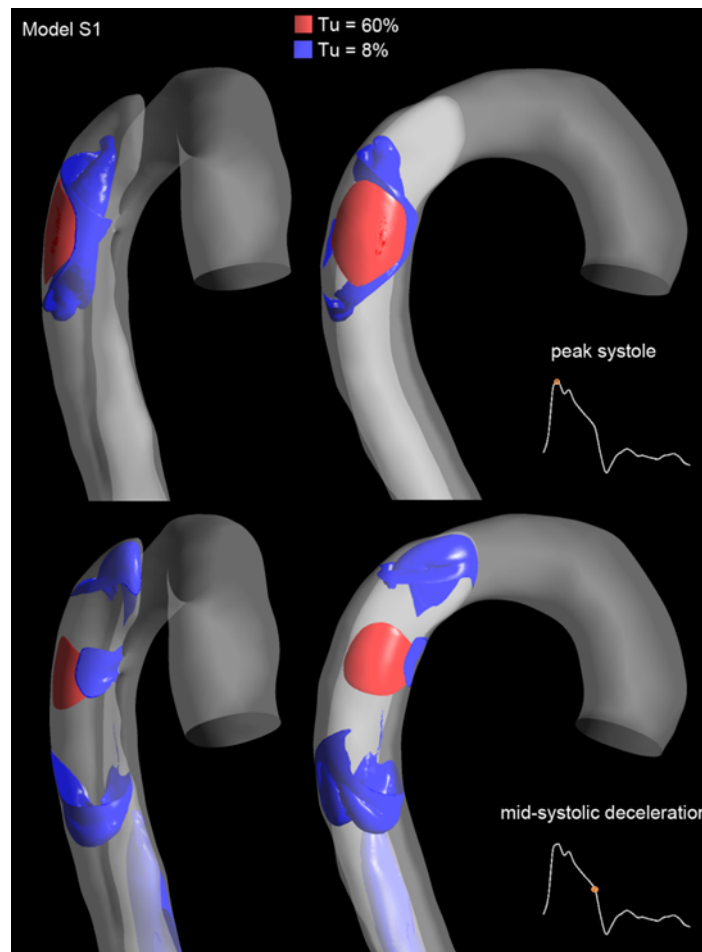


Figure 5.12: Turbulence intensity isosurfaces of the aortic dissection model S1 at peak systole (top) and mid-systolic deceleration (bottom).

Figure 5.13 presents the turbulence intensity levels in model S5. Because of the presence of two entry tears, two regions of Tu levels of 8% are induced by the flow injected from the true lumen in the vicinity of tears on the posterior surface at peak systole. Areas of high turbulence intensity up to 40% can be found in each region just opposite the tears, however the primary tear causes a larger area of high turbulence intensity than the secondary tear. At mid-systolic deceleration phase, turbulence intensity in the false lumen is much higher than at peak systole, with Tu reaching 60% opposite the tears. A larger area of high Tu level, which is distal to the secondary tear, can be observed in the abdominal false lumen. The same Tu level also exists in the middle segment of true lumen which is proximal to the secondary tear.

Comparing models S1 to S5, the distribution of Tu levels differs owing to changes in anatomy. However, high turbulence intensity ($>40\%$) can be seen in both models at similar locations near the tears. Model S1 has slightly higher turbulence intensities than model S5 at peak systole, and both models have comparable Tu levels in mid-systolic deceleration.

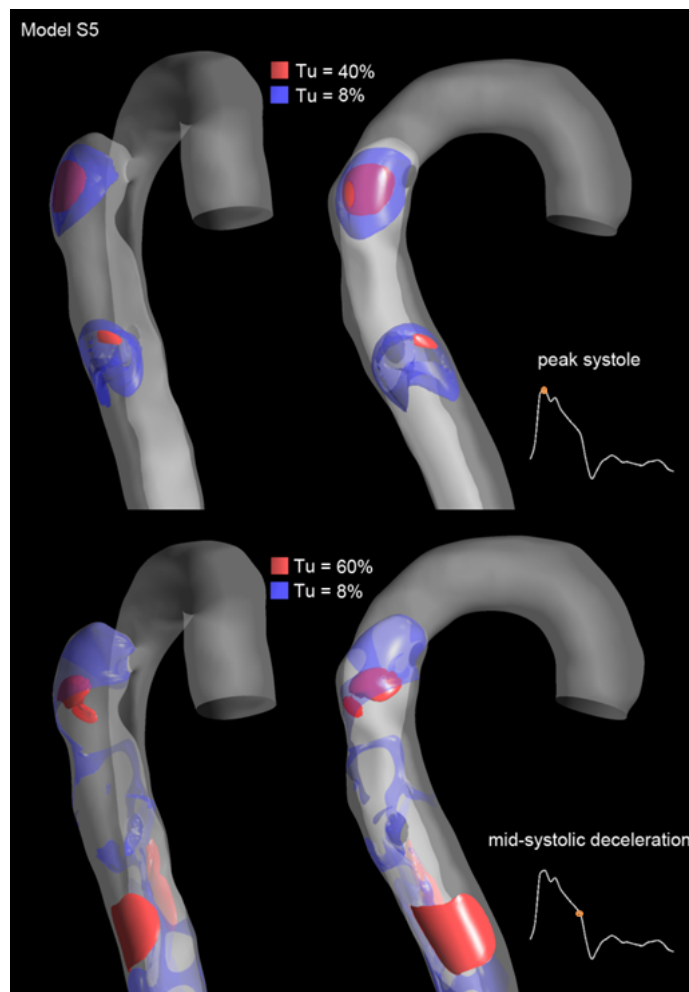


Figure 5.13. Turbulence intensity isosurfaces of the aortic dissection model S5 at peak systole (top) and mid-systolic deceleration (bottom).

5.5.6 Discussion

There is a considerable body of evidence suggesting that haemodynamic factors are involved in the initiation, growth and progression of aortic diseases. Among these factors, WSS at the endothelium has probably received the most attention. Much has been learned about its pathogenic influence in the case of atherosclerosis, where it influences plaque localization, progression and rupture (Malek et al. 1999; Slager et al. 2005; Ali & Schumacker 2002). WSS, which is the tangential stress derived from the friction of the flowing blood along the inner surface of a blood vessel, has been demonstrated to induce morphologic changes in the endothelial lining of the aorta (Fry et al. 1969). As shown in Figures 5.8 and 5.9, extremely high levels of TAWSS (>18 Pa) were found at the tear in the dissection models. During the period between models S1 and S5, significant enlargement of the primary tear diameter occurred. The exceptionally high level of wall shear stress found here suspected to play an important role in the degenerative endothelial lesion at the site. High WSS has been suggested as the main biomechanical factor regulating both neointimal formation and vascular remodeling (Wentzel et al. 2003). It also stimulates the endothelial cells to produce plasmin, nitric oxide and transforming growth factor β causing matrix breakdown by expression of plasmin, matrix—metalloproteinases and smooth muscle cells apoptosis (Lehoux et al. 2006; Li et al. 2005; Slager et al. 2005b). This could lead to weakening of the aortic endothelium, and also cause degenerative lesions of the dissected wall, altering wall thickness even eventual rupture (Ekaterinaris et al. 2006; Sakalihasan et al. 2005). Hence, the high shear stress exerted on the dissected wall around the tear, could lead to further degeneration and erosion in this area, thus causing enlargement of the tear. On the other hand, as the aortic wall is cleaved into two parts in the dissected aorta, the torn wall is severely weakened with compromised elasticity and tensile strength (Butcher 1960). Moreover, Akiyama and his co-workers found an increased expression of matrix metalloproteinase (MMPs) (responsible for matrix degradation) after the onset of aortic dissection (Akiyama et al. 2006), while Wang et al. found increased expression of aortic collagens and connective tissue growth factors (Wang et al. 2006); all of which were expected to reduce the aortic distensibility and systemic compliance. Thereafter, the tear is prone to further enlargement under high WSS. Considering the enlargement rate of the primary tear in the surveillance period, the tear grew more rapidly in Stage I while remained more or less stable in Stage II. Correspondingly,

different maximum TAWSS values were observed in the models indicating that higher WSS may induce more aggressive lesions on the tear. Hence, magnitude of WSS could probably affect the degeneration process of tear.

On the other hand, high wall shear stress has also been associated with platelet activation in blood. Much of the literature regarding the effects of bulk shear stress suggested that shear stress activates platelets either directly or indirectly (Brown et al. 1975; Wurzinger et al. 1985; Kroll et al. 1996). Shear stress at low levels had no measurable effect on platelet, but as the magnitude and exposure duration of WSS were increased, higher activation value could be detected in blood flow (Nobili et al. 2008). Platelets have long been regarded as the preeminent cell involved in pathologic thrombosis. It is also hypothesized that the non-physiological flow patterns and stresses which activate and enhance the aggregation of blood platelets could primarily initiate and maintain thromboembolism (Bluestein 2004). The high WSS at tear site of the dissection models is suspected to activate platelets in the blood flowing through the tear, hence leading to a flow environment more prone to thrombus forming in the false lumen compared to other parts of the aorta.

According to the geometries from each scan presented in Figure 5.2, a continuous formation of thrombus happened in the false lumen during the surveillance period. The thrombus formed mainly in the thoracic segment proximal to the tears. Based on the analysis of wall shear stress described earlier, very low and highly oscillating WSS as well as relative longer residence time could be found at the same sites. The distribution pattern of low and oscillating WSS in regions of low and circulating flow is shown to be closely related to the development of atherosclerotic lesions (Ku et al. 1985). Oscillatory shear stress in contrast to steady laminar shear stress has also been suggested to stimulate atherogenic phenotype and abnormal endothelial cell function, leading to further progression of atherosclerosis (Malek et al. 1999). Recirculating flow in the regions may enhance the delivery of activated platelets and monocytes to the arterial wall where longer residence time increases the likelihood of attachment. The pivotal role of haemodynamic factors in thrombogenesis has also been recognized in thrombosis research. The long residence time has been suggested to be critical for fibrin clot formation (Reininger et al. 1995). Increased plasma levels of the substrate fibrinogen have been implicated as a major factor in thrombus formation (Ernst 1993; Reininger et al. 1994). Moreover, long residence time and low wall shear stress are suggested as major determinants for the polymerization of fibrin under flow conditions (Reininger et al. 1994; Tippe et al. 1993; Friedrich et al. 1994). Hence, the very low

levels of WSS, high OSI and long residence time of flow in localized regions of the false lumen may act together to significantly cause the accumulation of blood clots on the surface of the false lumen, thus, leads to thrombosis in these regions.

Turbulence intensities of 8% can be found in the false lumen with localized high levels up to 40% indicating the presence of turbulence during part of the cardiac cycle. Disturbance and turbulence in blood flow can influence physiological parameters and processes, such as flow resistance, pressure, WSS, wall remodeling, inflammation and mass transport from the blood to the vessel wall (Giddens et al. 1976; Slager et al. 2005). Turbulent blood flow has also been proposed to contribute to thrombus formation (Stein & Sabbah 1974; Bellhouse & Bellhouse 1969) and intravascular haemolysis (Roberts et al. 1975).

The geometry of the dissection model analyzed in this chapter is relatively uncomplicated compared to some of the subjects presented in the Chapter 4. The dissection did not cause major alteration to the main geometrical features of the aorta. Although the true lumen was partially compressed by the false lumen, no significant narrowing or tortuous section could be found. Generally, regions of curvature and non-uniformity experience complicated flow containing regions of low and high mean shear stress as well as areas of flow reversal and possible flow separation. The normal anatomy leads to a relative stable flow conditions in the true lumen. The size of the primary tear is also found to be extremely small which has minimised the amount of flow going into the false lumen. The flow rate at the primary tear was only 6% of the total aortic flow at initial scan. Although the value increased slightly due to enlarged tear size, the flow rate through the primary tear was still very low. Studies found that with limited false lumen flow, thrombus formation was more likely to take place (Eagle et al. 1986; Mohr-Kahaly et al. 1989). A secondary entry tear developed in the middle of the descending aorta. Although the secondary tear induced an additional amount of flow into the false lumen (about 20%), as the location is quite distant from the aortic arch and primary tear, its impact on flow pattern in the proximal thoracic false lumen is minor. However, the progression of secondary tear is important and requires attention and close surveillance. The reason behind the development of secondary tear is not discussed here, as the etiology of tear is related to aortic wall weakening associated with the high wall stress mechanism as well as connective tissue disorders.

5.6 Summary

The role of the hemodynamic parameters identified in the multiple cases study presented in Chapter 4 was further examined in this chapter based on longitudinal data acquired from a single patient. The surveillance period of the patient was divided into two phases with specific geometric changes. The initial CT data of each phase was utilized for CFD simulations. The simulation results, including the wall shear stress distribution, residence time, and turbulence intensity, were analyzed and contrasted with geometric changes of the dissected aorta. The significant enlargement of the primary tear diameter in stage 1 is thought to be a consequent of the high levels of TAWSS acting on the edge of the tear, since as high wall shear stress may induce more aggressive lesions on the tear. The high WSS at the tear site could also active platelets in the blood flowing through the tear, thereby promoting thrombus formation in the false lumen. Very low and highly oscillating wall shear stress as well as longer relative residence time could be found at the same sites where thrombus was formed in the false lumen. A turbulence zone was found with high intensity near the proximal tear, which might also contribute to the rapid thrombosis process in the dissected aorta. The flow rate in the false lumen, which was very low owing to the small size of the entry tear, might also play a part in the rapid thrombus formation observed in this patient. The results shown in this chapter are the first attempt to link hemodynamic parameters with the progression of aortic dissection. Our data provided preliminary evidence for the possible erosion effect of high wall shear stress on the tear, the influence of low and oscillating wall shear stress on thrombosis process, and the correlation between the flow rate and false lumen patency. However, similar studies on a larger scale are required to assess the significance of these findings.

Chapter 6

Model validation using MR flow data

6.1 Introduction

The computational model applied to the patient-specific studies described in the previous two chapters involves a number of assumptions, including exclusion of the aortic arch branches, a flat velocity profile at the inlet, constant pressures at the outlet boundaries, and rigid walls. In order to validate the model, a comparison is made between the computational simulation results and the flow data extracted from 3D phase contrast MR images in this chapter. As introduced in Chapter 2, phase contrast MR flow imaging is probably the only imaging technique that can provide measurement of blood velocities in vivo with good spatial and temporal resolutions. In this chapter, phase contrast MR images were considered as the 'gold standard' for measuring blood flow patterns in dissected aorta.

6.2 Patient-specific model generation

Data acquired from a patient (not involved in the patient-specific studies described earlier) with a typical type B aortic dissection were adopted in this validation study. The patient is male and was 56-year old at the time of first diagnose. He was examined with CT scan initially, and was diagnosed as type B dissection at St. Mary's hospital. The patient was subsequently scheduled for a MR scan for further examination of the dissecting condition.

As shown in Figure 6.1(a), the generation of the model geometry was based on the initial CT images covering the whole aorta. The CT slice thickness is 2 mm, and the spacing between slices is 1 mm. The pixel resolution of the images is 0.86 mm. Approximately 300 slices were needed for the geometry generation. The transparent picture (Figure 6.1(b)) of the aorta is displayed from the right side of the model geometry, from which

the proximal entry tear can be seen clearly. The anatomical MR images of this patient were also available, but due to their relatively low axial resolution, they were only used for registration and localization of imaging planes between the CT and MR data.

Phase contrast MR imaging was performed at three planes in the aortic dissection in order to provide sufficient data for validation while minimizing the scan time for the patient. The parameters of the phase contrast MR scan are given as follows: TE 2.6 ms, TR 4.7 ms, Flip Angle 15 degrees, pixel spacing 1.3281 mm, and 8 mm slice thickness. At the imaging planes 1 and 3, the encoding velocity V_{enc} was 200 mm/s for FH (foot-head) direction and 100 mm/s for AP (anterior-posterior) and RL (right-left) direction. At the imaging plane 2, the V_{enc} was 200 mm/s for AP direction, and 100 mm/s for the other two directions. The locations of the imaging planes are shown on the transparent model in Figure 6.1(b). Plane 1 is located in the proximal ascending aorta in order to obtain velocity profiles distal to the aortic valve. Plane 2 is in the aortic arch between the root of the left subclavian artery and the site of proximal entry tear. Locating this plane was difficult in this case, as the tear occurred very close to the left subclavian artery, leaving very limited space for the imaging plane to avoid either extending to the artery branch or interrupting the entry tear. Flow imaging at plane 2 was used to assess the amount of flow left through the three branches on the aortic arch, as well as velocity profiles prior to the tear. Plane 3 is in the middle of the thoracic descending aorta distal to the proximal entry tear covering both the true and false lumen. The flow data from this plane were used to compare with those from the computational simulation for model validation.

Figure 6.1(c) presents the computational model used for validation, where the inlet coincided with imaging plane 1 in the ascending aorta. To keep the approach consistent with those of the patient-specific studies presented earlier, the validation model was also simplified by excluding the three branches in the aortic arch and other small branches in the descending aorta. As mentioned earlier, the false lumen originated from the proximal site of the left subclavian branch root and propagated down at the lateral side of the thoracic descending aorta. It not only propagated in the longitudinal direction and stayed in parallel to the true lumen, but also expanded in the circumferential direction around the true lumen toward the anterior side of the true lumen at the middle of the descending aorta. The false lumen continued to twist to the right and posterior side of the aorta, and propagated back to the lateral side in the distal segment of the abdominal aorta. As it extended to the left iliac artery below the abdominal bifurcation,

two outlets (one for each lumen) were included in the model, both being located in the abdominal descending aorta far distal to the proximal entry tear as well as the imaging plane 3 (as shown in Figure 6.1(c)). The length of the descending aorta is approximately 381 mm. The diameter of the proximal entry tear is about 22 mm in the circumferential direction and 25 mm in the longitudinal direction, with the tear being only 0.4 mm below the top of the aortic arch. The false lumen didn't propagate upward due to the restriction of the left subclavian artery. No other middle tears could be identified in this case.

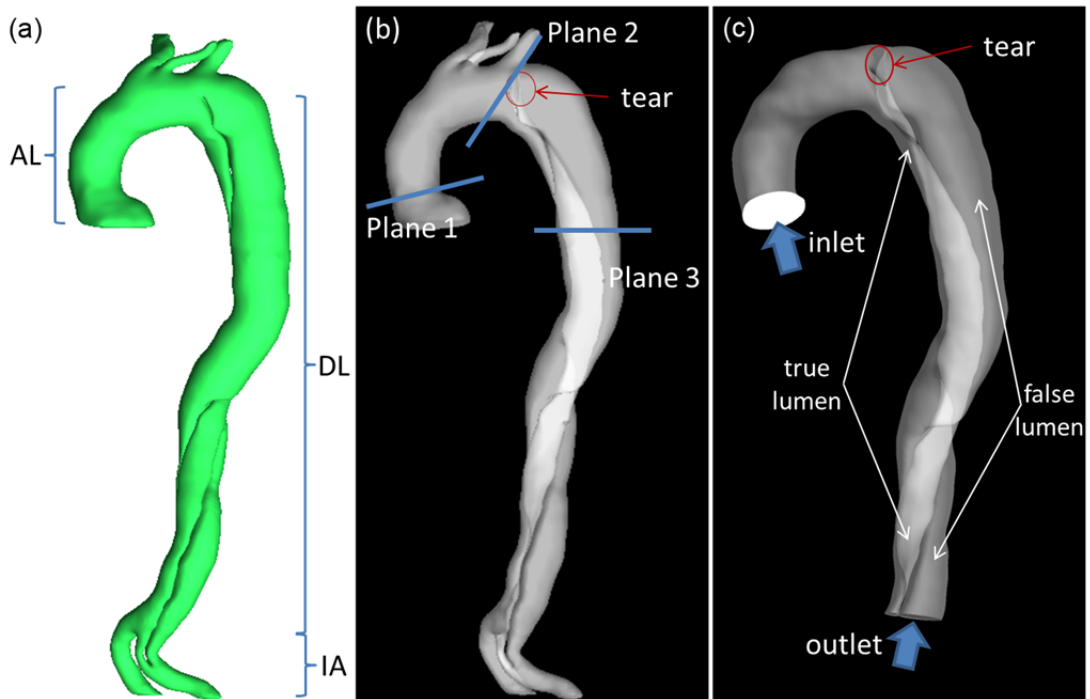


Figure 6.1: Reconstructed geometries of the aortic dissection used in validation. (a) The entire aorta including the ascending aorta lumen (AL), the aortic arch branches, the descending aorta lumen (DL), and the iliac arteries (IA), but excluding the branches off the descending thoracic and abdominal aorta; (b) the locations of three imaging planes where phase contrast MR velocity mapping was acquired, and (c) the computational model used in validation, with arrows indicating the locations of inlet, outlet, tear, false and true lumen.

6.3 Flow simulation

Simulation conditions adopted for the multiple cases and single case studies were also applied to the validation model. These include the SST Tran model to account for possible turbulence effect, a Newtonian assumption for blood with a constant viscosity

of $4.0 \text{ mPa} \cdot \text{s}$ and a density of 1060 kg/m^3 . The aortic walls were assumed to be rigid with no-slip condition. All the simulations of the validation study were carried out in ANSYS CFX 12.

6.3.1 Boundary conditions

Relevant flow boundary conditions used in the simulations were extracted from the patient-specific phase contrast MR images. The flow data at each imaging plane were recorded at 29 time points along a cardiac cycle, and the duration of one cardiac cycle was 0.98 s. The flow rate at imaging plane 1 (ascending aorta root) and imaging plane 2 (aortic arch after the three main branches) were calculated and presented in Figure 6.2. The length of the systolic and diastolic periods was 0.38 s and 0.6 s, respectively. The peak velocity happens at 0.2 s, and the maximum reversal flow velocity at 0.42 s. The maximum flow rate is $446 \text{ cm}^3/\text{s}$ in the ascending aorta, and $370 \text{ cm}^3/\text{s}$ at the aortic arch. Hence, the flow lost through the three main branches on the arch is $76 \text{ cm}^3/\text{s}$, which is about 17% of the total flow rate from the heart. This ratio is close to the value (15%) adopted in the multiple cases and single case study for compensating the flow lost through the upper extremities' branches.

The flow waveform derived from the imaging plane 2 was specified at the model inlet in the ascending aorta with a flat in-plane profile, which was the same as adopted in the patient-specific studies. Based on the inlet area, the mean and maximum Reynolds numbers are 850 and 3512 respectively, and the Womersley number is 10.4. A low inlet turbulence level of 1.5% was chosen to represent initial disturbances in the flow and allow transition to occur realistically. At the model outlets, a relative static pressure of 0 Pa was applied to both surfaces. A uniform time step of 0.001s was used. All simulations were carried out for three cardiac cycles to achieve a periodic solution, and the results of the last cycle were extracted for comparison.

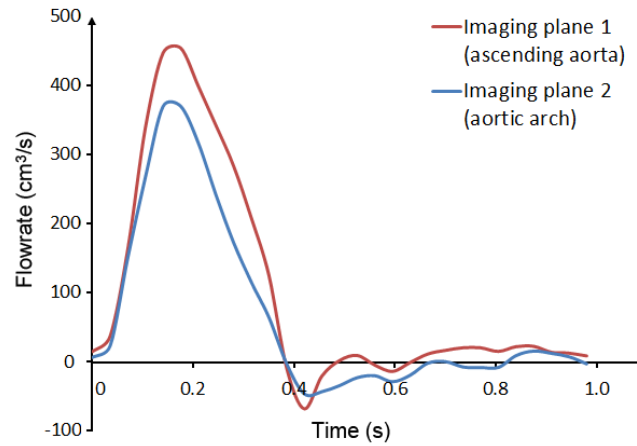


Figure 6.2: The flow rate waveforms at imaging plane 1 and plane 2 as defined in Figure 6.1 (b).

6.3.2 Mesh sensitivity test

The reconstructed model was imported into ANSYS ICEM CFX for mesh generation. Unstructured mesh was assigned to the model with 3D tetrahedral cells combined with prismatic cells in the fluid boundary layer at the wall. A very fine near wall resolution and a minimum of ten layers of prismatic elements were ensured, and enhanced mesh density and local refinement were also applied to the tear region. Mesh independence tests were carried out with an initial mesh consisting of 2,600,000 elements, and finer mesh by increasing the number of elements in the prismatic layer and mesh density. The results in terms of maximum wall shear stress (WSS) and turbulence kinetic energy were compared between different meshes. The differences in these parameters were less than 4% between the initial 2,600,000 elements mesh and a 3,200,000 elements mesh, and less than 3.5% between the 3,200,000 elements mesh and a 4,700,000 elements mesh. Hence, the mesh of 3,200,000 elements was considered to be sufficient for the validation study.

6.4 Results and discussion

The analysis of results includes comparisons for model validation and analysis of hemodynamic parameters in the model based on CFD results. The flow patterns obtained from the simulation were compared with the velocity data extracted from the phase contrast MR images. The flow distribution in the true and false lumen, and the flow velocity profiles at the level of the imaging plane 3 were analyzed and discussed.

6.4.1 Flow distribution in the true and false lumen

Because of the presence of two lumens in the descending aorta in type B aortic dissection, the total flow was divided into the true and false lumen. As found in the multiple cases study, the flow distribution in the two lumens was significantly affected by the size and location of the proximal entry tear based on the assumption of equal pressure at the end of each lumen. The pressure at the outlets could influence the amount of flow into the lumen as it reflects the level of distal resistance to flow in the model domain. The computed flow rates in the true and false lumens were compared with the corresponding MR measurement. Figure 6.3 shows the comparison of time-varying flow rate at the location of imaging plane 3 obtained from the CFD simulation and the corresponding flow rate extracted from MR flow data acquired at imaging plane 3.

In CFD simulation, the maximum flow rate in the false lumen was $293 \text{ cm}^3/\text{s}$, and was $72 \text{ cm}^3/\text{s}$ in the true lumen. Hence, about 80% of the total flow was diverted to the false lumen. As shown in Figure 6.3, the flow rate waveforms from MR images present a similar systolic profile to the CFD simulation with a slightly lower flow rate in the false lumen. Based on the MR data, $269 \text{ cm}^3/\text{s}$ of flow went into the false lumen which comprised about 76% of the total flow. Differences between the computed and measured flow rates exist but these are considered reasonable. A number of factors could have contributed to the differences observed, such as the flow calculation from the phase MR data which could be easily affected by imaging noise, identification of the lumen edge on MR image, and the motion of the flap,.

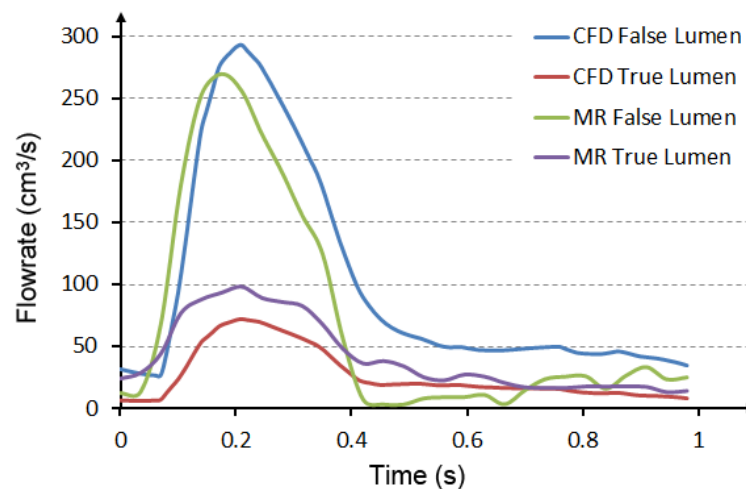


Figure 6.3: The flow rate waveforms of the true and false lumen from both CFD simulation results and phase contrast MR velocity data.

Referring to the relationship between the anatomic features of the proximal entry tear and the flow rate into false lumen concluded in the multiple cases study, the relatively large size of the entry tear and its closeness to the arch top were very likely to have contributed to the large amount of flow into the false lumen in this case. As described earlier, the longitudinal diameter of the proximal entry tear is 25 mm, the ratio of the circumferential diameter of the tear to aorta diameter is about 65%, and the distance between the tear and the arch is 0.4 mm. These geometric and flow parameters fit very well to the linear regression lines obtained in the multiple cases study.

6.4.2 Comparison of velocity profiles

Further comparison was made for the time-varying velocity profiles between the MR measurements and flow simulation at plane 3 (defined in Figure 6.1(b)). As the 3D phase contrast MR images provide the velocity information in three directions at the imaging plane, the comparison was made for all three velocity components. Figures 6.4 – 6.7 present the velocity contours in FH (foot-head), AP (anterior-posterior), and RL (right-left) directions extracted from the MRI data, compared with the computational results at four time points along the cardiac cycle, respectively. In the left column of each figure, the specific time point and the direction of velocity are displayed. Both sets of data are displayed in the foot-head (inferior-superior) direction. The corresponding magnitude image from the phase-contrast MR scan is also included which indicates the shape and size of the false lumen (FL) and true lumen (TL) at plane 3. As can be seen, the false lumen is 4 times larger than the true lumen at this location. The red color represents velocities from head to feet, anterior to posterior, and right to left in the FH, AP, and RL velocity contour maps, respectively, while the blue color represents velocities in the opposite directions. Different color scales are used for different directions and time points according to the range of velocity values.

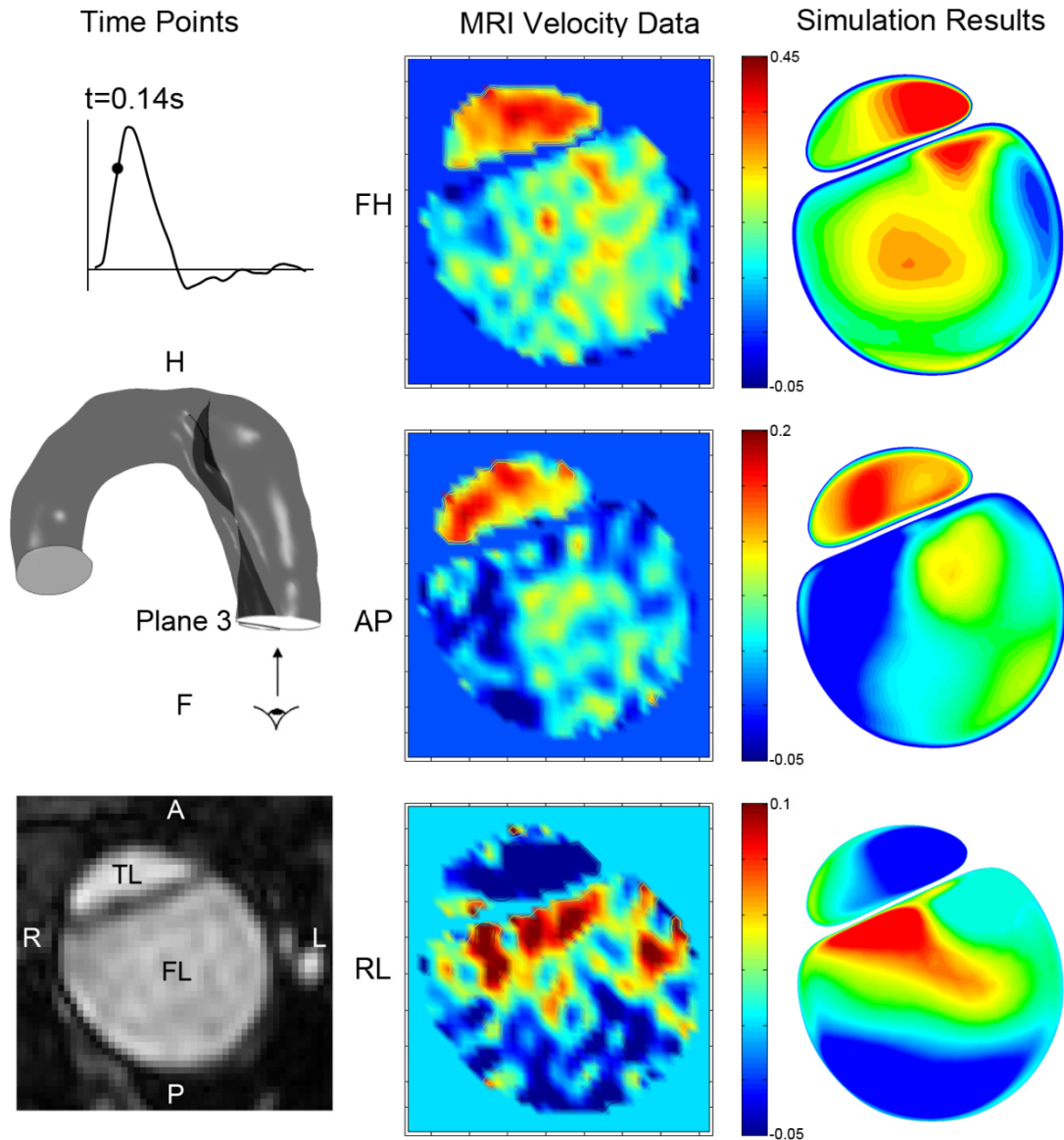


Figure 6.4: Comparison of velocity profiles in FH, AP and RL directions at mid-systolic acceleration phase of the cardiac cycle between MR velocity data (in m/s) and simulation results.

Figure 6.4 presents the velocity profiles at mid-systolic acceleration phase ($t=0.14s$). At this time point, the main direction of the flow was from superior to inferior with a maximum velocity of 0.45 m/s occurring in the true lumen. The high velocity flow was skewed to the left and anterior side of the true lumen due to the curvature of the lumen at this location. The simulation result presented the same distribution in the true lumen area with higher velocity at the anterior and left side and lower in the right side. The flow in the false lumen showed more spatial variation than in the true lumen. The simulation result captured the relatively high velocity at the left anterior side near the

flap and the middle area of the false lumen, as well as a narrow area of reversed flow at the left side. Velocities in the AP and RL directions were lower than in the FH direction. Both the MR data and simulation results presented the flow towards the posterior side in the true lumen with higher value at the right side. In the false lumen, the computational model predicted the velocity component towards posterior at the middle and left posterior area, and towards anterior at the right and right-posterior area. The velocity component in the RL direction was mainly from left to right in the true lumen with a small region of reverse flow at the right-posterior corner and anterior side near the wall, while two main contrary velocity trends in the RL direction existed in the false lumen. The anterior half of the false lumen was dominated by flow towards the left side, and the velocity component in the posterior half towards the opposite direction. The simulation results agreed well with the MR data in velocity profiles by capturing the magnitude and velocity direction in the two lumens. Velocity profiles in the three directions revealed the presence of clockwise helical flow patterns in the false lumen, while the flow pattern in the true lumen was more organized with minor reverse flow at the right posterior corner caused by the curvature of the lumen.

The velocity profiles at peak systole ($t=0.2s$) are displayed in Figure 6.5. The flow patterns in the true lumen at this time point presented a similar distribution to those at the mid-systolic acceleration phase but with a larger velocity magnitude. The simulation results successfully predicted the same velocity profile in the true lumen. The well-organized flow pattern in the true lumen was probably attributed to the compressed lumen area which restricted the occurrence of secondary flow. The flow in the false lumen was more complicated. The main velocity was still pointing down in the interior direction with higher velocity values in the left area. This feature was also found in the simulation result. The velocity components in AP and RL directions changed significantly from the mid-systolic acceleration phase. The AP velocity component was mainly towards the anterior direction with reverse flow in the middle anterior and posterior area, which was correctly captured by the computational simulation. The velocity component in the RL direction was quite disturbed. The simulation results had caught the positive flow in the right anterior area and negative flow in the left area, but failed to present the flow towards right in the area of posterior side. This was probably owing to the small velocity component (<0.1 m/s) in the RL direction at this time point, which was suggested to be affected by the MR velocity uncertainties (Wood et al. 2001). The flow pattern in the false lumen at peak systole is likely to be highly disturbed and even turbulent based on the non-uniform velocity profiles of AP and RL components.

The simulation results were found to have captures the most important flow characteristics presented by MR images at this time point.

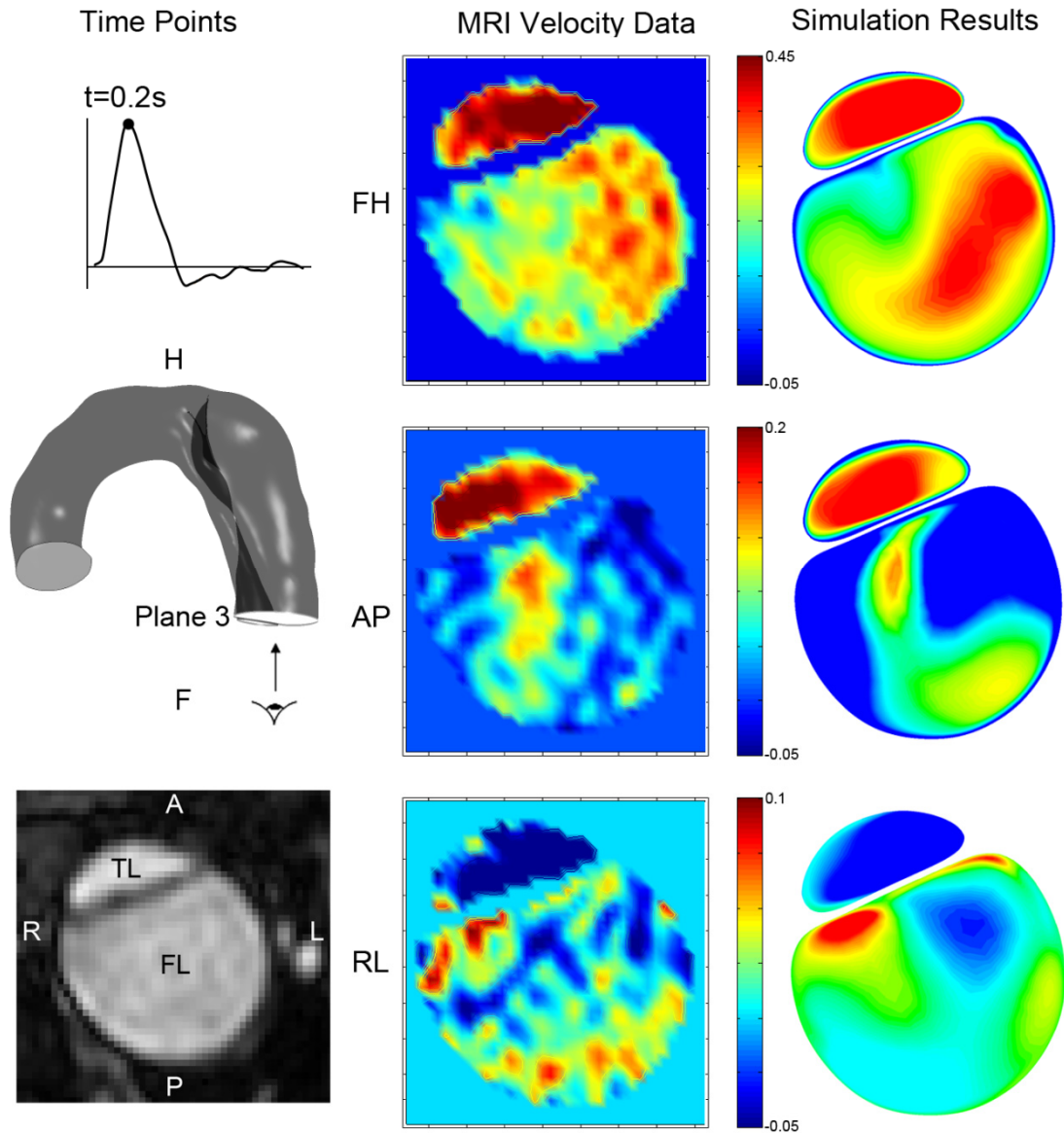


Figure 6.5: Comparison of velocity profiles (in m/s) between MR velocity data and simulation results in FH, AP and RL directions at peak phase of the cardiac cycle.

Figure 6.6 presents the velocity comparison at mid-systolic deceleration phase ($t=0.32s$). The flow in the true lumen was mainly moving downwards in the inferior direction. The flow pattern was similar to those at mid-systolic acceleration and peak systole. The simulation results have captured the main flow characteristics in the true lumen, including the detailed velocity gradient and changes in local areas, such as the decreased FH velocity component at the right and anterior side, the decreased AP velocity component at the left side, and small area of reversal RL velocity component in

localized area of the right and right anterior side. Moreover, the simulation results also successfully predicted the velocity distribution in the false lumen. The flow recirculation in the FH direction could be found. Unlike velocity profiles at the previous two time points, the flow was moving down along the right and posterior side of the false lumen, while reversed flow could be observed in the left anterior area. In the AP direction, as most flow was moving towards the anterior direction, a localized area near the posterior wall of the false lumen was dominated by flow in the opposite direction from posterior to anterior. The RL velocity component was in the left direction in the anterior half of the false lumen with the maximum value in the middle, and was in right direction at the right posterior and posterior side. Hence, flow at the mid-systolic deceleration phase was not only swirling helically in clockwise direction, but also included retrograde flow along the left anterior wall of the false lumen. As can be seen from Figure 6.6, the velocity profile calculated from computational results matched well with the MR velocity data.

The comparison of velocity profiles between the MR measurement and simulation results was also carried out for an early diastole phase when the maximum reverse velocity occurred in the proximal ascending aorta ($t=0.4s$) (as shown in Figure 6.7). The true lumen was dominated by flow in the inferior direction. The velocity component in the AP direction remained in the posterior direction with a mean value around 0.1 m/s. The RL velocity components were very small with negative flow in the right direction at the left side of the true lumen. In the false lumen, the FH velocity component continued the similar pattern as observed at the mid-systolic deceleration phase but moved slightly in clockwise direction with higher velocity in the right and right posterior area of the false lumen. The reversed flow was located in the left half of the lumen with increased velocity magnitude of 0.25 m/s compared to the mid-systolic deceleration phase. The area with posterior velocity component expanded to the left side of the false lumen. The profile of the RL velocity component still included the positive flow region in the anterior half, and negative flow in the posterior half of the false lumen. The elevated flow in the left direction was concentrated along the flap with a maximum value above 0.2 m/s. Figure 6.7 demonstrated that the simulation results and MR velocity data were in a good agreement at the early diastolic phase.

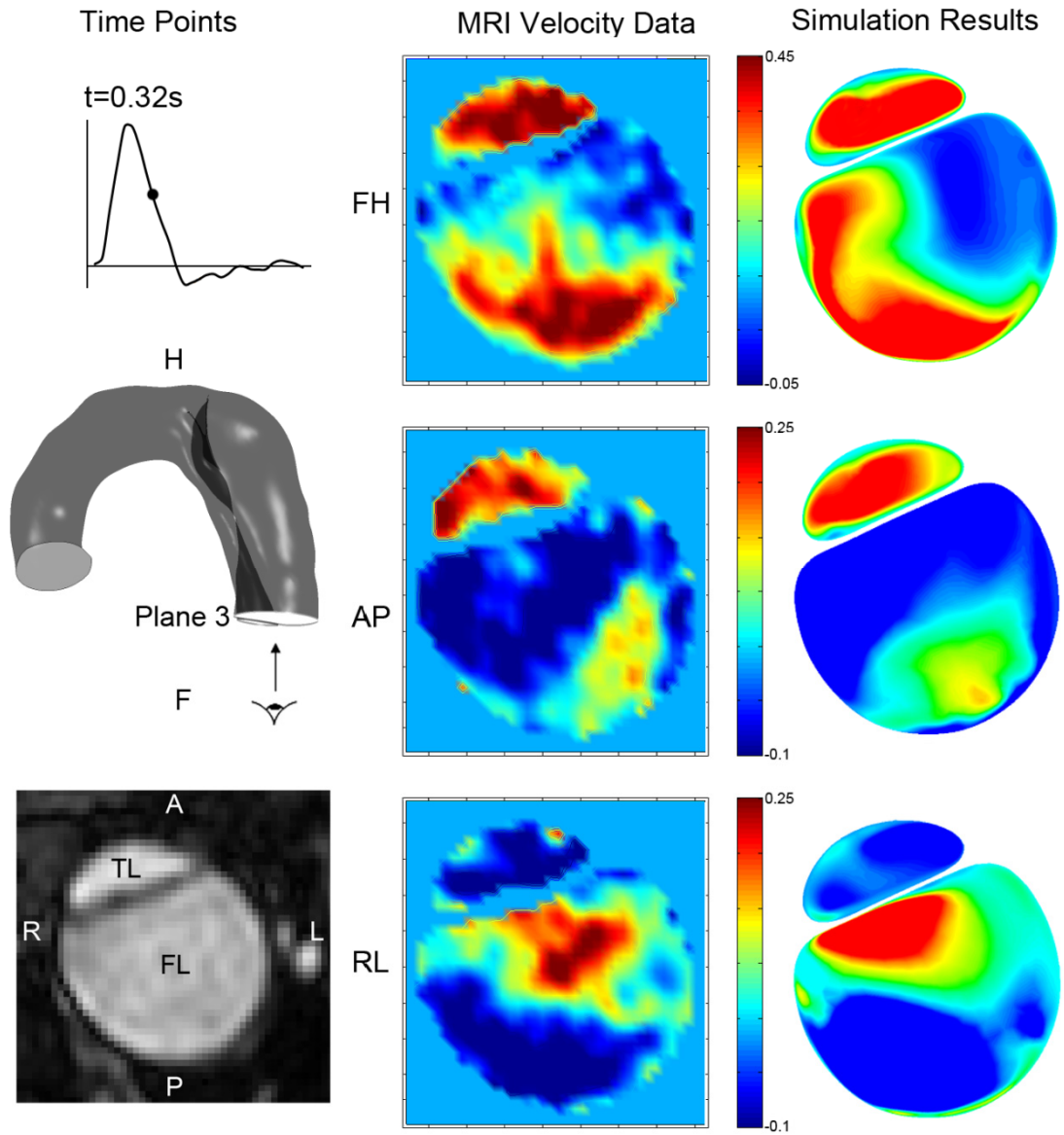


Figure 6.6: Comparison of velocity profiles (in m/s) between MR measurement and simulation results in FH, AP and RL directions at systolic deceleration phase of the cardiac cycle.

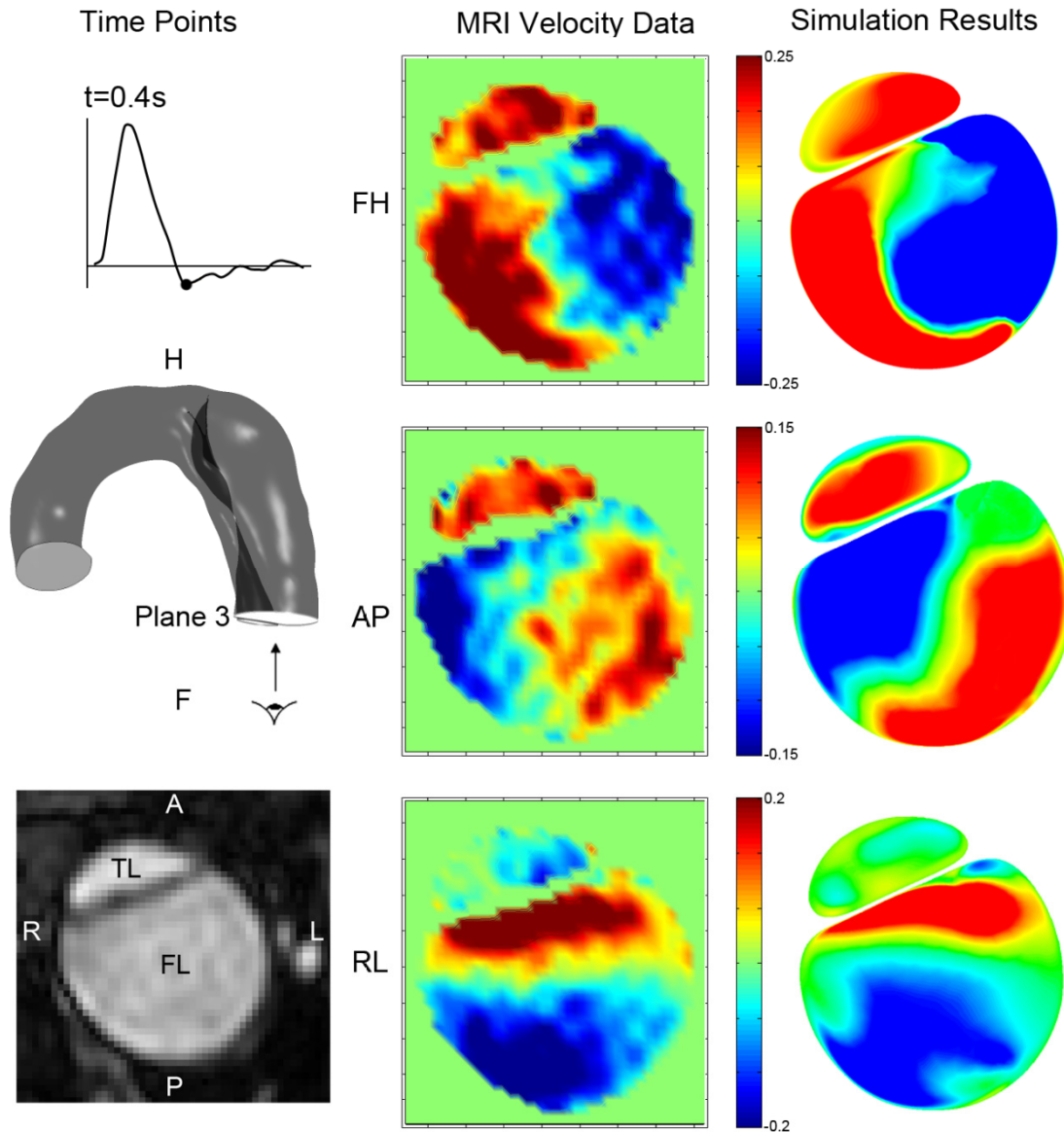


Figure 6.7: Comparison of velocity profiles (in m/s) between MR measurement and simulation results in FH, AP and RL directions in early diastole when the reverse flow is at the maximum.

6.4.3 Analysis of flow pattern and haemodynamic parameters

The validation study was accomplished by comparisons of flow distribution in the two lumens and velocity profiles in the descending aorta between the MR velocity data and computational simulation results. In order to obtain a complete picture of the flow patterns and haemodynamic situation in this model, the simulation results were further analyzed.

Figure 6.8 presents the particle paths in the model over 12 cardiac cycles. Around 100

particles were emitted at the inlet in the beginning. The pathlines suggested a complicated flow pattern in the dissected aorta. Retrograde flow could be seen in the aortic arch, which was caused by the vertical flap at the distal arch. Most of the flow went into the false lumen through the proximal entry tear along the anterior wall of the aortic arch, while the rest into the largely compressed true lumen. The false lumen was four times larger than the true lumen, and formed a bulge at the proximal region of the entry tear. As discussed in the last section, both the MR data and simulation results predicted a fairly organized flow pattern in the true lumen and highly disturbed flow with strong recirculation in the false lumen. The flow characteristics can also be obtained from the pathlines displayed in the figure. The flow was accelerated rapidly when passing through the tear, and rushed onto the left and anterior wall of the false lumen opposite the tear. It is obvious that the flow was almost straight forward in the true lumen, while the false lumen was dominated by helical and retrograde flow especially in the upper part where the imaging plane 3 was located.

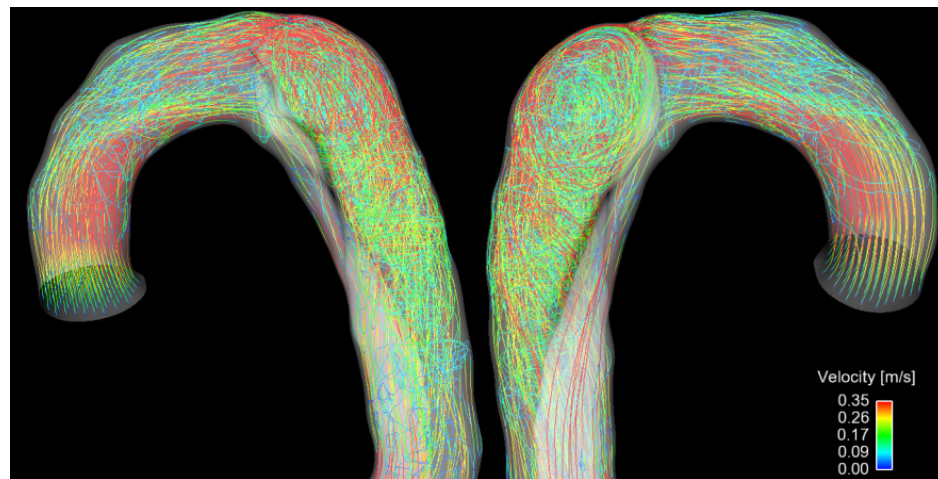


Figure 6.8: Particle paths of blood flow in the validation model from right anterior (left) and left posterior (right) view angles.

The TAWSS and OSI contours on the lumen wall of the dissected aorta are displayed in Figure 6.9. The TAWSS contours show the highest value of 11.3 Pa on the edge of the entry tear, which is consistent with the TAWSS distribution patterns of the other patient-specific models analyzed in the study. A moderately high TAWSS can be found on the anterior surface of the false lumen bulge where the flow impinged on after passing through the tear. Moderate TAWSS values can be found on the lateral surface of the false lumen and the downstream part of the true lumen, while the other part of the model experienced normal or low TAWSS around 0.2 Pa. The flow reversal and

recirculation induced large region of high OSI values of up to 0.5. The organized flow has led to a quite uniform and less variable OSI pattern in the true lumen. Corresponding to high TAWSS values, the tear and the anterior wall of the false lumen bulge present a region of low OSI values close to zero. The curvature of the arch induced flow reversal and directional changes presenting a moderate OSI value with a number of localized areas of zero value. The posterior surface of the false lumen bulge and the anterior surface of the distal false lumen experienced high OSI owing to the unsteady flow reattachment.

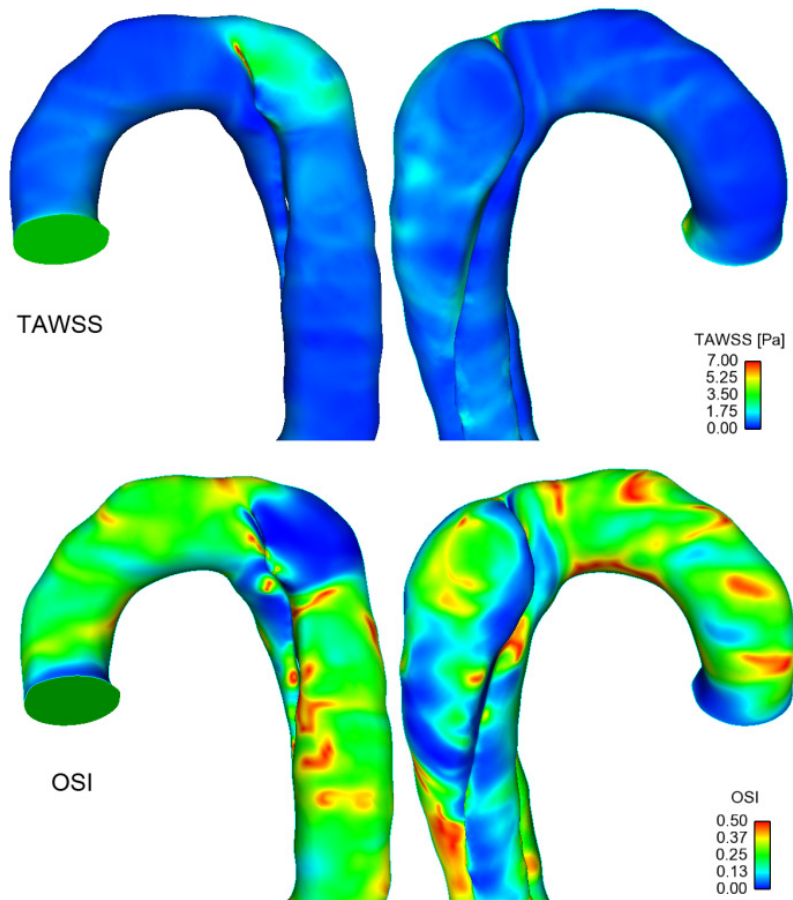


Figure 6.9: TAWSS (top) and OSI (bottom) contours in the validation model from right anterior (left) and left posterior (right) view angles.

Based on the complex velocity profiles demonstrated by both the MR data and simulation results, the flow in the validation model was highly disturbed, and may even become transitional and turbulent in the false lumen. Owing to the application of SST Tran model, the turbulence characteristics of the flow was also analyzed. Figure 6.10 shows the isosurfaces of Tu levels at the mid-systolic deceleration phase. The velocity profiles have proved the presence of retrograde and highly helical flow in the false

lumen at this time point. As can be seen from Figure 6.10, a large region of Tu levels of 5% was located in the upper part of the thoracic false lumen. The Turbulence intensity can reach 44% in the middle of this region where the AP velocity profile revealed a flow reversal. The high Tu levels were probably induced by the flow which was jetted from the entry tear, subsequently impinged on the anterior lumen surface and expanded in the false lumen bulge. A localized small region of 5% Tu can also be seen in the distal part of the thoracic false lumen.

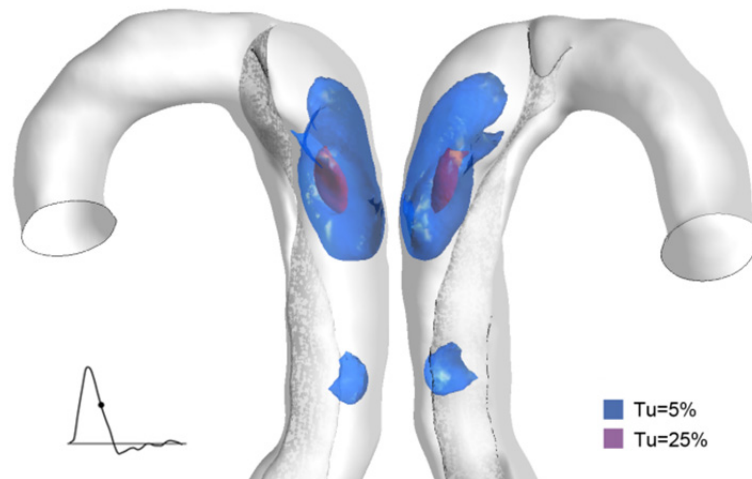


Figure 6.10: Turbulence intensity isosurfaces of the validation model at midsystolic deceleration phase.

6.4.4 Discussion

Flow rate in the false lumen is considered as a key feature for false lumen patency, which is the most important predictor of adverse early and later outcomes (Eggebrecht et al. 2005). One of the key findings of the multiple cases study was the correlation between the size and location of the proximal entry tear and the false lumen flow rate. This relationship was based on the computational results of ten patient-specific models with a number of assumptions and simplified boundary conditions. In this validation study, the flow rate in the false lumen calculated from the computational simulation was compared with that from the MR data. As can be seen in Figure 6.3, the computational model gave a comparable result to the MR data with similar flow rate waveform especially during systole as well as the percentage of flow in the false lumen (80% vs. 76%). The size and location of the proximal entry tear and the percentage of false lumen flow rate extracted from the MR data were found to fit well to the regression lines presented in Figures 4.4-4.6. The normalized root-mean-square deviations (RMSD) of the flow rate data of the validation model from the regression lines derived from the ten

patient-specific cases are 0.8%, 6.5%, and 3.2% for the ratio of tear circumferential diameter and aorta diameter, the tear longitudinal diameter and distance between the tear and arch top, respectively. Although the regression lines were based on limited number of cases, they could represent general relationships between the geometric parameters and the flow distribution in dissected aorta.

Further careful comparison was carried out between the velocity profiles extracted from MR images and the simulation results at the upper middle level of the descending aorta. The velocity data were compared in each of the three directions for a more detailed assessment. As shown in Figures 6.4 - 6.7, velocity profiles from the simulation results were comparable to those from the MR data. The profiles in the true lumen were well organized with similar patterns during the systolic period of the cardiac cycle. No retrograde flow was found in the true lumen as the velocity component in the FH direction was mainly pointing downwards (from head to feet) throughout the cardiac cycle. Velocity components in the other two directions also showed consistent patterns in pointing towards the posterior and right direction respectively, which were caused by the bending, curvature, and cross-section changes of the true lumen. The organized flow pattern in the true lumen, which has been demonstrated in many other cases included in this study, was probably owing to the compressed size and relatively straight geometry of the lumen. Velocity profiles in the false lumen presented much more complicated flow patterns. At the mid-systolic acceleration and peak systole, the main direction of the flow was from superior to inferior with the highest velocity close to the left and anterior wall. Reversed flow started to appear in the FH direction during the mid-systolic deceleration period demonstrating the presence of retrograde flow in the left anterior region of the false lumen. The flow reversal continued to the early diastolic phase with expanded area and elevated velocity in the superior direction. The velocity components in AP and RL direction both presented reversed flow during the whole cardiac cycle. The profiles demonstrated the presence of highly helical flow swirling in clockwise in the false lumen. Although the flow patterns are extremely complex as shown in the velocity profile figures, the computational model has successfully captured the regions of flow reversal and recirculation qualitatively and quantitatively. The good agreement has confirmed the reliability and validity of the computational model utilized in the multiple cases and single case studies in providing quantitative data on flow patterns and hemodynamic parameters in dissected aorta. Differences can be observed between the MR measured velocity profiles and the simulation results in localized regions at some time points, especially when the velocity is low. This difference is most

likely caused by the imaging noise of the MR images, which has a more appreciable effect when the velocity magnitude is relatively low hence more sensitive to the noise. The rigid wall assumption, which excluded the windkessel function of the proximal aorta and the wall motion at the acute phase of the dissection, may also contribute to the minor difference observed here.

The flow pathlines shown in Figure 6.8 displayed the disturbed and highly helical flow pattern in the false lumen as well as organized flow in the true lumen. This was confirmed by the high turbulence intensity levels of up to 44% in the false lumen proximal to the entry tear. This region was found to be the most likely place to develop disturbance and turbulence flow in the dissected aorta, as demonstrated by the multiple cases study. The distribution of TAWSS and OSI in the validation model was characterized by high TAWSS on the edge of the entry tear and low TAWSS on the surface of upward extension part of the false lumen, similar to the other patient-specific cases included in this study. A number of localized areas of high OSI are found on the false lumen surface due to the flow disturbance. These general features of wall shear stress and OSI are probably applicable to most of the dissection models.

6.5 Summary

To validate the computational model of aortic dissection utilized in the multiple cases and the single case study, 3D MR images, which contain the velocity information of the flow in three perpendicular directions, were used for validation. Comparisons of velocity profiles were made in three directions of the velocity components between the simulation results and MR data. A very good agreement was demonstrated in both the velocity profiles and the flow distribution between the two lumens. The comparison results have proved the reliability and validity of the computational model and the simulation approach. Combined with the analysis of the hemodynamic conditions, the validation model has also supported the results concluded from the multiple cases study and the single case study.

Chapter 7

Conclusion and Recommendations

7.1 Main conclusions

This study involved a group of patients who have suffered from uncomplicated type B aortic dissection. As the most suitable treatment for these patients is still a dilemma for surgeons, the aim of the study is to identify the haemodynamic factors that are associated with late dilatation and aneurysmal degeneration in uncomplicated type B aortic dissection, with an ultimate goal to assist surgeons in choosing the optimal treatment protocol for individual patient. By means of computational fluid dynamics, the present study investigated the flow patterns and haemodynamic factors in type B dissection models that were reconstructed from patient-specific CT images.

The thesis includes three subsets of studies for different research purposes, and a total of 12 patient-specific models were thoroughly analysed. Realistic pulsatile flow, transitional turbulence flow model, and patient-specific geometries were applied in the flow simulations. The multiple cases study involved 10 patients with typical type B aortic dissections, and detailed flow analysis was carried out for each model to investigate anatomical and flow characteristics in dissected aorta, especially the correlations between the morphological factors, and the flow patterns and haemodynamic parameters. The single case study was based on a series of follow-up scans of a patient who has been under surveillance for a long time but stayed stable. Flow analysis was performed on the initial and mid-term models to assess the role of the key haemodynamic and morphological factors identified from the multiple cases study in the progression of aortic dissection. The computational model, applied to the patient-specific study, was then validated by quantitative comparisons of flow velocity contours

between the simulation results and the flow data extracted from the 4D phase contrast MR images. Velocity components in three orthogonal directions, which could show the secondary flow patterns, were included in the validation.

The main findings of the thesis are as follows:

- The geometry of the aorta affected by type B aortic dissection can be extremely complex with large variation from patient to patient. Morphological 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. These morphological factors, which determine the flow pattern and haemodynamic environment in dissected aorta, are believed to play an important role in the long-term development of aortic dissection.
- The location and size of the primary tear determine the amount of flow circulating in the false lumen. The results of multiple cases study demonstrate that flow in the false lumen (expressed in terms of percentage of the total aortic flow in the thoracic aorta) is strongly correlated with (i) the longitudinal diameter of the primary tear, (ii) the ratio of circumferential diameter of the primary tear to aorta diameter, and (iii) the distance between primary tear and arch top. Larger primary tear diameter (both longitudinal and circumferential) or shorter distance from the top of aortic arch can lead to increased flow rate into the false lumen. As large amount of blood flow would keep false lumen patent and less likely to be thrombosed, aortic dissection patients who have a large primary tear with a proximal location may be at higher risk of developing aneurysm or late degeneration.
- General characteristics of flow patterns in dissected aortas have been demonstrated to be extremely complex with recirculating and disturbed flow dominating in the descending aorta especially in the false lumen. High turbulence intensity, up to 70%, can be found in some of the patient-specific models. The results indicate that the flow is likely to be turbulent, and the region surrounding the tear is the most possible site experiencing the highest levels of disturbed or turbulent flow.

- The turbulence intensity in dissected aorta is found to be significantly influenced by the relative stenosis of the true lumen. The dissection models with high levels of turbulence intensity are characterised by a relative smaller narrowing scale (defined as the ratio of the diameter of the narrowed true lumen to the unaffected aorta). Hence, the flow is more likely to be turbulent in the dissected aorta where the true lumen is highly compressed by the false lumen.
- High WSS can be found on the edge of the tear in all the dissection models, while low WSS was normally located in the superior region of the false lumen that had extended upward. The high levels of WSS acting on the edge of tear could enlarge the primary tear diameter, since high WSS may induce more aggressive lesions on the tear. The helical and recirculating flow in the dissected aorta also induced high OSI values in localized regions on the lumen surface. Very low and highly oscillating WSS as well as longer relative residence time could be found at the same sites where thrombus was formed in the false lumen. The high WSS at the tear site which could activate platelets in the blood flowing through the tear, and the extremely low and highly oscillating WSS, as well as long relative residence time, could promote thrombus formation in the false lumen, thereby reducing the risk of late degeneration.
- The computational model has been validated by comparing flow distributions between the true and false lumens and flow velocity profiles between the simulation results and in vivo phase contrast MR images. The good agreement achieved gives credence to the application of the utilized model, including the assumptions and boundary conditions, as well as the application of SST-Tran turbulence model. The evaluation study shows the promise of the model in capturing complex flow patterns in patient-specific models of type B aortic dissection, thus providing a promising method for further research.

In this study, systemic examinations of the flow patterns and haemodynamic factors in dissected human aortas have been performed, and possible links have been identified between certain morphological and haemodynamic parameters and the progression of aortic dissection. The results have provided preliminary evidence for the important roles of high and low WSS, oscillating WSS, location and size of primary tear in the development of dissection, which will require further assessment on a larger scale study.

7.2 Model assumptions and limitations

A number of model assumptions and limitations exist in the present study, including the assumption of rigid aortic wall, blood as a Newtonian fluid whereas it is in fact a shear-thinning fluid, exclusion of smaller arterial branches in patient-specific models, and limited number of cases. These assumptions and limitations are likely to have some influences on the predicted flow patterns and implications of our findings.

7.2.1 Rigid wall assumption

The wall of the patient-specific model was assumed to be rigid with no displacement although it is compliant in vivo. The flap and wall motion were not incorporated in the simulation of patient-specific cases due to the unavailability of wall thickness and the mechanical properties of the dissected wall. As discussed in Chapter 3, the similar density of dissected wall, thrombus and other tissues around the aorta makes it impossible to accurately acquire the geometry of the dissected aortic wall especially the intimal flap from standard CT and MR images. In a dissected aorta, neither the true nor the false lumen is bounded by a complete wall as the intimal tear splits the aortic wall in the media layer. The intimal flap comprises the intima and part of the media, whereas the outer wall of the false lumen contains the rest of media and entire adventitia. The heterogeneous mechanical models required for different parts of the dissected aortic wall are currently unavailable. Furthermore, the degree of dissection in the media layer varies from subject to subject inducing different compositions of media tissue in the intimal flap and outbound layer of the false lumen. This diversity leads to specific mechanical property for each subject model. Also, as dissection commonly extends to the abdominal aorta even affecting the iliac arteries, in order to get accurate simulation results, the dissection model should ideally cover the whole dissected aorta. The large size and complexity of the model will demand extensive computational resources for fluid-structure interaction (FSI) simulations.

Ganten et al. (2009) investigated the intimal flap and wall motion in a type B aortic dissection by using dynamic, ECG-gated CT imaging technique. It was found that the aortic wall distensibility in aortic dissection could be remarkably reduced when compared to healthy subjects, and the average narrowing degree induced by the flap motion was 4.4%. The effect of wall motion on the flow patterns and wall shear stress distribution was investigated in a thoracic aortic aneurysm model by incorporating FSI simulation (Tan et al. 2009). The study demonstrated a marginal difference in the results of the rigid and FSI simulations in the aneurysm model. Therefore, carrying out

expensive FSI simulations may not be necessary at the current stage. But it would still be desirable to include wall compliance to study the effects of flap and wall motion on the flow patterns in aortic dissection model. Moreover, the “windkessel” function of the proximal aorta, which converts intermittent flow from the heart to a continuous and steady flow across the capillaries, can alter the blood pressure and flow rate waveforms in the descending aorta, thus inducing possible changes in flow patterns in the distal aorta. Hence, it would be desirable to consider the “windkessel” effect and incorporate a compliant proximal aorta into FSI model. In the future, when a better understanding of the material properties of each layer of aortic wall and a higher computing power become available, as well as advanced imaging modalities providing better wall identification, this assumption can be relaxed.

7.2.2 Blood as a Newtonian fluid

The blood was treated as an incompressible and Newtonian fluid in the patient-specific flow models. Although blood does not exhibit a constant viscosity at all flow rate, it is widely accepted that blood behaves in a Newtonian fashion in most arteries (Ku 1997). Previous numerical studies have also indicated that the influences of shear thinning properties of blood are not significant for flow in large arteries (Perktold et al. 1991; Cho & Kensey 1991). As shear rates in the dissection model could be quite low especially in the proximal region of the false lumen, blood may behave as a non-Newtonian fluid in localised areas. In order to examine the effect of non-Newtonian viscosity of blood in aortic dissection, the Quemada model, which calculates the apparent viscosity based on a minimum energy dissipation analysis (Quemada 1978), was incorporated into the transitional flow model on one of the aortic dissection models. Compared with the results of the Newtonian simulation, the non-Newtonian model predicted a very similar TAWSS and pressure distribution with a slightly lower peak value. Hence, this assumption is unlikely to have a qualitative effect on the predicted flow pattern and TAWSS distribution in the dissection model.

7.2.3 Simplified patient-specific model geometry

The patient-specific models usually include the entire aorta depending on the extent of dissection. The aorta, starting from the root of ascending aorta to the iliac bifurcation, branches into a number of arteries supplying blood to various organs. Due to the unavailability of boundary information for the branches, the dissection models in this study were simplified by excluding all the branches off the aorta. Shahcheraghi et al. (2002) reported about 15-20% of the total blood is distributed to the upper extremities’

vessels on the aortic arch. To compensate for the flow lost through the three arch branches, the original velocity waveform applied at the inlet was scaled down to ensure realistic flow rate into the descending aorta where type B aortic dissection occurs. Except the three branches off the aortic arch, other arteries become successively smaller in diameter. The small branches are likely to have limited influence on the overall flow patterns of the dissection model, especially the region near the site of entry tear, which is of the most interest in this study.

7.2.4 Limited patient-specific cases

In this thesis, ten patient-specific cases were included in the multiple cases study, which were characterized by typical type B aortic dissection. Although similar patterns of WSS distribution and strong correlations between morphological factors and flow distributions in dissected lumens have been found from the simulation results, it is necessary to perform flow analysis on a larger number of patients to further test the findings for statistical significance. The longitudinal study and model validation study were also limited to one case for each. Recruiting more cases with follow-up scans would be highly desirable to further investigate the role of haemodynamic factors in the progression of aortic dissection with various long-term outcomes. As type B aortic dissection is a relatively rare cardiovascular disease, it is difficult to recruit a large number of suitable patients for flow analysis. Collaborations between hospitals and specialised medical centres could probably solve the problem by providing a broader medical image database of dissection patients. Phase contrast MR images for more dissection models are also essential for a more comprehensive validation. Although phase contrast MR imaging is currently not a routine diagnostic method for aortic dissection, its powerful function in identifying dissection and tear site has been noticed and gradually adopted in diagnosis and surveillance of aortic dissection patients. This would allow a thorough validation analysis on the dissection model utilized in this study.

7.3 Suggestions for future work

7.3.1 Haemodynamic investigation with dynamic wall motion

In the study, the absence of the wall motion in the flow analysis of patient-specific cases is considered as a major limitation. The lack of information on material properties of dissected aortic wall and pulsating pressure in the true and false lumen makes it difficult to obtain reliable results from fluid-structure interaction study on patient-specific cases. Although as mentioned in the previous section, the average wall motion of aortic dissection subjects is limited, it is still necessary to estimate the effects of the dynamic

wall motion on flow in patient-specific models to further complete the study. One proposed method as a first step towards this goal is to set up a patient-specific model with prescribed wall motion measured from cine MR imaging.

To set up such a model includes two important steps. The first step is to obtain realistic wall motion from medical images of dissection patients. Current time-resolved imaging modalities, such as ECG-gated dynamic CT or cine MR, can be utilized for the development of patient-specific dynamic motion models as it can generate cross sectional images of the aorta dissection at multiple time points during a cardiac cycle. Ganten et al. (2009) examined a group of 32 patients with conservatively treated type B dissection by using a 16-row multidetector-row CT. The motion of the flap and outbound wall has been successfully observed from 20 time frames per heart cycle. The high resolution of CT images makes it possible to record even small movements of the dissected wall. 4D MR could also capture the images of dissected wall, as well as patient-specific flow information, at multiple time points throughout the cardiac cycle by specifying suitable trigger time and acquisition window. Once the cross-sectional images are performed along the length of dissected aorta at any time point, the realistic motion of the entire flap and outbound wall could be achieved.

The second step is to incorporate the measured wall motion into the flow model. Based on the time-resolved CT or MR images, the geometries of the true and false lumen can be reconstructed at various time points. The deformation of the lumen area can be incorporated by specifying the coordinate of each nodal point of the lumen mesh as a function of time. Torii et al. (2010) used an in-house finite-element program with the lumenal-wall displacement prescribed in CFD as boundary conditions on the wall to assess the effects of dynamic vessel motion on coronary hemodynamics. A fully subject-specific model of the geometry, motion and input flow conditions of the right coronary artery, was developed based on MR acquisitions, and the computational results showed the effect of vessel motion on velocity profiles in the right coronary artery. The idea and methods of incorporating prescribed wall motions in CFD as boundary conditions could be applied to dissection models to investigate the effects of flap and wall motion on aortic dissection haemodynamics.

7.3.2 Material properties of dissected aortic wall

It has been suggested by previous researches that increasing wall stress on aneurysmal wall could be the ultimate cause of aneurysm rupture. Hence, to further continue this study, knowledge of wall stresses in an aortic dissection may be helpful in evaluating the

need for immediate surgical intervention to avoid rupture of dissected wall. The wall stress analysis in aortic dissection must be preceded by the development of a suitable material model for aortic dissection, which is currently unavailable. Patient-specific material parameters of the dissected aortic wall are essential for reliable stress analysis of clinical relevance. The parameters are difficult to determine via non-invasive methods.

A variety of methods have been developed and implemented to explore the material properties of normal and diseased aortic tissue with respect to tensile, inflation, tearing, splitting, and peeling tests performed on human, porcine, and canine aortic tissues. These previous tests include tensile tests in radial, circumferential, and axial directions (MacLean et al. 1999; Mohan & Melvin 1982; Vorp et al. 2003), and inflation tests (Mohan & Melvin 1983; Groenink et al. 1999). The mechanical testing methods could be applied to dissected aorta wall specimens to obtain the material parameters, such as tensile strength, ultimate stress of inflation, and tear breaking stress. The experimental data from dissection specimens can be used to determine and estimate the material parameters of dissected wall model.

Also, as the three main components of arterial wall, including the rubberlike protein elastin, the stiff fibrous protein collagen, and smooth muscle cells, were found to be structured in medial lamellar units in the media layer of the aorta (Sommer et al. 2008), this structure makes the media prone to be cleaved parallel to the elastic lamellae, and the dissection could happen in any level of the media. Hence, the thickness and composition of flap and outbound dissected wall are different from patient to patient. The mechanical testing method could also be utilized to examine wall tissue with different level of dissections in media to understand the effect of media layer thickness on the material properties of dissected wall.

Appendix: List of Publications

Journal Publications

Cheng, Z., Tan, F. P. P., Riga, C. V., Bicknell, C. D., Hamady, M. S., Gibbs, R. G., Wood, N. B., Xu, X. Y. (2010), 'Analysis of Flow Patterns in a Patient-specific Aortic Dissection Model', J. Biomech. Eng. 132(5):051007.

Xu, X. Y., Borghi, A., Nchimi, A., Leung, J., Gomez, P., Cheng, Z., Defraigne, J. O., Sakalihasan, N. (2010), 'High Levels of 18F-FDG Uptake in Aortic Aneurysm Wall Are Associated with High Wall Stress', Eur. J. Vasc. Endovasc. Surg. 39: 295-301.

Xu, X. Y., Leung, J. H., Borghi, A., Cheng, Z., Wood, N. B. (2008), 'Subject-specific Analysis of Biomechanical Forces in Aortic Aneurysms', Aortic aneurysm: New insights into an old problem Liege: Les Editions de l'Universite de Liege, pp. 101-114.

Cheng, Z., Riga, C. V., Chan, J., Hamady, M. S., Wood, N. B., Cheshire, N. J. W., Xu, X. Y., Gibbs, R. G. J. (2011), 'Computational Simulation of the Aorta in Acute Type B Dissection'. Submitted to Journal of Vascular Surgery.

Conference Proceedings

Biomechanics Analysis of an Abdominal Aortic Aneurysm using Patient-specific Data (poster & oral presentation), International Meeting on Aortic Diseases: New insights into an old problem- CHU Liege, Belgium, September, 2008.

Comparison of Flow and Wall Shear Stress Patterns in Different Patient-specific Models of Type B Aortic Dissection (poster presentation), International Meeting on Aortic Diseases: New insights into an old problem- CHU Liege, Belgium, September, 2008.

Flow and Wall Shear Stress Patterns in a Patient-specific Model of Aortic Dissection (poster presentation), Bioengineering 08, Imperial College London, September 2008.

Comparison of Flow and Wall Shear Stress Patterns in Different Patient-specific Models of Type B Aortic Dissection (poster presentation), Cardiovascular Technology Network, 3rd Symposium, Institute of Biomedical Engineering, National Heart and Lung Institute and Education Centre, Royal Brompton Hospital, London, December, 2008.

Comparison of Flow and Wall Shear Stress Patterns in Different Patient-specific Models of Type B Aortic Dissection (oral presentation), The 4th Symposium on Biomechanics in Cardiovascular Disease: Shear Stress in Vascular Biology, Rotterdam, April, 2009.

Elucidation of the Role of Morphological Changes and Biomechanical Forces in the Progression of Type B Aortic Dissection (oral presentation), The 6th World Congress of Biomechanics (WCB 2010), Singapore, August, 2010.

Computational Flow Analysis of Type B Aortic Dissection (oral presentation), Endovascology 2011, Shanghai, China, October, 2011.

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