Numerical simulation and measurements of hemodynamics for coronary artery bypass

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**NUMERICAL SIMULATION AND
MEASUREMENTS OF HEMODYNAMICS IN
CORONARY ARTERY BYPASS**

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**SCHOOL OF MECHANICAL & AEROSPACE ENGINEERING
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2005

Numerical Simulation and Measurements of Hemodynamics in Coronary Artery Bypass

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Abstract

Hemodynamics is widely believed to correlate with the stenosis of coronary artery bypass graft (CABG). Although some researchers had investigated distal anastomosis, further studies upon the proximal anastomosis and even the complete bypass model, including both proximal and distal anastomoses, are still necessary. Therefore in this project, flow characteristics and hemodynamic parameters (HPs) distributions of proximal anastomosis and the complete bypass model were studied in order to enhance the understanding of the stenosis pathophysiological process and provide useful information for sleeve design and medical doctors. To validate the numerical simulation results, Particle Image Velocimetry (PIV) measurements were also carried out.

Three proximal anastomosis models (viz. 45° forward facing, 45° backward facing and 90° anastomotic joints) were firstly designed to mimic the proximal anastomosis. The simulation results showed a flow separation region along the graft inner wall immediately after the heel at peak flow phase and it decreased in size with the increase of grafting angle. Meanwhile stagnation point was found along the graft outer wall with small shifting during the physiological cycle. Fluctuations and oscillations of instantaneous wall shear stress (WSS) were also found around the proximal anastomotic joint. Near the anastomosis, there was a region, where the time-averaged WSS was low and the oscillation shear index (OSI) was high. In addition, there were also two regions near the anastomosis, where the time-averaged WSS was high and the OSI was relatively low. In general the disturbed flow (stagnation point, flow separation and vortex) and abnormal HPs distributions would lead to graft stenosis. In contrast to the other two models, the 45° backward facing model would result in better patency rate as it has reduced the region of disturbed flow and abnormal HPs.

In addition, a fair match between numerical and PIV experimental data was observed in terms of the flow characteristics, the velocity vectors and WSS distributions of proximal anastomosis models. The overall difference between them ranged from 8 to 54 percent and the error range maintained similarity for different time phases. It is evident from the findings that PIV measurement can obtain quantitative results with reasonable accuracy as LDA and validate the results of numerical simulation, which is able to provide much detailed information with enough mesh density.

Furthermore, numerical simulation for the whole anastomosis model reported disturbed flow (flow separation / reattachment, vortical and secondary flow) at proximal and distal anastomoses, especially at the distal anastomosis. In the heel vicinity of distal anastomosis, a large recirculation region with low momentum persisted within the cycles, which increase the potential of intimal hyperplasia (IH). The flow separation and noticeable secondary flow observed near the toe of distal anastomosis would also result in disease there. High-OSI-and-low-WSS and Low-OSI-and-high-WSS regions were observed at both proximal and distal anastomoses, especially at the toe and heel regions of distal anastomosis. These regions are thus speculated to initiate the atherosclerotic lesion and would further worsen the situation by modifications in permeability indicated with the increases of WSSG. The comparisons of segmental average of HPs further proved that IH might be more prone to form in the distal anastomosis than in the proximal anastomosis, especially along the suture line at the toe and heel of distal anastomosis. Further comparisons with other models indicate that the surgeon should consider the influence of anastomosis geometry in order to improve the graft patency rate and this would help in the optimal design of sleeve connector.

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Nomenclature

a_i	Coefficient of polynomial fitting, $i=1, 2, 3 \dots n$ for degree of polynomial approximation respectively
a_{nb}	Influence coefficients for neighboring cells
a_p	Coefficient value at the center of the cell
b	The contribution of constant part from source term and boundary conditions
B_n	Fourier coefficients
d	Diameter of the tube (m)
D_G	Diameter of graft (m)
f	Frequency in Hertz
F_i	External body force (N/m ³)
i	$\sqrt{-1}$, unit imaginary number
J_0	The first kind of Bessel function of order 0
J_1	The first kind of Bessel function of order 1
N	The total number of Fourier transform terms
p	Static pressure (Pa)
$p(x, t)$	Static pressure (Pa) at different axial location (x) and time (t)
Q or $Q(t)$	Flow rate at time t (m ³ /s)
Q_G	Mean flow rate in the graft during the pulsatile flow cycle (m ³ /s)
r	Radius with respect to the center axis of the tube (m)
R	Radius of the tube (m)
Re	Reynolds number, defined as $Re = \rho u d / \mu$
Re_G	Reynolds number of graft, defined as $Re_G = \rho u D_G / \mu$
R^Φ	Unscaled residual
R_s^Φ	Scaled residual
S_m	Mass added to the continuous phase from the dispersed second phase (e.g., due to vaporization of liquid droplets) and any other mass sources (kg/m ³ ·s)
t	Time (s)
T	Period (s)
u or $\bar{u}$	The average cross sectional velocity (m/s)
u_i	Velocity in i direction (m/s)
$u(r, t)$	The axial velocity (m/s) at different radial location (r) and time (t)

Nomenclature

$U(r)$	The distribution of axial velocity across the tube of radius R (m/s)
u_{∞}	Free-stream velocity (m/s)
$u(\xi)$	Velocity at local normal distance to the wall (ξ), with direction parallel to the wall (m/s)
$\partial u / \partial n _{\text{wall}}$	The normal velocity gradient at the wall (s^{-1})
x_i	Location in Cartesian coordinate (m), $i=1, 2, 3$ for x, y, z directions respectively
Y_0	The second kind of Bessel function of order 0
y_P	Distance to the wall from the adjacent cell centroid (m)

GREEK SYMBOLS

Φ_{nb}	Variable values for neighboring cells
Φ_P	Variable values at the center of cell
α	Womersley number, defined as $\alpha = R\sqrt{\omega / \nu}$
δ	Boundary layer thickness (m), defined as $\delta = \sqrt{\frac{\nu x}{u_{\infty}}}$ for steady flow and $\delta = R/\alpha$ for pulsatile flow
ε	Error, defined as $\varepsilon = (f_2 - f_1) / f_1$, where f_1 and f_2 are the solutions on fine and coarse grids respectively
δ_{ij}	Kronecker Delta, which equals to 1 for $i=j$ and 0 for $i \neq j$
ξ	Local normal distance to the wall (m)
μ	Dynamic viscosity of the working fluid ($\text{Pa}\cdot\text{s}$)
ρ	Density of the working fluid (kg/m^3)
τ_G	Poiseuille type wall shear stress at the graft corresponding to the mean flow rate in the graft (Pa), defined as $\tau_G = \frac{32\mu Q_G}{\pi D_G^3}$
τ_i	Wall shear stress in Cartesian coordinate (Pa), $i=x, y, z$ for x, y, z directions respectively
τ_w	Wall shear stress (Pa), defined as $\tau_w = \mu(\partial u / \partial n) _{\text{wall}}$, where $\partial u / \partial n _{\text{wall}}$ is the normal velocity gradient at the wall
ν	Kinematic viscosity of the working fluid (m^2/s)
ω	Angular frequency in radian per second of the oscillatory motion, defined as $\omega = 2\pi f$

List of Abbreviations

bFGF	Basic fibroblast growth factor
BJT	Bipolar Junction Transistor
CABG	Coronary artery bypass graft
CAT	Computed Axial Tomography
CFD	Computational Fluid Dynamics
CT	Computed Tomography
DOS	Distal outlet segment
DR	Diameter ratio
EBT	Electron beam tomography
EC	Endothelial cell
ECM	Extracellular matrix
ETS	End-to-side
FCPP	Femoro-crural patch prosthesis
GCI	Grid convergence index, $GCI^{fine} = F_s \varepsilon / (r^P - 1)$, where p is the order of the numerical method; F_s is safety factor; for unstructured grids, the grid refinement ratio $r = (N_1 / N_2)^{1/D}$, N_1 and N_2 are numbers of elements on fine and coarse grids respectively, and D is the dimensionality of problem.
GE	Gradient-echo
GPs	Glycoproteins
HP	Hemodynamic parameter
HUW	Higher upwind
IA	Interrogation area
IH	Intimal hyperplasia
IHT	Intimal hyperplasia thickening
IVC	Interposition of vein cuff
LDA	Laser Doppler anemometry
LDL	Low-density lipoprotein
MIH	Myointimal hyperplasia
MR	Magnetic resonance

List of Abbreviations

NO	Nitric oxide
NWRT	Novel near-wall residence time
OSI	Oscillatory shear index, defined as $OSI = \frac{1}{2} \left(1 - \frac{\left \int_0^T \tau_w dt \right }{\int_0^T \tau_w dt} \right)$
PDGF	Platelet derived growth factor
PIV	Particle Image Velocimetry
POS	Proximal outlet segment
PRF	Point response function
PTFE	Polytetrafluorethylene
PUDWSR	Pulse ultrasonic Doppler wall shear rate
QUICK	Quadratic upwind interpolation of convective kinematics
RPG	Radial pressure gradient
SE	Spin-echo
SMC	Smooth muscle cell
SNR	Signal-to-noise ratio
Time-averaged WSS	Time-averaged wall shear stress (Pa), defined as $WSS = \frac{1}{T} \int_0^T \tau_w dt$
Time-averaged WSSG	Normalized Time-averaged wall shear stress gradient, defined as $WSSG = \frac{1}{T} \frac{D_G}{\tau_G} \int_0^T \sqrt{\left(\frac{\partial \tau_x}{\partial x} \right)^2 + \left(\frac{\partial \tau_y}{\partial y} \right)^2 + \left(\frac{\partial \tau_z}{\partial z} \right)^2} dt$
TTL	Transistor-Transistor-Logic
WBC	White blood cell
WSR	Wall shear rate (s^{-1}), defined as $WSR = \partial u / \partial n _{wall}$
WSS	Wall shear stress (Pa), defined as $WSS = \mu(\partial u / \partial n) _{wall}$, where $\partial u / \partial n _{wall}$ is the normal velocity gradient at the wall
WSSG	Normalized wall shear stress gradient, defined as $WSSG = \frac{D_G}{\tau_G} \sqrt{\left(\frac{\partial \tau_x}{\partial x} \right)^2 + \left(\frac{\partial \tau_y}{\partial y} \right)^2 + \left(\frac{\partial \tau_z}{\partial z} \right)^2}$

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CHAPTER 1

INTRODUCTION

1.1 Background

Just like all tissues in the body, heart requires oxygenated blood in order to function properly. Blood nourishes the heart through the left and right coronary arteries. However, coronary artery may be narrowed by fatty lesions in arterial walls, named atherosclerosis as shown in Figure 1-1. Once atherosclerosis has developed, there may be further narrowing of the coronary arteries by formation of blood clot, called thrombosis. Whatever the reason in reducing blood flow (fatty build up, blood clot, or spasm) the result is the same, not enough blood and oxygen reaching the heart muscle, and subsequently the heart muscle begins to fail and finally dies. When the blood supplying to the heart muscle is not sufficient for 15-30 minutes or is even stopped, the heart muscle will be impaired, and results in a heart attack or a myocardial infarction. Reducing blood supply also causes an electrical instability of the heart, which makes it impossible to pump blood again. When the heart stops pumping, the supply of blood to the brain will be cut off. If blood flow is not restored within five minutes, it can result in permanent damage to the heart and brain or even death.

Neither the heart nor the brain damage can be repaired. Therefore the injury leaves behind a permanent disability. Aging men and women are more prone to coronary artery disease and the number of disease increases over years. Just as demonstrated in the Heart and Stroke Statistics Report of 2004 in USA, since 1900 cardiovascular diseases have kept as the No. 1 killer in the USA every year except 1918. Among them, coronary artery disease

occupies 54% of deaths from cardiovascular disease. The estimated direct and indirect cost of coronary artery disease in the United States of 2004 is \$133.2 billion. In addition, heart diseases also constitute about 24.2% of the total deaths in Singapore, making it a second killer after cancer.

Figure 1-1 View of diseased coronary artery

Well-known risk factors of coronary artery disease are family history, high blood pressure, smoking, diabetes, excess body fat, and physical inactivity. Therefore healthy diet and medications that lower blood cholesterol can help to slow down the process that clogs arteries. Exercise and losing weight, under doctor's supervision, is also helpful to strengthen heart. Quitting smoking is essential to protect heart and reduce the chances of future heart attack. However, if heart attack has already happened, medications that control blood pressure and heart rate can help in reducing the chances of another heart attack. Balloon angioplasty, a non-surgical procedure is also employed to treat patients with the disease. In the procedure, a catheter with a balloon on its tips is inserted into an artery in the leg. It is then guided into the narrowed coronary artery. Once there, the balloon is inflated, widening the narrowed area and increasing blood flow to the heart. To increase the long-term success of the angioplasty, a stent is usually implanted during the

process (Fabregues et al., 1998). However, for cases of serious blockages in the coronary arteries, coronary artery bypass graft (CABG) surgery has to be conducted, which creates an alternate route of blood supply.

During the surgery, a connection is made between the major blood vessel of the body - the aorta (or its subsidiary branches) - and the blocked coronary artery, beyond the area of obstruction, using a variety of conduits (leg veins or other arteries) as shown in Figure 1-2. In this way, even though nothing is done about the blockage itself, blood is provided to the heart via the "bypass". Hence the term, coronary bypass surgery is derived. (Hochman, 1982).

Figure 1-2 View of the heart with grafts

The most commonly used conduits are saphenous veins, which are stripped from a patient's legs to correct varicosity, and are removed at the same time, when the bypass operation is performed. Besides saphenous veins, there are also some suitable choices for the graft, such as internal mammary artery (an artery from the chest), gastroepiploic artery

(which supplies the stomach), radial artery (which nourishes the hands), inferior epigastric artery (which runs in the wall of the abdomen), subscapular artery (on the back of the chest), splenic artery (which supplies the spleen) and intercostal artery (which runs just inside the rib cage). Meanwhile synthetic veins such as Dacron, Teflon and Polytetrafluoroethylene (PTFE) veins are also available in the commercial market and have been used as substitutes of the saphenous vein graft. These man-made synthetic veins are only used if the extracted autogenous vein (from the patient's body) is not suitable for the bypass operation.

In this anastomotic operation, one end of the vein graft is sewn to the aorta, the main artery (known as proximal anastomosis), and the other end is attached to coronary artery below the area of blockage (known as distal anastomosis). In this way, the oxygen-rich blood is taken directly from the aorta, bypasses the obstruction and flows through the graft to nourish the heart muscle. The average size of a saphenous vein of an Asian adult ranges from 3.5 to 6.5 mm in diameter and the coronary artery diameter varies around 2mm and could be even as small as 1.25 mm.

Since the introduction of saphenous vein grafting in the late 1960s, CABG, with or without arterial conduits, remains the treatment standard for management of intractable angina due to coronary artery occlusive disease. According to the statistics of American Heart Association, 571,000 of bypass procedures were performed on 355,000 patients in 1999. The trends in cardiovascular surgery shown in Figure 1-3 indicate that there has been an increase in the number of bypass operations over the years and maintained the same level in 2000 and 2001.

Figure 1-3 Statistics data on bypass operations

However, the CABG was not without complications (Vorp, 1997). The saphenous vein, which is the most commonly used vessel for grafting, provides only palliation of the ongoing process. Approximately 15% to 20% vein grafts occlude in the first year, and half occlude within the first 2 years. Thereafter, the annual occlusion rate is 1% to 2% from 1 to 6 years and 4% to 5% from 6 to 10 years. At 10 years, approximately 60% of vein grafts are patent; only 50% of these vein grafts remain free of significant stenosis (Shah et al., 2003). The internal mammary artery has a higher 1-year patency rate of 98% and 10-year patency rate of 90%. In addition, the radial artery has a 1-year patency rate of 93.5% and a 5-year rate of 83%. The pathology in the grafts documented by angiography and histologic examinations includes acute thrombosis and intimal hyperplasia during the first postoperative year and onset of progressive atherosclerosis beyond 3 to 5 years (Shah et al., 2003).

It is therefore not unexpected that numerous research works were carried out intensively to investigate the occlusion symptom or commonly known as stenosis. Previous studies have shown that vascular surgery, biological and mechanical factors are involved in the formation of stenosis, which includes mitogenic factors, platelet activation and chronic

endothelial injury (injury induced during surgery), hemodynamic factors, compliance mismatch between graft and host vessel, and interactions between blood and graft material (Nerem, 1992; White et al., 1993; Keynton et al., 2001).

Among these, hemodynamic factors were proved to be the most important factor (Friedman et al., 1992; Stewart and Lyman, 1992; Hofer et al., 1996; Vorp, 1997). It was suggested that hemodynamic parameters (HPs) encapsulate “disturbed flow” that may trigger a cascade of abnormal biological process leading to intimal thickening and/or thrombi formation. In turn, sufficiently high and sustained HP values can be employed to determine susceptible site for the onset of blood vessel disease (Kleinstreuer et al., 2001). These HPs included low wall shear (Rittgers et al., 1978; Binns et al., 1989), low and oscillating shear (Bassiouny et al., 1992), high wall shear (Fry, 1969; Friedman, 1992), “safe-bandwidth” of the wall shear stress (WSS) (Kleinstreuer et al., 1991), wall shear stress gradient (WSSG) (Henry et al., 1996; Kleinstreuer et al., 1996) and oscillation shear index (OSI) (He and Ku, 1996).

Furthermore, factors such as wall curvature (Lei et al., 1995; Rowe et al., 1999; How et al., 2000), wave form (White et al., 1993; Kleinstreuer, 1996; Ethier et al., 1998), anastomosis angle and flow rate ratio (Pietrabissa et al., 1990; Fei et al., 1994; Hughes and How, 1995 and 1996; Henry et al., 1996; Inzoli et al., 1996; Loth et al., 1997) are also proved to influence the development of stenosis. To determine the influence of these factors, several experimental techniques have been utilized to study the flow patterns of vascular anastomoses, including flow visualization using dye-injection (Crawshaw et al., 1980), laser illumination of particles suspended in the fluid (White et al., 1993; Hughes and How, 1996) and the hydrogen bubble technique (Keynton et al., 1991). Velocity

profiles and WSS have also been determined using the photochromic tracer techniques (Ojha, 1993; Ojha et al., 1993) and laser Doppler anemometer (LDA) (Keynton et al., 1991; Loth et al., 1997). Particle Image Velocimetry (PIV) (Bates et al., 2001; Heise et al., 2004) has also been implemented to investigate the hemodynamics. Recently, numerical simulation has become a popular and an extremely valuable tool for performing a systematic study of complex flow patterns in anastomosis (Xu et al., 1992; Steinman et al., 1993; Perktold et al., 1991; Fei et al., 1994; Lei et al., 1996; Hofer et al., 1996; Kleinstreuer et al., 1996; Lei et al., 1997).

Whereas one may see that earlier studies only reported in subsections of the bypass, especially in the distal anastomosis. However, high stresses associated with flow disturbances may be present at the proximal anastomosis and platelet activation is likely to occur within the vascular prosthesis and activated platelets formed proximally may be conveyed along the graft and accumulate at the distal anastomosis in the regions of low shear rate. The site at which intimal hyperplasia develops would be determined by the distal geometry, but the extent and initiation of the process may be influenced by the nature of the flow at the proximal anastomosis (Hughes and How, 1995). In addition, Lee and co-workers (2001) have also observed that local flow conditions at the distal anastomosis were influenced by the flow conditions at the proximal site. Also, few investigations have been conducted on the complete bypass graft with both proximal and distal ends (Lee et al., 2001). Therefore, it is necessary to fully explore the flow structure in the proximal anastomosis, by firstly establishing the conditions of the flow at upstream and then study the whole anastomosis model including both by-pass and host tubes as a system.

Accordingly, computer modeling is used initially in the present study in order to enhance the understanding of the stenosis pathophysiological process. The outcomes of present work will provide useful information for doctors and serve as the basis for the design of the biocompatible sleeve device, which could minimize the surgical injury and enhance the longevity of coronary artery bypass procedures.

In addition, among the present studies, the comparison of numerical results with experimental data has either not been conducted or has been conducted in a simplified model using a flow visualization method (Steinman et al., 1993; Hofer et al., 1996, Cole et al., 2002c) or LAD measurements (Lei et al., 2001 and Bertolotti et al., 2001). Although PIV method was recently implemented for hemodynamics investigation (Bates et al., 2001; Heise et al., 2004) due to its high temporal resolution, the comparison between numerical simulation results and PIV measurements has not been performed until now. Therefore, in this study, comparisons between the numerical results and PIV measurements were carried out to verify the validity of numerical simulation.

1.2 Objectives and Scopes

The project is carried out in order to accomplish the following aims:

1. To design and build physical models of varying anastomotic angles to mimic the proximal anastomosis of the bypass at the aorta-coronary section.
2. To investigate effects of various parameters, such as flow angle, velocity profiles, HPs distributions etc., on the patency of bypass graft under both steady and pulsatile flow conditions, by means of numerical simulation for the proximal anastomosis models.
3. To evaluate the different proximal anastomosis models in terms of expectant patency rate according to the flow characteristics and HPs distributions.

4. To validate the numerical simulation results with those observed from PIV measurements for the proximal anastomoses.
5. To design and build physical model for mimicking the whole anastomosis of the CABG, including both proximal and distal anastomoses.
6. To investigate the hemodynamics of the whole anastomosis model under both steady and pulsatile flow conditions for better understanding the stenosis pathophysiological process.

Both flow field and HPs distributions are dealt with in this thesis, as they are demonstrated to contribute for the growth of intimal hyperplasia, and/or atherosclerosis. The investigation for steady flow is to provide some physical insight into the causes of specific flow features that may also exist in pulsatile flow. Steady flow investigation would allow these flow features to be specifically identified as geometric phenomena rather than unsteady phenomena.

In the numerical simulation, the computed sections are modeled as rigid tubes with the assumption that synthetic graft and diseased arteries are expected to be relatively stiff. The physiological data for the size of the graft and the coronary arteries were provided by a local medical institute, and is based on local Asian patients who have suffered from the disease and had been operated. Since saphenous vein graft is most commonly used and has lower patency rate than arterial grafts, the physiological data of saphenous vein graft will be quoted as the data of graft.

In this project, the PIV experiments for the proximal anastomosis models have been carried out. The experimental results were used to compare and validate the numerical

simulation. Due to the time constraint, the measurements on the whole anastomosis model were not performed. This is also partly due to the reasonably fair agreement between the PIV measurements and the numerical simulation for the proximal anastomosis models.

The overall initiative of this project is to design an interposition sleeve for joining the aorta to vein graft and vein graft to the coronary artery in a bypass operation. This sleeve will maintain an adequate arterial contour and will be speculated to reduce the chances of postoperative symptoms like endarterectomy, carotid aneurysm and kinks problems according to the hemodynamic analysis. The information collected in this report will provide a better knowledge on the correlation between the CABG and the patency rate. These would provide useful information for medial doctors and would help in optimizing the sleeve design.

1.3 Overview of the Contents

The thesis consists of eight chapters. After the brief introduction and the presentation of research objectives and scopes, the second chapter further discusses the works done on investigating the hemodynamics of bypass anastomosis and the graft failure in the literature, which includes the in-vivo and in-vitro experiments, as well as the numerical simulation. The general description of end-to-side anastomosis studies by other researchers to-date is also introduced. Chapters 3 and 4 described the methodologies of the numerical simulation and PIV measurements respectively, after which the simulation results for proximal anastomosis models are presented and discussed in Chapter 5. PIV experimental results for the proximal anastomosis models were demonstrated and compared with the simulation results in Chapter 6. Chapter 7 presents and discusses the numerical simulation results for whole anastomosis. Finally, conclusions are drawn and recommendations for future works are suggested in Chapter 8.

CHAPTER 2

LITERATURE REVIEW

This chapter reviews work done on coronary artery bypass grafting in the literature. The bypass graft failure modes and the pathological reasons are firstly reviewed. Then the role of hemodynamics upon the coronary artery bypass anastomosis are reported, followed by a summary to give a general overview about the importance, investigating methods and up to date findings of hemodynamics in the coronary artery bypass anastomosis.

2.1 Bypass Graft Failure

Since the introduction of saphenous vein grafting in the late 1960s, coronary artery bypass grafting, with or without arterial conduits, remains the treatment standard for management of intractable angina due to coronary artery occlusive disease. However, it soon became evident that the saphenous vein provided only palliation of ongoing process, which is further complicated by vein graft atherosclerosis. Approximately 15%-20% of vein grafts occlude in the first year, and half occlude within the first 2 years. Thereafter, the annual occlusion rate is 1% to 2% from 1 and 6 years and 4% to 5% from 6 to 10 years. At 10 years, approximately 60% of vein grafts are patent, only 50% of these vein grafts remain free of significant stenosis (Shah et al., 2003). Therefore, this section presents background on the bypass graft failure modes and current morphological knowledge.

2.1.1 Failure Modes

The pathology in the vein grafts documented by angiography and histologic examinations includes acute thrombosis and intimal hyperplasia (IH) during the first postoperative year and onset of progressive atherosclerosis beyond 3 to 5 years (Shah et al., 2003).

2.1.1.1 Thrombosis

Thrombosis is the formation of a blood clot, named as thrombus, inside an artery or vein.

Thrombosis develops by the same mechanisms that control hemostasis - the clotting system, which prevents blood loss in the event of vessel injury. As shown in Figure 2-1, the thrombus is primarily composed of platelets and red blood cells bound together by molecules in the cell membrane of the platelets, called membrane glycoproteins (GPs), by other proteins in the blood or inside the plaquelets, and by a network of polymerized plasma protein called fibrin (Colman et al., 1994).

Figure 2-1 Plaque fissuring and thrombus in human coronary artery. The thrombus (T) is comma shaped with a portion inside the plaque and a portion occluding the lumen. The torn edge of plaque cap is indicated by the arrow (taken from Davies, 1990)

An arterial thrombus is composed primarily of platelets, with some fibrin and trapped red cells, which are typically found distal to the platelet-rich part of the thrombus. An arterial thrombus is usually found superimposed on an atherosclerotic plaque, which fissured (or ruptured) to expose subendothelium plaque components to the blood as demonstrated in Figure 2-2 (Longest, 2002). Arterial thrombosis may also develop on artificial surfaces such as vascular grafts, heart valves and stents, as well as in aneurysms or injured arteries. An acute arterial thrombosis is often followed by a fibrin “tail” of trapped red blood cells, which extends downstream (Davies, 1990). Thrombi formed in the venous system are composed mostly of red blood cells, which are held together by a fibrin mesh, such as a fibrin tail.

Figure 2-2 Arterial thrombus including red blood cells, activated platelets and fibrin mesh (taken from Longest, 2002)

2.1.1.2 Intimal Hyperplasia

Intimal hyperplasia is the rapid abnormal continued proliferation and overgrowth of smooth muscle cells (SMCs) in response to endothelial injury or dysfunction (Chervu and Moore, 1990). This process results in an intimal thickening, which consists of SMCs and fibroblasts as well as collagen, elastin and proteoglycans. Figure 2-3 illustrates the intimal

thickening process of rat carotid artery after injury obtained by Clowes (2003). To better understand the pathological process, Figure 2-4 shows a diagrammatic representation of a muscular artery.

Figure 2-3 This series of photographs shows how a normal rat carotid artery (panel A- histologic cross-section) responds to injury. Angioplasty of the artery removes the surface endothelium (panel B). By two weeks (panel C), SMCs have migrated from the media into the intima (region above the elastic layer marked by the arrow) and have begun to proliferate (IH). The thickening of the wall reaches a maximum by three months (panel D). (taken from Clowes, 2003)

Figure 2-4 Diagrammatic representation of a muscular artery (taken from <http://greenfield.fortunecity.com/rattler/46/artries.htm>)

Although the IH process may reach a steady state level, which allows the luminal area to remain at a size, it can also grow unchecked, eventually leading to a severe obstruction of the lumen with subsequent ischemia in tissues further distal. Intimal hyperplasia is often viewed as an accelerated form of atherosclerosis due to the similarities in the lesions, e.g.

predominance and monoclonality of SMCs; in early stages SMCs proliferate and migrate from media toward intima; in later stage, contain large quantities of extracellular matrix (ECM). Ross (1986) advanced the response to injury hypothesis to propose that IH may be an early lesion on the pathway to atherosclerotic plaque. However, in similar sized plaques those developing due to hyperplasia tend to have a higher concentration of SMCs, less numbers of macrophages and T lymphocytes and a lower concentration of lipid accumulation than do atherosclerotic lesions.

2.1.1.3 Atherosclerosis

Atherosclerosis (note that in Greek, 'athero' and 'sclerosis' mean 'gruel' and 'hardness' respectively) is the progressive narrowing and hardening of arteries over time. It involves the buildup of deposits of fatty substances, decaying muscle cells, cholesterol, calcium and other substances in the inner lining of an artery as shown in Figure 2-5. This buildup is called plaque (atheroma). Plaque can grow and can considerably narrow the artery, so the artery becomes constricted and the elasticity is reduced. Therefore the amount of blood able to travel through it is reduced. The number and thickness of plaques increases with age, which builds up over many years. Figure 2-6 illustrates the progress of atherosclerosis.

Figure 2-5 Cross-sectional image of artery with atherosclerosis (taken from <http://www.nlm.nih.gov/medlineplus/ency/imagepages/18018.htm>)

Figure 2-6 Progress of atherosclerosis (taken from <http://www.guidant.com/condition/pop7.html>)

Initially, there is no endothelial denudation injury and so platelets interact with the intact endothelium. That is not to say that the endothelial function is normal, but simply that no adhesion of aggregates is present (Davies, 1994). There is ample evidence of functional endothelial abnormality at this stage of atherosclerosis (DiCorleto and Chisholm, 1986). As the atherosclerotic lesion progresses, there are gaps in the endothelial surface within which lipid-filled monocytes are impacted, and the presence of foam cells in peripheral blood suggests that some are emigrating from the intima. Platelets then adhere to the exposed connective tissue matrix underlying the endothelial defects, and this is the stage in which a true thrombogenic dimension is involved in atherosclerosis. The attached platelets play a major role in plaque growth by stimulating SMC migration and proliferation even though they may not significantly influence initiation.

2.1.2 Theories on Bypass Graft Failure

While the pathogenic mechanisms responsible for the development of thrombosis, IH and atherosclerosis remain elusive. It is generally believed that these pathological changes are remodeling process wherein a change in the mechanical environment (fluid shear, wall

stress, etc.), which stimulates cellular responses (changes in gene expression, mass transport, etc.) and subsequently results in the remodeling (Vorp, 1997; Nerem, 1992).

2.1.2.1 Biological Factors

Vascular endothelium, which lines the inside of the vessel wall and resides on a basement membrane anchoring the endothelial cells (ECs) to the vessel walls, plays an important role in many vascular functions. These include: provision of a nonthrombogenic and nonadherent surface to the blood; provision of a permeability barrier to blood constituents; maintenance of vascular tone; formation and secretion of growth-regulatory molecules and cytokines; maintenance of the basement membrane collagen and proteoglycans and the ability to modify (oxidize) lipoproteins (Ross, 1993). The ECs sense the mechanical forces acting on them through mechanotransducers, which may include integrins, G-proteins, and ion-channels, and regulate vascular functions by synthesizing and secreting numerous activator molecules (Davis, 1995). The presence of abnormal mechanical forces on the endothelium may lead to high cell turnover and leaky junctions, bond rupture of the EC, and changes in gene expression. These effects can then trigger excessive release of mitogens and growth factors and lead to subsequent SMC proliferation and excessive platelet aggregation (Chervu and Moore, 1990).

Smooth muscle cells, which comprise most of the media, are believed to migrate into the intima and proliferate during IH formation, although this proliferation rate varies widely. It has been shown that the SMCs undergo apoptosis (programmed cell death) and that their density in the media is lower compared to baseline levels in the early stage of vessel wall injury (Liu et. al., 2000). It is believed that EC-released mitogens and growth factors (e.g. NO, ET-1 and PDGF) are responsible for SMC migration and proliferation (Kraiss et. al., 1991), but the specific pathways are still uncertain.

The ECM proteins have been found to affect the fate of atherosclerotic lesions and to modulate cell migration, activity of growth factors and local concentrations of atherogenic lipoproteins (Knox et. al., 1986). Fibroblasts may be involved in synthesizing ECM proteins such as elastin and procollagen. These activated fibroblasts may be cells that originate in the adventitia and migrate to the intima (Shi et. al., 1997). The involvement of fibroblasts in IH formation is reminiscent of the process of wound healing, but it is distinguished from wound healing by its persistent synthetic activity which may be due to either humoral or mechanical factors that are known to sustain myofibroblast phenotype (Grinnell, 1994).

Nitric oxide (NO) is an important determinant of vascular homeostasis and an effector molecule critical to blood vessel function. It acts as a very potent endogenous vasodilator, helps in maintaining the nonatherogenic character of the healthy blood vessel wall, and works with other mediators (e.g. TGF- β 1) to keep vascular SMCs quiescent. Nitric oxide counteracts pro-proliferative agents such as platelet derived growth factor (PDGF) and basic fibroblast growth factor (bFGF), inhibits leukocyte and platelet response, which contribute to thrombosis, and decrease the expression of cell adhesion molecules released by vascular endothelium. So a vascular NO deficiency may promote restenosis (Janero and Ewing, 2000).

Monocytes and cholesterol (oxidized low-density lipoproteins (LDL)), also aided by endothelial cytokines and adhesion molecules, accumulate in the intima creating foam cells (Murase et al., 1998). Monocytes become macrophages within the intima and ingest oxidized LDL, secreting more mitogens and chemoattractants. Oxidized LDL appears to be cytotoxic to macrophages, causing them to rupture and release free cholesterol,

cytokines and procoagulants into the intercellular space. This creates an atherosclerotic plaque with fatty streaks consisting of a mass of lipid-engorged monocytes and free lipids covered by a fibrous cap of connective tissue (Virmani et al., 2000). Older plaques can develop into a calcified lesion or nodule. The origin of the calcification is not precisely known, but it appears to be associated with healed plaque. With a rigid matrix, the artery is unable to remodel, causing further cellular proliferation to push the fibrous cap out into the lumen. The rupture of this fibrous cap exposes tissue factors and collagen to the blood forming a nidus for thrombus formation.

2.1.2.2 Vascular Injury

Injury to the vessel wall, especially the endothelium, is believed to be the initiator of atherosclerosis (Schachter, 1997). In animal modeled synthetic or venous bypass grafts, IH was found to be most prominent along the suture line where trauma is present (Bassiouny et al., 1992). At the suture site itself, four distinct endothelial lesions have been identified (Pagnanelli et al., 1980): a large intimal hole due to needle perforation; a variable length of intimal tear continuous with the needle hole; a variable number of patches of denuded subendothelium surrounding the needle hole and variable degrees of platelet aggregation and white blood cell (WBC) adhesions extending from the needle hole over a wide area of the vessel. These injuries to the vessel wall result in deposition of mural thrombi on the suture line, necrosis of the vessel wall where it is compressed by the suture, and intramural hemorrhage in the early stages produced by damage caused by passing the suture materials through the vessel wall (Shiroma and Kusaba, 1996). Clowes et al. (1983) were first to demonstrate clearly that acute injury to the intima and media could produce hyperplasia. Subsequent studies have shown that such injury produces SMC proliferation, which occurs at a rate proportional to the degree of the injury (Chervu and Moore, 1990).

In 1986, Ross even provided two pathways about how the injury causes atherosclerosis, which was illustrated in Figure 2-7. In Figure 2-7, the pathway demonstrated by the clockwise arrows to the right has been observed in experimentally induced hypercholesterolemia. Monocytes attach to endothelium, as shown in Figure 2-7 (B), which may continue to secrete growth factors (short arrow in Figure 2-7 (B)). Subendothelial migration of monocytes may lead to fatty-streak formation and release of growth factors such as PDGF (short arrow in Figure 2-7 (C)) as demonstrated in Figure 2-7 (C). Fatty streaks may become directly converted to fibrous plaques (as observed from Figure 2-7 (C) to (F)) through release of growth factors from macrophages or endothelial cells or both. Macrophages may also stimulate or injure the overlying endothelium. In some cases, macrophages may lose their endothelial cover and platelet attachment may occur, as seen in Figure 2-7 (D), providing three possible sources of growth factors – platelets, macrophages, and endothelium (short arrows in Figure 2-7(D)). Some of the SMCs in the proliferative lesion itself may form and secrete growth factors such as PDGF (short arrows in Figure 2-7(F)) as seen in Figure 2-7 (F). An alternative pathway for development of advanced lesions of atherosclerosis is shown by the Figures 2-7 (A) to 2-7 (F) through 2-7 (E). In this case, the endothelium may be injured but remain intact. Increased endothelial turnover may result in growth factor formation by ECs as shown by Figure 2-7 (A). This may stimulate migration of SMCs from the media into the intima, accompanied by endogenous production of PDGF by smooth muscle as well as growth factor secretion from the “injured” endothelial cells as illustrated in Figure 2-7 (E). These interactions could then lead to fibrous-plaque formation and further lesion progression as shown in Figure 2-7 (F).

Figure 2-7 The updated response to injury hypothesis of Ross (1986)

2.1.2.3 Mechanical Factors

As IH and atherosclerosis are commonly found in locations where abnormal mechanical forces are also present, it is possible that an abnormal mechanical stimulation may cause the wound healing process to go unchecked.

2.1.2.3.1 Wall Shear Stress Related Factors

Although the precise mechanism(s) have not been established, mechanical factors must be involved in localization of atherosclerosis. It is worth to know that some studies were carried out to link the hemodynamic parameters with atherogenesis in arterial bypasses and other branching blood vessel configurations since ECs have been shown to be shear sensitive (Davies, 1991). These parameters included WSS, wall shear stress gradient (WSSG) and oscillation shear index (OSI) etc, and were reviewed as following.

Texon (1957): Low pressure theory

This publication was the first attempt to link fluid dynamics with atherogenesis. In sites of arterial curvature, it was proposed that the pressure at the inner wall would decrease significantly to become negative and hence would pull the endothelium into the lumen initiating the disease process when the blood is forced to turn around the curve. However, the radial pressure gradient is very small and hence significant decrease in pressure will not occur. So the effect proposed in this theory is not likely to happen. However, this publication contributed towards the thinking process on hemodynamic effects on the endothelial cells and initiation of atheroma.

Fry (1968): High shear stress theory

His study was based on the theory that high shear stresses will erode the endothelium and the morphological alterations in the lumen will also alter the transport of species across the endothelial barrier into the arterial wall. Through the in-vivo experiments on dogs, he concluded that ECs appeared to be normal if the time averaged shearing stresses were below $379 \pm 85 \text{ dynes/cm}^2$ ($37.9 \pm 8.5 \text{ Pa}$).

Caro et al. (1971): Shear-dependent mass transport theory

They observed that in the aorta, atherosclerotic lesions occur along the inner wall of curvature where there is low shear stress. Hence their proposal is that cholesterol is actually synthesized in the arterial wall and diffuses into the lumen where it is washed away by the blood stream. In the regions of high wall shear stresses (and hence velocity gradients), more cholesterol is washed away by the blood flow. On the other hand, where the shear stress is low, excess cholesterol is deposited on the surface of the lumen

initiating atheroma development. Thus, it is the shear-dependent mass transport that is responsible for atheroma growth.

Thus low and high wall shear stress theories were debated for several years. With the development of more sophisticated measurement techniques and computational fluid dynamic algorithm, more detailed analysis become possible. In addition, advent of sophisticated imaging modalities such as MRI, computed tomographic (CT), and ultrasound imaging, morphologically realistic 3D geometrical reconstruction of the segments of interest also became available. Studies on arterial sites of interest thus resulted in additional theories as well.

Ku et al. (1985): Oscillatory shear index

They studied the oscillatory nature of shear stress induced by pulsatile blood flow in the carotid artery bifurcation. Adopting the low shear stress hypothesis, they put forward an OSI, which is a measure of the temporal and spatial variation of the local WSS, and attempted correlation with atheroma development. In general it varies between 0.0 and 0.5. OSI values near reattachment and separation points are 0.5. Regions that experience no reverse flow have OSI values of zero.

Kleinstreuer et al. (1991): WSS bandwidth theory

The postulate is that very low, oscillating shear stress initiates atherosclerotic lesions and low and high wall shear stresses contribute to the growth of plaque formation. A safe bandwidth of WSS was suggested with a lower limit and a higher limit. Wall shear that falls outside these limits will result in plaque formation and the magnitude beyond these limits will determine the rate of growth of the plaque.

Depaola et al. (1992): The temporal and spatial wall shear stress gradient

The WSSG attempts to capture the aggravating effects of changing surface forces on the endothelium. They postulated that large spatial WSSG induces morphological and functional changes in the endothelium, which contribute to elevated wall permeability and hence possible atherosclerotic lesions. Whereas spatial gradients of the WSS may provide reasonable answers to predicting susceptible regions due to elevated wall permeability, the spatial WSSG cannot identify very low, nearly uniform WSS regions that may be prone to atherosclerotic lesions.

Buchanan et al. (2003): Wall shear stress angle gradient (WSSAG) theory

They investigated the flow simulations and monocyte deposition patterns for a rabbit's abdominal aorta. The WSSG, WSSAG and normalized monocyte deposition fraction were correlated with the distribution of monocytes along the abdominal aorta. These results suggested that the transport and deposition pattern of monocytes to arterial endothelium played a significant role in the localization of lesions.

Longest and Kleinstreuer (2003): Novel near-wall residence time (NWRT) model

They conducted experimentally validated particle-hemodynamic simulations for two end-to-side anastomotic configurations, in order to assess the potential role of platelet-wall interactions. Specifically, sites of significant particle interactions with the vascular surface had been identified by a novel near-wall residence time (NWRT) model for platelets, which included shear stress-based factor for platelet activation as well as endothelial cell expression of thrombogenic and anti-thrombogenic compounds. Results indicated that the composite NWRT model for platelet-wall interactions effectively captured a reported shift in significant IH formation from the arterial floor, thus indicated

the potential significance of platelet-wall interactions coinciding with regions of low WSS in the development of IH.

In spite of all these theories, a single theory is not able to completely explain the plaque initiation and growth. It should also be remembered that with injury to the endothelium, the plaque formation and development would also depend very heavily on the transport of LDL-cholesterol and its absorption into the subendothelial region. Some evidences have also been presented in the literature that regions of hypoxia also contribute towards plaque formation. Availability of oxygen is a limiting factor in the ability of cells to metabolize lipids and some models have suggested that in regions of stagnation and recirculation, the concentration of lipid is high (due to large residence time) whereas oxygen concentration is reduced (due to non-availability of red blood cells with oxygen in the region of stagnation and recirculation).

2.1.2.3.2 Compliance Mismatch

In the case of arterial bypasses, compliance mismatch between an artery and graft is regarded as another mechanical factor that may lead to IH formation. Studies by Abbott et al. (1987) and Bassiouny (1992) have shown that a higher degree of compliance mismatch (graft stiffer than artery) results in a greater amount of IH formation, although Wu et al. (1993) did not show a similar trend in host arterial IH formation. While the presence of compliance mismatch may also be associated with reduced fluid shear stress in the anastomotic region and with increased wall shear concentration at the suture line, a controversy still exists which questions the role of mechanical factors upon IH formation. No matter what the primary mechanical stimulator is, it seems that compliance mismatch alone, without trauma, only causes limited amounts of IH formation (Okuhn et al., 1989).

2.1.2.3.3 Turbulence

It has been shown that the high and low frequency component of turbulence can cause damage to collagen and elastin, resulting in weakness and dilation (Boughner and Roach, 1971). Increased velocity gradients such as occur with turbulence were also reported to cause vascular endothelial damage (Fry, 1968). Hence turbulence can cause damage to the three major components of the vessel wall (collagen, elastin, endothelium) and can consequently decrease the modulus of elasticity of the host artery. Eiken (1961) experimentally showed that thrombotic deposits occur on luminal surfaces at sites of turbulence. The question, which remains unanswered, is whether the turbulence occurs on the coronary artery bypass graft.

2.2 The Role of Hemodynamics upon the Anastomosis

As discussed above, there is now considerable evidence that hemodynamics plays an important role for the occlusion symptom of bypass. Over the years, investigators have sought to relate the fluid dynamic variables with the vascular graft healing and failure by using in-vivo animal studies, in-vitro flow modeling studies and numerical simulations. The obvious advantage of in-vivo studies is the ability to study mammalian tissue, but the hemodynamic conditions are not easily controlled or measured. This insufficiency can be overcome by the in-vitro flow modeling studies. However, except for short-term studies, the hemodynamically mediated biologic response of intact, living blood vessels is difficult to study in-vitro. Comparing with in-vivo and in-vitro studies, numerical simulation allows the detailed study of many complex hemodynamic factors, such as particle streamlines in various grafting configurations, which are difficult and expensive to study accurately by means of in-vivo or in-vitro experiments. Therefore numerical simulation has become popular with the advent of computational fluid dynamics and the availability of high powered computing platforms. Of course, numerical simulation based

investigations are limited to only elucidate the fluid mechanic parameters and are difficult to detail a resulting biological response (Vorp, 1997).

In general, hemodynamic based studies play an important role in vascular graft research and development. The main purpose is to establish the correlation of fluid dynamic variables with biological factors, such as mitogenic factors, platelet activation and etc.

2.2.1 In-Vivo Study

Animal experiments or human implantations are performed by many scientists as a means to provide first-hand feedback from graft implantation. In-vivo studies demonstrated that there is evidence of hemodynamic influences on the endothelium, intimal thickening and monocyte recruitment.

As far as 1972, Imparato et al. studied intimal and neointimal fibrous proliferation, which caused the failure of arterial reconstruction, using mongrel dogs as animal models. Their histologic examination of specimens revealed fibrous intimal proliferation occurring at the sites of the anastomoses, the vein wall opposite to the anastomotic toe and in the graft conduit. Later in the study of an end-to-side anastomotic configuration, they also found that intimal fibrous plaques developed at the proximal end of the host arterial, where no surgical manipulations had been performed (Imparato et al., 1974), which suggested the contribution of hemodynamics to the formation of the intimal plaque.

In 1979, Echave et al. found that IH ingrown from the recipient vessel into the Polytetrafluoroethylene (PTFE) graft, by applying the 6.5mm to 4.5mm tapered PTFE graft for femoral popliteal and femoral tibial bypass. Later, Berguer et al. (1980) found

that the vein graft carrying low flow rates appeared to develop more IH than those carrying high flow rates when performing an end-to-end anastomosis in dogs.

LoGerfo et al. (1983) firstly investigated the precise location and progression of anastomotic hyperplasia and its possible relationship to flow conditions through studying the femoro-femoral Dacron grafts of 28 dogs. Transmission electron microscopy showed that the hyperplasia consisted of collagen-producing SMCs and was significantly greater at the downstream anastomosis, which was progressive with time and led to the failure of Dacron arterial grafts.

Morinaga et al. (1985) further investigated the effect of WSS on the intimal thickening of arterially transplanted autogenous vein in dogs. In group I, grafts were implanted under flow conditions of 79.7 ± 3.2 ml/min of the normally high flow rate with 33.1 ± 1.9 dynes/cm² of low WSS. In group II, grafts were implanted under conditions of 2.9 ± 1.8 ml/min of the normally low flow rate with 178.8 ± 11.0 dynes/cm² of high WSS. The intimal thickness after implantation in group I was statistically significant comparing with group II, which revealed that WSS, not the rate of blood flow was the essential hemodynamic factors related to IH.

In 1986, Kuwano et al. performed serial histologic observations on the healing process of expanded PTFE vascular grafts in dogs. Lesion growth was found within 3mm of the anastomoses. Pannus developed smoothly from both ends of the graft. Therefore they suggested that thrombi organization followed by nodular lesions might be one of the major factors that led to the formation of IH.

Moreover, Binns et al. (1989) also studied the effect of WSS on vascular healing. Forty PTFE grafts with internal diameters of 3, 6 and 8mm were inserted end-to-end in the femoral and carotid arteries of 10 mongrel dogs. Total flow and diameter were measured. In addition, grafts were stained with Evans blue dye, fixed by pressure perfusion, and analyzed by computer for anastomotic neointimal thickening, graft pseudointimal thickening and degree of endothelial coverage. The results identified that low shear stresses produced greater amounts of pseudointimal thickening within PTFE grafts and neointimal thickening at their anastomoses than those produced by high shear stress.

Kenneth et al. (1991) investigated the effect of varying blood flow rates on the accumulation of thrombotic material within arteries, with the use of shear rate as an index of flow across the inner wall surface. The findings reflected that the formation of thrombus on altered arterial surfaces was highly dependent on the flow characteristics at the blood-intimal interface. Regions of high shear rate appeared to be most prone to thrombus growth, with increasing platelet and fibrin deposition.

To further investigate the localization of experimental anastomotic intimal thickening in relation to known biomechanical and hemodynamic factors, Bassiouny et al. (1992) implanted both bilateral iliofemoral saphenous veins (extracted from the animals) and synthetic PTFE grafts in 13 mongrel dogs. The regions of intimal thickening in the histological sections were identified and quantified with the use of oculomicrometry, which revealed two separate and distinct regions of anastomotic intimal thickening (or IH formation) as shown in Figure 2-8.

Figure 2-8 Distribution of IH in recipient artery following end-to-side anastomosis (taken from Bassiouny et al., 1992)

The first region of IH formation was along the suture line, which was greater in PTFE anastomoses than in vein anastomoses. The second distinct type of intimal thickening was developed on the arterial floor and was the same in both PTFE and vein anastomoses. To characterize the flow patterns inside the distal anastomosis, transparent silicone models were constructed from the castings of the anastomosis and flow visualization method was used. Intimal thickness was absent along the graft hood where flow was laminar and high shear with short particle residence time. Arterial floor intimal thickening developed in a region corresponding to the stagnation zone where low and oscillatory shear prevailed. Flow patterns associated with relatively low shear and long particle residence time were also found along the heel and lateral wall of sinus where suture line intimal thickness was presented. Therefore they concluded that the suture line intimal thickening, which represents vascular healing, was more prominent with the PTFE anastomosis and may be related to compliance mismatch. Arterial floor intimal thickening was unrelated to graft type and developed in regions of flow oscillation and relatively low shear.

In another study done by Sise et al. (1992), PTFE interposition grafts were used for carotid reconstruction in 23 patients during a 7-years period. The function of this interposition as illustrated in Figure 2-9, was to maintain adequate arterial control to reduce chances of endarterectomy, carotid aneurysm and kinks after carotid

reconstruction. They proposed that PTFE can be used effectively for carotid reconstruction but there seemed to be a higher risk for patients to suffer a second restenosis.

Figure 2-9 Configuration of PTFE interposition graft used in reconstruction of carotid bifurcation (taken from Sise et al., 1992)

Staalsen et al. (1995) implanted Polyurethane grafts of 8mm in diameter into 10 pigs in order to study the effect of the anastomosis angle (15° , 45° and 90°) on the flow fields at the end-to-side anastomoses. The effect of the anastomosis angle on the flow field was investigated by means of color-flow Doppler scanning to identify the range of angles that were associated with the least flow disturbances. The results suggested that the smallest anastomosis angle (15°) was associated with the least flow disturbances at the toe and one diameter downstream. This study confirmed the in-vivo existence of regions with low and reverse velocities at the preferential sites in vascular end-to-side anastomoses where neointimal hyperplasia tends to form.

In addition, Wu et al. (1995) studied the effects of increased shear stress on the aggregability of platelets on the surface thrombosis and endothelialization in nine dogs

implanted with 6mm diameter Dacron grafts. It was found that high shear stress graft had less flow surface thrombus, more endothelialization, and a thinner surface lining than a low shear stress graft.

Sterpetti et al. (1996) investigated the production of growth factors - PDGF and bFGF after PTFE and vein arterial grafting. Fifteen 1cm long segments of PTFE and 15 vein grafts were interposed in 30 rats at the level of abdominal aorta respectively. Four weeks after implantation, the animals were killed and the tissue was studied in organ culture for release of PDGF AA, PDGF BB and bFGF. The results identified that PTFE grafts released a greater quantity of growth factors (PDGF AA and bFGF) than did vein graft, which could explain, in part, the occurrence of distal anastomotic myointimal hyperplasia.

In 1996, Caro et al. used magnetic resonance imaging techniques to examine the geometry of arterial curvature and branching in-vivo and in casts. The distribution of axial velocity in the associated flow was also measured. It was found that the geometry was commonly non-planar, which affected the velocity and wall shear distribution.

Jones et al. (1997) firstly recorded the in-vivo velocity profiles of canine end-to-side ilio-femoral anastomotic grafts with a pulsed Doppler ultrasound velocimeter. The geometries were obtained from casts of the anastomotic region, and flow rates were measured with electromagnetic flow probes. Three cases including a “standard” geometry, a stenosed geometry and a case with below average flow rate were reported as shown in Figure 2-10. Although the flow patterns require some interpretation since only one component of the velocity is measured and the Doppler angle is not known a priori, the velocity profiles are still adequate to determine the flow patterns in the anastomosis. Observed flow features

included flow separation at the hood and toe, movement of the floor stagnation point and skewed profiles in the proximal outflow segment. Out-of-plane curvature and lateral displacement of the anastomosis inlet appeared to have a strong effect on the flow fields. In addition, compliance affected the instantaneous flow rates within the proximal and distal branches. In conclusion, variations in graft geometry may be an important determinant of the spatial distribution of the IH.

Figure 2-10 Summary of flow pattern in three different cases
(taken from Jones et al., 1997)

Keynton et al. (1999) applied a specially designed pulse ultrasonic Doppler wall shear rate (PUDWSR) measuring device to evaluate the effect of graft caliber, a surgically controllable variable, upon local hemodynamics, which, in turn, played an important role in the eventual development of anastomotic hyperplasia. Tapered (4-7 mm I.D.) 6-cm-long grafts were implanted bilaterally in an end-to-side fashion with 30 degree proximal and distal anastomoses to bypass occluded common carotid arteries of 16 canines. The results stated that wall shear rate (WSR) varied widely within end-to-side distal graft anastomoses, particularly along the artery floor, and might play a role in the development of IH through local alteration of mass transport and mechano-signal transduction within the endothelium.

Another in-vivo study by Kissin et al. (2000) demonstrated different amounts of IH in anastomoses with either a synthetic or a venous Miller's cuff. Based on the assumption that the synthetic and venous Miller's cuffs constructed with the same geometry should result in a similar hemodynamic environment in both anastomoses, they supposed that there should be no influence of the hemodynamic environment on the reduced amount of IH in the venous cuff. Instead, they speculated that the difference in material properties of cuffs (which may cause different degrees of compliance mismatch) or some biological factors originating from the venous cuff might be responsible for the reduced amount of IH seen with the particular case study.

In 2001, Keynton et al. further investigated the potential interaction between local hemodynamics and vascular wall response. Tapered (4–7 mm I.D.) 6cm long e-PTFE synthetic grafts were placed as bilateral carotid artery bypasses in six adult mongrel dogs with distal anastomotic graft-to-artery diameter ratios (DR) of either 1.0 or 1.5.

Immediately following implantation, simultaneous axial velocity measurements were made in the toe and artery floor regions at the plane of the anastomosis with radial increments of 0.35mm, 0.70mm, and 1.05mm using a specially designed 20MHz triple crystal ultrasonic WSR transducer. Mean, peak, and pulse amplitude WSR, their absolute values, the spatial and temporal WSSGs, and the OSI were computed from these velocity measurements. All grafts were harvested after 12 weeks implantation and measurements of the degree of IH were made along the toe region and the artery floor of the host artery in 1mm increments. While some IH occurred along the toe region and was significantly different between DR groups, the greatest amount occurred along the artery floor and no significant differences were found between different DR groups. Linear regressions were performed on the paired IH and mean, peak, and pulse amplitude WSR data as well as the absolute mean, peak, and pulse amplitude WSR data from all grafts. The mean and absolute mean WSRs showed a modest correlation with IH, which were even better correlated when using an exponential relationship. The overall best correlation was seen against an exponential function of the OSI. In addition, it was observed that over 75% of the IH occurred at or below a mean WSR value of 100s^{-1} while approximately 92% of the IH occurred at or below a mean WSR equal to one-half that of the native artery. Therefore, while not being the only factor involved, wall shear (and in particular, oscillatory wall shear) appeared to provide a stimulus for the development of IH.

Jackson et al. (2001) also studied the relationship between local hemodynamics and pathological response of the distal anastomosis by manipulation of the grafting angle. In their studies, end-to-side anastomoses of the right carotid to the left carotid arteries of rabbits were performed at anastomotic angles of less than 10 degrees (acute), 45 degrees (intermediate), or 90 degrees (right angle), and then the upstream left carotid arteries were

ligated to simulate pathologic occlusion. The result indicated that very different pathologic changes to the vessel wall were elicited when hemodynamics was manipulated by altering the anastomotic branch angle.

As a conclusion, the in-vivo studies revealed the pathological factors for the failure of bypass, which showed the great relationship with hemodynamic factors, especially the WSS. In-vivo WSRs were often estimated from either volume flow rate or single-point velocity measurements together with the no slip assumption at the wall and a simple linear regression, although a new, in-vivo transducer was capable of determining WSRs nonintrusively from velocities at three points along a line perpendicular to the vessel wall using a second or third-order polynomial curve fit (Keynton et al., 1995). Therefore to further understand the role of hemorheologic and hemodynamic factors in vascular graft healing, more researchers have explored the fluid phenomena by in-vitro study or numerical simulation.

2.2.2 In-Vitro Study

For end-to-side anastomosis, most research works focused on experimental studies using such techniques as laser Doppler anemometry (LDA), flow visualization, Particle Image Velocimetry (PIV), electrochemical and Pulsed Doppler Ultrasound techniques. The anastomotic geometries used in these studies include simple, rigid straight tubes intersecting with each other as well as more realistic, compliant anastomotic configurations. The inlet waveforms used include simple steady flow and purely sinusoidal waveforms as well as more physiological waveforms.

2.2.2.1 Laser Doppler Anemometry Measurements

In order to examine the effects of junction angle and flow rate on the local velocity field, Keynton et al. (1991) performed a steady flow in-vitro study on the distal arterial bypass

graft junctions. Three anastomotic models with 30° , 45° and 60° junction angles were fabricated using Plexiglas tubing of 25.4 mm in diameter. Both LDA measurements and flow visualization (using Hydrogen bubbles) were performed. The results revealed skewed velocity profiles towards the outer wall with a flow split around a clear stagnation point along the outer wall as shown in Figure 2-11. Axial velocities and shear rates along the outer wall were found to be higher than those along the inner wall and occurred in the order of 45° , 60° and 30° junction angles. In summary, this study clearly identified changes in wall shear, which varied with the anastomotic angle and flow rate.

Figure 2-11 Flow pattern and velocity profile for $Re = 205$ at various anastomotic angles (taken from Keynton et al., 1991)

Friedman et al. (1992) carried out LDA measurements to estimate the WSR histories for investigating the effect of arterial compliance and non-Newtonian rheology on the correlations between intimal thickness and wall shear. Although they used a minimally diseased human aortic bifurcation to replicate in rigid and compliant flow-through casts, the results were useful for considering the proximal anastomosis. In the study, both casts

were perfused with the same physiologically realistic pulsatile flow. The pulse pressure in the compliant cast produced radial strains similar to those expected from postmortem measurements of the compliance of the original tissue. The compliant cast was perfused with a Newtonian fluid and the other one whose rheology was closer to that of blood respectively. Intimal thickness was measured at corresponding sites in the original vessel and linear regressions were performed between these thickness and several normalized shear rate measures obtained from the histories. The correlations showed a positive slope - that meant the intima was thicker at sites exposed to higher shear rates, which was consistent with earlier results for relatively healthy vessels, but the slope was relatively small. There was no significant effect of either model compliance or fluid rheology on the slopes of the correlations between the intimal thickness and any normalized measured shear rate.

To investigate the role of a compliant wall upon the near wall hemodynamic flow field, two models of the carotid bifurcation were constructed by Anayiotos et al. (1994). The inner geometry were identical for both models, although one was made of compliant material while the other one was rigid. Velocity under pulsatile flow condition was measured with a single component laser system and WSR was estimated from new wall data. Wall motion in the compliant model was measured by a wall motion transducer and the maximum diameter varied between 4-7 percent in the model with the greatest change at the intersection of axis. The trend of mean shear stress distribution in both models was similar, although the magnitude in the compliant model was observed to be smaller by about 30 percent than the rigid one at most locations. The difference between two models in peak shear stress was greater and occasionally reached as much as 100 percent with the

compliant model consistently having smaller positive and negative peaks. The results indicated prominent influence of compliance.

In 1997, Loth et al. carried out LDA measurements of velocity and WSS inside a PTFE vascular graft model under steady flow conditions. The WSS distribution, computed from near-wall velocity gradients, revealed a relatively low WSS region on the wall opposite to the graft near the stagnation point approximately one artery diameter in axial length at the mid-plane. It was suggested that these sites might be susceptible to arterial remodeling and intimal thickening because of the low WSS region created by the stagnation flow.

Recently, with the emergence of Miller cuff, which was interposed between the graft and arterial to enhance the patency rate of grafts, Rowe et al. (1999) and How et al. (2000) began to investigate the local hemodynamics due to the cuff geometry.

Rowe et al. (1999) studied the flow pattern of two different types of precuffed grafts and compared them with the flow patterns in the Miller cuff and the conventional end-to-side anastomoses using flow visualization. The WSR was calculated from the near-wall velocity acquired using LDA. The flow structures in the precuffed grafts were similar to those observed in the Miller cuff, which may be the 'ideal' geometry to improve the clinical performance of PTFE bypass grafts.

How et al. (2000) further compared the WSS distribution in the conventional end-to-side (ETS) anastomosis and the anastomosis with the interposition of vein cuff (IVC). The results showed that the vein cuff did alter the mean WSS distribution within the recipient artery and removed the area of low WSS at the heel as shown in Figure 2-12, which may

explain the redistribution of myointimal hyperplasia (MIH) away from important sites in the recipient artery.

Figure 2-12 Mean WSS distributions for a flow split of 50:50 in the (a) ETS and (b) IVC anastomoses. The horizontal dashed lines at $\pm 0.5 \text{ N/m}^2$ represent the range of low mean WSS that has been associated with a high increase in MIH (taken from How et al., 2000)

Li and Rittgers (1999, 2001) investigated the effect of different flow ratios between the proximal outlet segment (POS) and the distal outlet segment (DOS) on flow patterns and the distribution of hemodynamic factors in the distal anastomosis. Flow visualization method was used to determine the overall flow patterns and velocity measurements were made with LDA. The statistical results showed significant difference for the mean WSS between different flow ratio cases along the graft hood, but no significant differences were detected along the artery floor. There was also no significant difference for the spatial WSSG along both the artery floor and the graft hood, where significant difference of mean OSI can be observed. Comparing these mechanical factors with histological findings of IH formation obtained by previous canine studies, they suggested that the regions exposed to a combination of low mean WSS and high OSI were the most possible places subject to the formation of IH.

In 2002, Loth et al. further investigated the relative contribution of WSS and injury in experimental intimal thickening at PTFE end-to-side arterial anastomoses. The distribution of intimal hyperplasia thickening (IHT) was determined from seven canine iliofemoral PTFE grafts after 12 weeks of implantation with computer assisted morphometry. An upscaled transparent model was constructed according to the in-vivo anastomotic geometry, and WSS was determined at 24 axial locations from LDA measurements of the near wall velocity under pulsatile flow conditions similar to those presented in-vivo. Nonlinear multivariable logistic analysis was used to model IHT as a function of the reciprocal of WSS, distance from the suture line, and vascular conduit type (i.e. PTFE versus host artery). Vascular conduit type and distance from the suture line independently contributed to IHT. An inverse correlation between WSS and IHT was found only for those regions located on the juxta-anastomotic PTFE graft. Since IHT was small in all the canines studied, there may be difference between the intimal thickening observed in their study and that observed in human vascular anastomoses. However, they provided a basis for further investigation with more realistic physiological models.

Anayitos et al. (2002) studied the hemodynamic features of two anatomic models of saphenous-vein CABGs. One model simulated an anastomosis with both diameter and compliance mismatch and a curvature at the connection, analogous to the geometry observed in a conventional cardiothoracic procedure. The other model mimicked an anastomosis with a flow stabilizing anastomotic implant connector, which improved current cardiothoracic procedures by eliminating the distal vein bulging and curvature. Physiologic flow conditions were imposed on both models and qualitative analysis of the flow was performed with dye injection and a digital camera. Quantitative analysis was performed with LDA measurement. The results demonstrated that the presence of the

bulge at the veno-arterial junction, contributed to the formation of accentuated secondary structure (helices), which progressed into the flow divider and significantly affected radial velocity components at the host vessel up to four diameters downstream of the junction. The model with the implant, achieved more hemodynamically efficient conditions on the host vessel with higher mean and maximum axial velocities and lower radial velocities than those of the conventional model. The presence of the sinus might also affect the magnitude and shape of the shear stress at locations where intimal thickening occurred. Thus, the presence of the implant created a more streamlined environment with more primary and less secondary flow components which might then inhibit the development of intimal thickening, restenosis and ultimate failure of the saphenous vein graft.

2.2.2.2 Flow Visualization Measurements

In the field of flow visualization, the works by Karino and his coworkers were quite important and significant. They initiated a series of morphologic and fluid mechanical studies on the localized pathogenesis and development of intimal hyperplasia (and atherosclerosis) by developing a new technique to prepare isolated transparent natural blood vessels from animals and human post-mortems. Thus, this has, for the first time, enabled the study of exact flow patterns and distributions of fluid velocity and shear rate existing in various region of disturbed flow in the mammalian circulation by directly observing and photographing the behavior of tracer particles and blood cells flowing through the isolated transparent blood vessels (Motomiya and Karino, 1984; Asakura and Karino, 1990). Further histological examinations of the transparent vessels realized firstly the correlation between the flow patterns and the exact anatomic locations of intimal thickening (Ishibashi et al., 1995).

The investigation by Motomiya and Karino (1984) of flow patterns in the human carotid artery bifurcation demonstrated that a recirculation zone which consisted of a pair of complex spiral secondary flows, symmetrical about the common median plane of the bifurcation, was formed in the carotid sinus over wide ranges of inflow Reynolds numbers and flow rate ratios. This recirculation zone was suggested to act as a promoter of the vascular diseases, atherosclerosis and thrombosis, which tend to be localized in this region.

Applying the same technique to the human coronary arteries, Asakura and Karino (1990) found that atherosclerotic plaques and wall thickenings in left and right coronary arteries were localized almost exclusively on the outer wall of one or both daughter vessels at major bifurcations and T-junctions, which left the flow-divider free of lesions, and along the inner wall of curved segments. Through studying of flow patterns in such vessels, it was discovered that the flow at these sites was either slow or disturbed with the formation of slow recirculation and secondary flow and furthermore, the wall shear stress was low.

The exact locations and sizes of intimal thickening and characteristics of the flow prevailing at sites of anastomoses were studied in detail by Ishibashi et al. (1995) using flow visualization and cinemicrographic technique. It was found that a perfect correlation existed between the preferred sites of intimal thickening and the regions of slow recirculation flows with low wall shear stresses. In both 90-degree and 45-degree anastomosed vessels, intimal thickening developed only in those vessels in which formation of slow recirculation flows was observed. It was also found that although a pronounced and localized intimal thickening developed in 45-degree anastomosed

vessels, the degree of circumferential constriction caused by both surgical procedures and development of intimal thickening was much mild in 45-degree than in 90-degree anastomosed vessels.

According to this series of studies, they concluded that the key hemodynamic factors involved in the localization of intimal thickening (and atherosclerosis) were low velocity of flowing blood and the resultant low shear stresses acting on the vessels (Ishibashi et al., 1995). The mechanism, which leads the vessels to a pathologic state of intimal hyperplasia or atherosclerosis, may due to the arrest or permanent adhesion and concentration of the particles (lipoproteins, platelets and monocytes) on the endothelium by the low fluid velocity. The local difference in the morphology of endothelial cells due to different wall shear stress may also provide different permeability to water, solutes and macromolecules, thus leading to different biological and biochemical functions (Asakura and Karino, 1990).

In addition, other researchers also carried out important works in this field. In 1989, Shu et al. constructed an elastic, transparent Silastic flow model to represent the detailed geometry of anastomoses. Dye injection technique was used to study the flow patterns, detailed flow measurements were carried out with LDA and the WSS was calculated from the velocity profile gradients near the wall at two phasic angles as shown in Figure 2-13. The results showed that more variations of WSS were limited around the joint of anastomosis, where it is prone to the IH.

Figure 2-13 WSS distributions at two phasic angles for two planes are shown at the left and right sides respectively (taken from Shu et al., 1989)

White et al. (1993) investigated the flow behavior of distal anastomoses under steady and pulsatile flow conditions. Flows in the scaled-up, transparent models were visualized with white, neutrally buoyant particles, which were photographed under laser illumination and recorded on videotape. Strong three-dimensional helical patterns, which formed at the anastomotic junction, were prominent features of the flow fields. Comparisons with the limited qualitative data available on intimal thickening in vascular graft anastomoses suggested a relation between localization of vascular intimal thickening and those surfaces experiencing low shear and long particle residence time.

In order to provide a detailed description of spatial and temporal variations of WSS within the end-to-side arterial anastomosis, Ojha (1993) introduced a photochromic tracer technique to provide an overall view of the velocity field and to determine the instantaneous value of the WSS in a 45-degree anastomosis model under pulsatile flow conditions of a 2.9 Hz sinusoidal waveform with a Womersley number of 7.9. Figure 2-14 highlighted the WSS variations over the flow cycle at six different locations. Flow separation was produced just beyond the toe and the stagnation point was seen to

fluctuate quite sharply on the bed over a distance of about one tube radius upstream from the site across the toe. The sudden motion of the stagnation point around peak flow further produced sharp temporal gradients of the WSS. When compared to the sites where IH tends to occur, a strong correlation was seen with low WSS at the heel and toe, and with the sharp temporal variations of the magnitude and spatial gradient of the WSS on the bed at the junction.

Figure 2-14 Variations of the WSS over the flow cycle at six different locations (taken from Ojha, 1993)

Later on, Ojha et al. (1993) advanced the study to investigate the fluid mechanical effects of a side-to-end proximal anastomosis and compared the results with their earlier study on the end-to-side distal anastomosis. The same photochromic tracer technique was adopted to determine the instantaneous WSS and to visualize the overall flow field under pulsatile flow conditions. The results showed that positive WSSs were very high at the toe and heel junctions, together with substantial nonperiodic fluctuations as illustrated in Figure 2-15. The peak WSS was about four times higher at the toe and about seven times higher at the heel than the maximum values observed at about four tube diameters upstream from the junction. On the bed of the host vessel, nonperiodic fluctuations were also observed, but

the shear stresses were mainly negative with magnitudes comparable to those seen upstream. With leakages of 11% and 28% from the mean flow through the blocked end of the host vessel, the shear stress pattern seemed to be significantly affected only at the toe for the higher leakage. Furthermore, when the mean Reynolds number was reduced, the magnitude of the variations in the WSS was reduced proportionately, except at the heel, where the reduction was much larger than expected. Comparing with the results of distal anastomosis, it was concluded that the preferential development of IH at the distal end-to-side anastomosis might be promoted by low WSS at the toe and heel, and probably by high shear stresses or shear stress gradients on the bed. It was found that the proximal junction could serve as a control for improving the patency rate.

Figure 2-15 WSS variations on (a) bed and (b) toe at $Z = -0.2$ and on (c) bed and (d) heel at $Z = 1.6$. For each instant of time, five measurements were made; range is indicated by bar and mean by dot. Solid curve is fitted profile through phase-averaged values (taken from Ojha et al., 1993)

In 1994, Ojha et al. further investigated the influence of angle on WSS distribution for an end-to-side anastomosis under pulsatile flow conditions using the same technique. Models with angles of 20° , 30° , 45° , and 60° were examined. For all angles, low shear stress was present at the heel and on the bed opposite the heel of the anastomosis as a result of the complete occlusion of the proximal end of the host vessel. Near the toe, increased flow separation occurred with increasing angle. On the bed across from the toe, increasing the

angle led to the increase of shear stress. In addition, the anastomotic angle significantly altered other properties of the shear stress field such as the mean and peak-to-peak magnitudes and cycle-to-cycle fluctuations in the region shown in Figure 2-16. All of these results were discussed in terms of possible roles of shear-induced IH.

Figure 2-16 WSS waveforms at indicated sites of the anastomoses. Points represent averages of five measurements, and connecting lines are spline-fitted profiles through data points (taken from Ojha et al., 1994)

Another effort to study the effects of geometry and flow division in models of the proximal and distal end-to-side anastomoses were done by Hughes and How (1995 and 1996). Flow models made of polyurethane elastomer were designed at three anastomotic angles of 15°, 30° and 45°. Flow visualization was conducted under steady and pulsatile flow conditions using planar illumination of suspended tracer particles. At the proximal anastomosis (Figure 2-17), the flow patterns were highly three-dimensional and were characterized by a series of vortices in the fully occluded distal artery ($Q_3 = 0$) and two helical vortices aligned with the axis of the graft. The presence of a patent distal artery ($Q_3 \neq 0$) had a significant effect on the overall flow pattern and led to the formation of a

large recirculation region at the toe of the anastomosis. The main structures observed in steady flow, such as vortices in the distal artery and helical flow in the graft, were also seen during the pulsatile cycle. However, the secondary flow components in the graft were more pronounced in pulsatile flow particularly during deceleration of the flow waveform.

At the distal anastomoses (Figure 2-18), the flow patterns were also highly three-dimensional and comprised of two helical vortices in the distal artery. A recirculation vortex was also formed in the occluded proximal arterial segment and a stagnation point existed on the floor of the artery. Under pulsatile flow, the secondary flow components in the distal artery became more pronounced during flow deceleration. The results agreed that IH occurred in regions of flow separation at the toe and the heel, and flow stagnation on the floor of the anastomosis.

Figure 2-17 Relative positions of the plane for illumination when viewing flow structures (taken from Hughes and How, 1995)

Figure 2-18 Relative positions of the plane for illumination when viewing flow structures (taken from Hughes and How, 1996)

Rhee and Lee (1998) investigate the effect of radial wall motion on the WSR distribution in the end-to-end anastomosis model. Rigid and elastic models were constructed and the WSR distributions were measured along the anastomosis using photochromic flow visualization method under pulsatile flow condition. The mean and peak of shear rate decreased along the divergent graft and the decreases were more significant in the elastic model. Although radial wall motion decreased the amplitude of higher harmonics of WSRs in the elastic models, attention should be paid when studying the arterial hemodynamics because the effect of radial wall motion is different for different geometry.

2.2.2.3 Particle Image Velocimetry and other Measurement Methods

In 2001, Bates et al. firstly adopted Particle Image Velocimetry (PIV) to investigate the flow structure inside a 30° Y-junction with different fillet radii at the intersection between the graft and the host artery with various Reynolds numbers and DOS to POS flow ratios. The two-dimensional instantaneous velocity fields confirmed the existence of a very complex flow, especially in the toe and heel regions for the different fillet radii and clearly identify features such as sinks, sources, vortices and strong time dependency.

Heise et al. (2004) further performed the PIV measurements for three silastic models representing Taylor patch, Miller cuff and femoro-crural patch prosthesis (FCPP) as shown in Figures 2-19 (a), (b) and (c) respectively. A large flow separation at the hood containing a clockwise rotating vortex was found inside the Taylor patch anastomosis. Additionally a smaller flow separation at the heel and a flow stagnation zone on the floor of the recipient artery were observed. Conversely, inside the Miller cuff a counterclockwise rotating vortex was seen inside a large heel flow separation. The FCPP also showed typical separation areas at the hood and heel of the anastomosis, although these were smaller than other anastomoses and no vortex creation was observed

throughout the cardiac cycle. With comparable inlet velocity level for the three anastomoses, a significant fluid acceleration was present at the antegrade as well as the retrograde outlets of the Taylor and Miller cuff, while the fluid acceleration at the antegrade outflow of the FCPP was small, which was due to the configuration of the antegrade FCPP leg. The shear stresses inside the flow separations of the three anastomoses were significantly lower than normal WSSs. High shear stress levels were found inside the transition zones between flow separation and high velocity mainstream. In general, flow pattern inside cuffed or funnel shaped anastomoses consisted of large flow separation zones, which are thought to be associated with IH development. In addition, fluid accelerations at the distal outlets resulted in pressure losses, which may contribute to impaired crural perfusion.

Figure 2-19 Photograph showing the silastic models of three femoro-crural anastomoses types used for femoro-crural reconstructions. A=Taylor patch, B=Miller Cuff, C=FCPP, arrows indicating flow directions (taken from Heise et al., 2004)

In 1994, Yamaguchi and Kohtoh described an experimental work on the flow situation through a branch model having a daughter tube bifurcated from a parent tube at 45 degree. Experiments were conducted utilizing an electrochemical method. The results proved that, even in steady flow, the WSS along the proximal wall in the daughter tube varied significantly with position in the form of a damped sine wave. For pulsating flow at the nondimensional pulsating frequency of 6.6, the above-mentioned tendency appeared to be severe and the distribution of its amplitude in pulsating flow was similar to that of WSS in steady flow.

Gaupp et al. (1999) investigated the characterization of vortex shedding in vascular anastomosis models using pulsed Doppler ultrasound with the flow circuit sketched in Figure 2-20. The results showed that higher vortex amplitude was found in the proximal anastomoses under resting flow waveform. Although the vortex amplitudes generally increased with angles of anastomosis, they were found to be higher in the 60° than in the 80° proximal anastomosis. Analysis of vortex structures identified prominent features at 40-50 Hz indicative of the short-duration oscillatory signals during the systolic deceleration phase expected from the passage of vortices. The study indicated that flow disturbances due to vortex shedding might be a common feature in femoropopliteal bypass grafts.

Figure 2-20 Sketch of the flow circuit in experiment (PA, proximal artery; DA, distal artery and G, graft) (taken from Gaupp et al., 1999)

In general, in-vitro experiments proposed much useful information on the hemodynamics of bypass anastomosis, especially distal anastomosis. However experiments often cost a lot and it was very difficult to obtain the accurate value of WSS. Therefore numerical simulation developed quickly with the advent of high capacity computer.

2.2.3 Numerical Simulation

Numerous research works had been carried out intensively by means of numerical simulation to investigate the occlusion symptom of the bypass. From the theoretical viewpoint of the governing equations for motion, the boundary conditions associated with the bifurcating flows are the primary determinants of the flow behavior. Hence, the geometry of the bifurcation, the inflow conditions, and the division of the flow into the branches all play strong roles in dictating details of the local flow fields. This fact can be perplexing to the fluid dynamists since individual variability is the rule rather than the exception for parameters such as branch angle, ratio of daughter branch to parent vessel area and the flow division (Giddens et al., 1993). Meanwhile the compliance mismatch between graft and host vessel, the interactions between blood and graft material and chronic endothelial injury are also associate with the failure of bypass. This variability presents a particular challenge when attempting to relate fluid dynamic variables with biological factors, such as the mitogenic factors, platelet activation and etc. So the reviews in this section are arranged according to these variables.

2.2.3.1 Geometry

2.2.3.1.1 Angle

In 1990, Pietrabissa et al. began to study the influence of bypass geometrical parameters, such as degree of coronary stenosis, the bypass diameter and the bypass angle, on the fluid dynamics around the distal anastomosis with a two-dimensional finite element model. The results showed that the development of a recirculation area immediately

downstream of the anastomosis and the magnitude of the recirculation increased with the angle, the bypass diameter and the degree of coronary stenosis.

Perktold et al. (1991) developed a pressure correction finite element method to investigate the flow and stress patterns in human carotid artery bifurcation models. The non-Newtonian behavior of blood was modeled by Casson's relation based on measured dynamic viscosity. The results showed that the magnitude of reversed flow, the extension of the recirculation zone in the outer sinus region and the duration of flow separation within the pulse cycle as well as the resulted WSS were clearly influenced by the bifurcation angle. In the case of large angle bifurcation, sinus flow separation accompanied with low negative WSS was found over the major part of the pulse cycle, which resulted in the formation of atherogenesis.

Fei et al. (1994) simulated steady flow in distal end-to-side anastomoses of iliofemoral artery bypass graft through various three-dimensional numerical models with varying angles from 20 to 70 degrees. The study aimed at examining flow patterns and WSR under various conditions of anastomotic angle and flow rates. The flow in graft became skewed toward the inner wall with increasing angle for the two Reynolds numbers of 100 and 205. Separated flow regions were seen along the inner wall for angles ≥ 60 deg at $Re=100$ and for angles ≥ 45 deg at $Re=205$ while a stagnation point existed along the outer arterial wall for all cases which moved downstream relative to the toe of the anastomosis with decreasing angles. Normalized shear rate increased with distance downstream of the stagnation point and with the anastomotic angle. Compared with the observations from chronic in-vivo studies, the results appeared to support the hypothesis of greater IH occurring in regions of low fluid shear.

Steady flow in two anastomosis models with different anastomosis angles (30° and 45° respectively) were simulated numerically by Henry et al. (1996). It was shown that areas known to be prone to IH, did correspond to areas of high spatial gradient of shear stress. Furthermore, the results also reflected that the level of shear and pressure variation to be lower in the 30° anastomoses.

Moreover, Lee et al. (2001) investigated the complete bypass tube flows under the steady flow condition. The changes of the hemodynamics were investigated with three parameters: the inlet flow Reynolds number (Re), anastomotic angle (α) and the position of the occlusion in the host tube. Higher inlet Reynolds number not only increased the flow rate but also strengthened the secondary flow in the bypass, which also escalated the high shear on the bed of zone III as shown in Figure 2-21 and modified the recirculation zone at the toe. Smaller anastomotic angle weakened the secondary flow and smoothened the overall flow, however it took longer suture line, which was not the usual practice and may induce other problems.

Figure 2-21 The configuration of the bypass tube
(taken from Lee et al., 2001)

2.2.3.1.2 Graft-to-host Diameter

Cheng and Taylor (1999) studied the effect of femorofemoral bypass graft diameter on hemodynamic conditions through the computational approach. The results revealed that under steady flow conditions, larger grafts reduced flow resistance, increased blood flow to the recipient limb and yet led to a decrease in shear stress.

Moore et al. (1999) studied blood flow patterns in anatomically realistic and simplified end-to-side anastomoses to determine how much an anatomically realistic geometry can be simplified without the loss of significant hemodynamic information. The results showed that for the specific case of an end-to-side anastomosis, simplified models provided sufficient information for comparing hemodynamics with qualitative or average disease locations. The ratio of the graft-to-host artery diameter was shown to be the most important geometric feature than others such as the local arterial caliber changes, out-of-plane curvature and small-scale surface topology.

2.2.3.1.3 Surface Features

Kleinstreuer et al. (1996) and Lei et al. (1996, 1997) employed the WSSG concept to generate a near-optimal graft-artery junction design through iterative improvement of the Taylor patch geometry. The models having large anastomotic flow areas, small continuously changing bifurcation angles and smooth junction wall curvatures can reduce the local time-averaged WSSG, thus enhance the patency of graft.

Longest and Kleinstreuer (2000) investigated the hemodynamics for a constant-diameter end-to-side base case, the VenafloTM graft and an improved graft-end configuration as illustrated in Figure 2-22. The geometric design of the new graft-end was based on the reduction of three time- and area-averaged hemodynamic parameters, i.e. the WSSG, WSSAG and radial pressure gradient (RPG). Considering the critical toe region, the

Venaflo™ graft demonstrated measurable improvements over the base case configuration in predicative computer simulation as well as in clinical trials. The performance improvements were further enhanced with the modification illustrated by the new design.

Figure 2-22 The geometries of three models (taken from Longest and Kleinstreuer, 2000)

Cole et al. (2002a, 2002c) further investigated the hemodynamics of cuffed arterial anastomoses, which involved the incorporation of a small section of vein (vein cuff) into the distal anastomosis of PTFE grafts to improve graft patency rates. Numerical simulations and in-vitro flow visualization experiments were conducted under physiological conditions to identify the flow behavior and to determine whether the improved performance of the cuffed system can be accounted for hemodynamic factors. The flow patterns at the cuffed anastomosis were observed to be significantly different from those of conventional end-to-side anastomosis. In the former case, the flow was characterized by an expansive, low momentum recirculation within the cuff. Separation occurred at the graft heel, and at the cuff toe as the blood entered the recipient artery. WSSs in the vicinity of the cuff heel were low, but high shear stresses and large spatial gradients in the shearing force acted on the artery floor during systole. In contrast, there

was less disturbed flow and less adverse shear stress distribution along the floor in the conventional model. In conclusion, aspects of the anastomotic hemodynamics were worsened when the cuff was employed. The benefits associated with the cuffed grafts may be related primarily to the presence of venous material at the anastomosis. So caution was advised with regard to using PTFE grafts, pre-shaped for resembling a cuffed geometry.

Figure 2-23 Symmetry plane of the cuffed bypass graft model (take from Cole et al., 2002a)

Besides the above investigations, Cole et al. (2002b) further performed numerical simulations of pulsatile, non-Newtonian blood flow through lifelike femorodistal bypass models as shown in Figure 2-24 to determine whether hemodynamic benefits arise from the modified geometry of the Taylor anastomosis. In a conventional bypass, the distal anastomotic flow exhibited considerable spatial and temporal variations. Steep spatial gradients in the shearing force acted along the floor during systole. The effect of the Taylor geometry was to reduce gradually the momentum of the blood approaching the junction. Thus, flow disturbances were abated, undesirable flow separation at the toe was diminished, and a less adverse floor shear stress distribution prevailed in that case. Intimal thickening should be alleviated at the toe in the Taylor model where separation was reduced, and where the thrombogenic graft surface was replaced with a vein patch.

Intimal hyperplasia on the floor may be inhibited in the Taylor model due to more favorable shear stresses. The improved flow through the patched anastomosis should contribute to its enhanced performance.

Figure 2-24 Symmetry plane of the Taylor bypass model (S1 indicates sites at which results are plotted) (taken from Cole et al., 2002b)

2.2.3.1.4 Nonplanarity

Sherwin et al. (2000) investigated the flow features of two distal anastomosis geometries, one planar and one non-planar as shown in Figure 2-25 under steady flow condition with numerical simulation and magnetic resonance imaging. The nonplanar three-dimensional flow notably altered the WSS distribution at the bed of the anastomosis, reducing the peak WSS by approximately 10 percent when compared with the planar model. Furthermore, an increase in the absolute flux of velocity into the occluded region, proximal to the anastomosis, of 80 percent was observed in the nonplanar geometry when compared with the planar geometry.

In 2002, Papaharilaou et al. carried out the similar investigations for the same two models under the pulsatile flow condition. The results also indicated a significant change in the spatial distribution of WSS and a reduction of the time-averaged peak WSS magnitude by 10% in the non-planar model as compared to the planar configuration. In the planar geometry the stagnation point followed a straight-line path along the host artery bed with a path length equal to 80% of a diameter. By contrast in the non-planar case the stagnation point oscillated about a center that was located off the symmetry plane

intersection with the host artery bed wall, and followed a parabolic path with a 0.7 diameter longitudinal and 0.5 diameter transverse excursion. In both models, regions of elevated oscillatory shear were spatially associated with regions of separated or oscillating stagnation point flow. The mean oscillatory shear magnitude in the nonplanar geometry was reduced by 22% as compared to the planar configuration. These changes in the dynamic behavior of the stagnation point and the oscillatory shear distribution introduced by out-of-plane graft curvature may influence the localization of vessel wall sites exposed to physiologically unfavorable flow conditions.

Figure 2-25 Model geometries of a distal 45° end-to-side anastomosis: planar (top) and non-planar (bottom) with numerical grid marked on vessel surfaces. All dimensions shown are scaled with vessel diameter (taken from Papaharilaou et al., 2002)

2.2.3.2 Flow Rate

Inzoli et al. (1996) studied the fluid dynamic conditions at the distal end of a 3-D aorta-coronary bypass model. The results showed the presence of low and high shear stress regions and illustrated the influence of flow rate distribution on the secondary flows. The performance of the near optimal graft-artery connectors designed by Kleinstreuer et al. (1996) and Lei (1996, 1997) were also evaluated through analyzing the effects of various flow input waveforms on the temporal and spatial WSSG distributions by Kleinstreuer et al. (1996).

In 1998, Ethier et al. investigated the flow waveform effects on the end-to-side anastomotic flow patterns. Femoral, iliac and coronary flow waveforms suitable for humans at rest were used. The results showed that peripheral flow waveform (iliac and femoral) produced large temporal and spatial WSSGs on the host artery bed than the coronary flow waveform, even though the average bed WSS magnitude were similar. If the anastomotic IH was promoted by large spatial and /or temporal gradients of WSS, IH was predicted less on the host artery bed of coronary bypass grafts than the peripheral bypass grafts.

The effect of proximal artery flow (ie, prograde, zero and retrograde flows) on the hemodynamics at the distal anastomosis was also investigated by Kute and Vorp (1999, 2001). Marked difference was found in both the magnitude and spatial distribution of WSS and WSSG, which suggested that the flow condition in the proximal artery was an important determinant of the hemodynamics at the distal anastomosis.

Beside the above investigations, Bertolotti and Deplano (2000) analyzed the flow patterns at the anastomosis of a stenosed coronary bypass. They built geometrical models of the host coronary artery with and without a 75% severity stenosis at three different locations from the anastomosis. The flow features, including velocity profiles, secondary motions and WSS, were compared for different configurations of the flow rate and of the distance of the anastomosis from the site of occlusion (called distance of grafting). The combination of the junction flow effects (counter rotating vortices) with the stenosis effects (confined jet flow) was particularly important when the distance of the grafting was short. Given that the residual flow issued from the pathologic stenosis being non-

negligible after two weeks grafting, models without stenosis cannot predict the evolution of the WSS in the vicinity of the anastomosis.

Figure 2-26 Geometry and meshes of the stenosed coronary bypass (taken from Bertolotti and Deplano, 2000)

To further investigate the post-operative realistic flows in stenosed coronary bypass, Bertolotti et al. (2001) simulated three-dimensional unsteady flows through the similar models by means of both finite element and experimental methods. The inflow rates were issued from in-vivo measurements in patients who had undergone coronary bypass surgery a few days before. A comparison between experimental and numerical velocity profiles coupled with the numerical analysis of spatial and temporal WSS evolution was investigated. The interaction between the graft and coronary flows was demonstrated. The phase inflow difference can partly be responsible for specific flow phenomena: jet deflection towards a preferential wall or feedback phenomenon that causes the flapping of the post-stenotic jet during the cardiac cycle. In conclusion, these typical flows showed the sensitivity to distance of grafting, inflow waveforms and the waveform phase differences.

2.2.3.3 Compliance Mismatch

Steinman and Ethier (1994) performed numerical simulation for an idealized 2-D distensible end-to-side distal anastomosis model, which solved the wall velocities simultaneously with the fluid velocity and pressure fields, while the wall displacements

were treated via an iterative update. Both the rigid and distensible cases indicated the presence of elevated temporal as well as spatial variations and low average magnitudes of WSS at sites known to be susceptible of the development of IH. Comparison between distensible-walled and corresponding rigid-walled simulations showed moderate changes in WSS at isolated locations, primarily the bed, toe and heel. However, other than these locations, only minor changes in overall WSS patterns were observed. Therefore they concluded that the effects of wall distensibility were less pronounced than those of changes in arterial geometry and flow conditions.

Perktold and Rappitsch (1995) studied the effect of distensible artery wall on the local flow field and the mechanical stress in the human carotid artery bifurcations with a numerical model. The comparison of results for a rigid and a distensible wall model demonstrated quantitative influence of the vessel wall motion, that was the global structure of the flow and stress patterns remained unchanged although the WSS magnitude decreased by 25% in the distensible model.

Two distensible models with different graft elasticity and one rigid model were used by Hofer et al. (1996) to investigate the effect of wall mechanics and fluid dynamics on end-to-side anastomoses. Time-dependent, three-dimensional Navier-Stokes equations were used to describe the motion of an incompressible Newtonian fluid, while a geometrically non-linear shell structure was used to model the motion of wall, which was iteratively coupled with the calculation of fluid motion. The results showed that graft elasticity acted as a regulating factor for the deformability and the stress concentration in the junction area, which supported the hypothesis that the pronounced formation of distal anastomotic

IH at the suture line was dependent on the wall mechanical factors such as intramural stress and strain.

Later on, Ballyk et al. (1998) investigated the influence of compliance mismatch on the end-to-end and end-to-side anastomoses. Greater influence of compliance mismatch can be found in the end-to-side anastomosis than the end-to-end model, which always led to less hyperplasia than end-to-side model. Therefore compliance mismatch might promote graft-artery IH by altering suture-line stresses.

Further study was carried out by Leuprecht et al. (2002), who suggested that the vessel wall mechanics and the compliance mismatch of the materials played the major role in the development and progress of intimal thickening along the suture line of the junction, as it was observed in the in-vivo study. It was also found that the migration of stagnation point played a role in the disease progress. The comparison between the conventional and Miller-cuff anastomoses demonstrated less shift of the stagnation point in the Miller-cuff.

2.2.3.4 Blood Property

In 1992, Xu et al. investigated the three-dimensional flow through canine femoral bifurcation models under physiological flow conditions through numerically solving the time-dependent three-dimensional Navier-Stokes equations. In the calculations, blood was assumed as a Newtonian fluid and a non-Newtonian fluid separately. The predicted velocity profiles were in good qualitative agreement with the in-vivo measurements. No great differences in velocity profiles were observed from the two fluids.

Gijssen et al. (1999) performed finite element simulations and LDA measurements of steady flow in a carotid bifurcation to investigate the influence of non-Newtonian

properties of blood on the velocity distribution. The axial velocity distribution was measured for two fluids: a non-Newtonian blood analog fluid and a Newtonian reference fluid. Striking differences between the measured flow fields were found. The axial velocity field of the non-Newtonian fluid was flattened, had lower velocity gradients at the divider wall, and higher velocity gradients at the non-divider wall. The flow separation, as found with the Newtonian fluid, was absent. In the computations, the shear thinning behavior of the analog blood fluid was incorporated through the Carreau-Yasuda model. The viscoelastic properties of the fluid were not included. A comparison between the experimental and numerical results showed good agreement, both for the Newtonian and the non-Newtonian fluids. Since only shear thinning was included, this seemed to be the dominant non-Newtonian property of the blood analog fluid under steady flow conditions.

2.2.3.5 Hemodynamic Parameters

Since ECs have been shown to be shear sensitive (Davies, 1991), extensive studies were carried out to link the hemodynamic parameters with intimal thickening in arterial bypasses and other branching blood vessel configurations. These parameters included WSS, WSSG and OSI etc, and were reviewed as following.

In 1991, Khodadadi investigated the wall pressure and shear stress variation for a two dimensional 90-degree bifurcation model with rectangular cross sections. Two dynamic recirculation zones and multiple zones of high and low shear stresses at various sites in the bifurcation were observed. Near-to-the-wall LDA velocity measurements were used to estimate the shear stress distribution on the walls. Qualitative agreement between the experimental and computed WSS values was obtained.

Numerical simulations of flow field within a two-dimensional 45-degree rigid-walled end-to-side distal anastomosis were carried out by Steinman et al. (1993). The numerical code was tested and the results agreed well with experimental studies (using photochromic dye tracer) when using steady and near-sinusoidal waveforms. Numerical simulations indicated elevated instantaneous WSS magnitudes at the toe and heel of the graft-host junction and along the host artery bed. These sites also experienced highly variable WSS behavior over the cardiac cycle, as well as elevated spatial gradients of WSS. These observations provided additional evidence that IH may be induced by the WSS over the cardiac cycle, high WSSG or a combination of the two parameters.

In terms of branching arteries, Lei et al. (1995) investigated the transient velocity vector and WSSG distributions by means of 3-D numerical simulation, which indicated that local WSSG was the single best indicator of nonuniform flow fields leading to atherogenesis.

At the 1995 Bio-Medical Fluids Engineering and Bioengineering Conference in USA, numerous studies about distal anastomoses and bifurcations with numerical simulation were published (Ballyk et al., Gatlin and Cuicchi, Kleinstreuer et al., Ojha, Perktold et al., 1995). Relatively slow recirculation flow; increased residence time and the oscillation of the stagnation point together with the low shear stress were thought to promote the development of IH by Ojha. However, Ballyk et al. and Kleinstreuer et al. suggested the stress gradients might contribute to the initiation of IH

He and Ku (1996) mimicked the pulsatile hemodynamics of the left coronary artery bifurcation using numerical method. Velocity was found skewing aroused from the

bifurcations and the arterial WSS was significantly lower in the bifurcation region. The time-averaged mean WSS varied from about 3 to 98 dynes/cm² in the left coronary artery. It was found that highly localized distribution of low and oscillatory shear stress along the walls strongly correlates with the focal locations of atheroma in the human left coronary artery. However, through numerical simulation, Henry et al. (1996), Kleinstreuer et al. (1996) and Lei et al. (1996, 1997) believed that high gradients of WSS might create the necessary conditions for IH formation.

With respect to the artery bifurcation, numerical studies were also performed by Perktold et al. (1998) and Shipkowitz et al. (1998). In a realistic coronary artery branch, the WSS component caused by the complex secondary velocity can be as high as the axial component (Perktold et al., 1998). Four-branch numerical model developed by Shipkowitz et al. (1998) showed that maximum stresses occurred at the apex region of the arteries and lower stresses induced at the lateral walls. The study also showed that shear stresses and flow rate ratios in the downstream were more affected by the inlet Reynolds number than the upstream arteries.

In 1998, Taylor et al. developed a comprehensive computation framework to solve the equations governing blood flow in a model of a normal human abdominal aorta under resting, moderate and vigorous pulsatile flow waveforms. Flow patterns and WSS were computed. A recirculation zone was observed to form along the posterior wall of the infrarenal aorta. Low time-averaged WSS and high shear stress temporal oscillations, as measured by an OSI, were present in this location, along the posterior wall opposite the superior mesenteric artery and along the anterior wall between the superior and inferior

mesenteric arteries. These regions were noted to coincide with a high probability of occurrence of sudanophilic lesions.

The comparison of computations with experimental data for the flow in end-to-side distal anastomoses, investigated by Taylor et al. (1998) and Lei et al. (2001), further proved the computational approach as a valid alternative to the experimental approach for quantitative hemodynamic studies.

Buchanan et al. (1999) investigated a rabbit's aorto-celiac junction as a representative atherosclerotic model, the hemodynamics of it was numerically simulated and three hemodynamic parameters – WSS, OSI and WSSG were compared. In comparing the segmental averages of the indicator functions and previously published intimal WBC densities, only the WSSG showed a statistically significant correlation. All three indicators had selective strengths in determining sites of early lesion growth around the aorto-celiac flow divider. At the proximal end of the flow divider on the lateral side of the orifice, there were elevated OSI and WSSG as well as low WSS. Regions of elevated wall permeabilities were comparable with the regions of elevated WSSG along the lateral and distal portions of the flow divider. Largely dependent upon the present input pulse with reverse flow, the OSI indicated relatively high values throughout the flow domain, however, it was important when utilized in conjunction with low WSS regions.

Shahcheraghi et al. (2002) studied numerically a three-dimensional and pulsatile blood flow in a human aortic arch and its three major branches for a peak Reynolds number of 2500 and a Womersley number of 10. The simulation geometry was derived from the three-dimensional reconstruction of a series of two-dimensional slices obtained in-vivo

using computed axial tomography (CAT) scan imaging on a human aorta. The numerical simulations were obtained using a projection method, and a finite-volume formulation of the Navier-Stokes equations was used on a system of overset grids. Their results demonstrated that within the aorta, WSSs were highly dynamic, but were generally high along the outer wall in the vicinity of the branches and low along the inner wall, particularly in the descending thoracic aorta. Within the branches, the shear stresses were considerably higher along the distal walls than along the proximal walls. Wall pressure was low along the inner aortic wall and high around the branches and along the outer wall in the ascending thoracic aorta. Comparison of numerical results with the localization of early atherosclerotic lesions broadly suggested preferential development of these lesions in regions of extreme (either maxim or minima) in WSS and pressure.

In 2003, Buchanan et al. investigated the flow simulations and monocyte deposition patterns for a rabbit's abdominal aorta. The deposition pattern traced a helical shape down the aorta with local elevation in monocyte adhesion around vessel branches. The cell deposition pattern was altered by an exercise waveform with fewer cells attaching in the upper abdominal aorta but more attaching around the renal orifices. Monocyte deposition was correlated with the WSSG and the WSSAG. The WSSG, the WSSAG and the normalized monocyte deposition fraction were correlated with the distribution of monocytes along the abdominal aorta. Furthermore, monocyte deposition was correlated with the measured distribution of monocytes around the major abdominal branches in the cholesterol-fed rabbit. These results suggested that the transport and deposition pattern of monocytes to arterial endothelium played a significant role in the localization of lesions.

Longest and Kleinstreuer (2003) conducted experimentally validated particle-hemodynamic simulations for two commonly implemented end-to-side anastomotic configurations, with and without proximal outflow, in order to assess the potential role of platelet-wall interactions. Specifically, sites of significant particle interactions with the vascular surface had been identified by a novel near-wall residence time (NWRT) model for platelets, which included shear stress-based factor for platelet activation as well as endothelial cell expression of thrombogenic and anti-thrombogenic compounds. Results indicated that the composite NWRT model for platelet-wall interactions effectively captured a reported shift in significant IH formation from the arterial floor of a relatively high-angle (30 deg) graft with no proximal outflow to the graft hood of a low-angle graft (10 deg) with 20% proximal outflow. In contrast, other WSS-based hemodynamic parameters did not identify the observed system-dependent shift in IH formation. However, large variations in WSS-vector magnitude and direction, as encapsulated by the WSSG and WSSAG parameters, were consistently observed along the IH-prone suture-line region. Of the multiple hemodynamic factors capable of eliciting a hyperplastic response at the cellular level, results of this study indicated the potential significance of platelet-wall interactions coinciding with regions of low WSS in the development of IH.

2.3 Summary and Conclusions

Based on the above literature findings, various means have been explored by researchers to understand in depth the effect of fluid hemodynamics on the development of IH. Generally, IH can be seen developing at regions on the bed and around the suture, the toe and heel (Figure 2-27). The suture line hyperplasia is believed to be a result of stress-induced remodeling caused by compliance mismatch, localized release of growth factors and the platelet deposition to the micro-crevices of the anastomosis. Intimal hyperplasia on the arterial bed is thought to be primarily caused by flow disturbances and an increased

release of growth factors by the constituent cells in response to the altered hemodynamics (Vorp, 1997). Hemodynamic study of the bypass is therefore very important.

Figure 2-27 Distribution of IH (black regions) in recipient artery following end-to-side anastomosis

It should be reminded that published literature on the flow characteristics in proximal and whole anastomoses is indeed rare. However, as Hughes and How (1995) have pointed out, the mitogens and activated platelets formed at the proximal anastomosis may convect down to the distal site. Studies of Lee et al. (2001) also indicated that local flow conditions at the distal anastomosis were influenced by the flow conditions at the proximal site. Hence, in order to clarify the hemodynamic factors that may promote IH, it is necessary to fully explore the flow structure in the proximal anastomosis, firstly establish the conditions of the flow at the upstream and then study the whole anastomosis model including both bypass and host tubes as a system.

Moreover, from the literature review, it is wise to use computer modeling in the present study at the initial stage, since it is less expensive than the experiment to carry out and has large capacity for including more parameters. Therefore three-dimensional numerical simulation was conducted in this project firstly on the proximal anastomosis models of true size in order to have a better understanding on the realistic situations of the flow

nature at the joint. Further comparisons between the numerical results and experimental measurements in the proximal anastomosis configurations will also be carried out to validate the numerical simulations, followed by the simulation of the whole anastomosis model.

CHAPTER 3

SIMULATION METHOD AND THEORY

It is well known that Computational Fluid Dynamics (CFD) is superior for the experiment due to its less expenses, accuracy and the ability to include more variations in the input parameters. Therefore in this project, numerical simulation is used as an extremely valuable tool for performing a systematic study of complex flow patterns such as proximal and whole anastomoses in the bypass surgery. To solve problems properly, firstly, some unimportant features, which are not essential to build the correct physical and numerical models, will be ignored. Secondly, the geometry, boundary condition and governing equations are determined discreetly. After that, domain geometry is divided into discrete control volumes as meshes and then governing equations are integrated over control volumes to get a set of algebraic equations before solving them to fully explore the flow field. Therefore in this chapter the numerical simulation method and theory will be presented according to the above-mentioned sequences.

3.1 Assumptions

To stress on main factors, which greatly influence the hemodynamical conditions of anastomosis, some assumptions are required to simplify the problem.

3.1.1 Newtonian Fluid

A Newtonian liquid is, by definition, one in which the coefficient of viscosity is constant at all rates of shear (Nichols and O'Rourke, 1990). Most homogenous liquids can be closely approximated by this characteristic, but suspensions of particles show deviations from it. As might be expected, such anomalous behavior becomes more apparent as the

particle size becomes appreciably large in comparison with the dimensions of the channel in which it is flowing.

Human blood consists of a suspension of red blood cells, white blood cells and platelets in a continuous aqueous medium (plasma) containing organic and inorganic salts, proteins (e.g., serum albumin, globulin and fibrinogen) and transported substances (e.g. glucose and urea). The volume percentage of red blood cells, the hematocrit, is typically 40-45% for an adult human. Therefore, blood is essentially a suspension of erythrocytes in plasma and shows anomalous viscous properties as following:

First of all, at low shear rates, the apparent viscosity increases markedly, when the hematocrit is higher than 14 percent. Brooks et al. (1970) examined the effect of hematocrit on the flow properties of human blood at shear rates up to 700sec^{-1} . An illustration of their findings is shown in Figure 3-1. Up to hematocrit of approximately 14% (H_n equals to 12.6%), the whole blood was found to be Newtonian, i.e. constant, at all rates of shear. As the hematocrit increasing, the viscosity increases and reaches an asymptotic value above approximately 100 sec^{-1} . At shear rate below 100 sec^{-1} the viscosity increases markedly with the increase in hematocrit. As a consequence, the viscosity of blood is associated with the shear rate and the percentage of hematocrit.

Figure 3-1 Relationship between viscosity and rate of shear for human erythrocytes suspended in their own plasma at 25°C for various volume concentrations H_n of the erythrocytes (hematocrit $\times 0.96$). Reported by Brooks et al. (1970).

Table 3-1 is taken from Minlor (1982), which shows shear rates in the human circulation calculated from radius and average blood velocity, with the assumption of parabolic flow. From the table, shear rates of aorta and arterial are found to be higher than 50sec^{-1} . Moreover, hematocrit for an adult is typically 40-45% and the elderly always have lower hematocrit than those of the younger. As it is known, bypass surgery is usually done on the elderly and is associated only with aorta, graft and coronary artery. Applying the high shear rate and the low hematocrit to Figure 3-1, the viscosity can be found almost constant with an asymptotic value ($3.8\text{-}5.8 \times 10^{-3}\text{Pa}\cdot\text{s}$), which agrees with the Newtonian fluid assumption for the blood in this study.

Table 3-1 Representative of shear rates at vessel walls in the human circulation (taken from Minlor, 1982)

Vessel	Shear rate at wall (sec^{-1})
Ascending aorta	50
Femoral artery	150
Arteriole	400

The second anomalous viscous property of blood is that in small tubes the apparent viscosity at higher shear rates is smaller than that of larger tubes. This progressive diminution with tube size begins to be detectable with tubes of less than 1mm internal diameter (i.e. about 100 times the major diameter of the red blood cells) and becomes marked in tubes of the order of 100-200 μ m in diameter (Reinke et al., 1986 and 1987). However, in this research the smallest diameter of all tubes is 2mm. This unique viscous property of blood for small vessels can be ignored.

Therefore the assumption that blood exhibits purely Newtonian viscosity is a valid approximation for the steady flow of the present study. In terms of physiological flow, the effects of very low velocities and shear rates at the end of each pulse have not been investigated directly. However, by means of dimensional analysis and scaling, Rohlf and Tenti (2001) recommend the use of the Womersley number as an indicator of whether non-Newtonian effects are important ($\alpha < 1$) or not ($\alpha > 1$), which is confirmed from both analytical and numerical studies. In the present investigation, the Womersley number is larger than 10, which further certifies the assumption of blood as Newtonian fluid.

Moreover, non-Newtonian characteristic of blood is also indicated not to be an important factor, when Xu et al. (1992) used power law to consider the effect of non-Newtonian characteristic of blood in the canine artery bifurcation with about 2mm diameters. Friedman et al. (1992) also compared the correlation between intimal thickness and WSS using Newtonian and a shear-thinning fluid individually, there was no significant effect of fluid rheology on this correlation.

On the other hand, one of the objectives in this study is to validate the numerical simulation by comparing with the experimental results, which use Newtonian fluid as working fluid to mimic the flow condition. Accordingly blood is assumed as Newtonian fluid with the viscosity of $4.08 \times 10^{-3} \text{ Pa} \cdot \text{s}$ and a density of $1,055 \text{ kg/m}^3$ in this project.

3.1.2 Laminar Flow

The laminar and turbulence flows have been studied extensively since the pioneering work of Reynolds (1883). The most frequently used fluid dynamic parameter in regard to turbulence is Reynolds number (Re). Re is a dimensionless quantity often used to describe the characteristics of steady flow through straight tubes at which transition from laminar to turbulent flow would occur. In steady tube flow, the Reynolds number is defined as:

$$\text{Re} = \rho u d / \mu \quad (3-1)$$

where ρ is the density of the fluid (kg/m^3), u is the average cross-sectional velocity (m/s), d is the diameter of the tube (m), and μ is the fluid viscosity ($\text{Pa} \cdot \text{s}$). In applications involving oscillating flows, the peak Reynolds number, defined as the Reynolds number at peak velocity is used. Transition from laminar to turbulent flow during steady flow in a straight and smooth tube typically occurs at a critical Reynolds number of about 2,300 (Nichols and O'Rourke, 1990). If the pipe is perfectly smooth, that transition can even be delayed to $\text{Re} > 5 \times 10^4$ (Wyganski and Champagne, 1973). However under the steady flow conditions of this study, the Re of graft, aorta and coronary artery is far below the critical Re when the tube is very smooth and would be described in detail at Chapters 5 and 7. Therefore blood flow can be assumed as laminar flow under the steady flow conditions of this study.

As far as physiological pulsatile flow is concerned, the onset of turbulence in a straight tube attracts a lot of investigations. For purely oscillatory flow with no mean component, studies have shown that transition occurs when the oscillatory Reynolds number ($Re_{osc} = u_{osc}d/\nu$ with u_{osc} = maximum cross-sectional average velocity, and $\nu = \mu/\rho$ is the kinematic viscosity) exceeds the critical Re defined as:

$$Re_{osc(critical)} = \text{constant} \times \alpha \quad (3-2)$$

where α is the Womersley parameter, which is defined as $r(2\pi f/\nu)^{0.5}$ and will be further illustrated later. The value of the constant in Eq. (3-2) ranges from 250 to 1000 (Merki and Thomann, 1975; Hino et al., 1976; Eckmann and Grotberg, 1991). Several authors have also investigated transition in pulsatile pipe flow, consisting of a mean flow with a superimposed oscillatory component. Nerem and Seed (1972) published the correlation shown as Eq. (3-3) for the onset of turbulence in the canine aorta:

$$Re_{peak(critical)} = \text{constant} \times \alpha \quad (3-3)$$

Eq. (3-3) is similar to the stability criterion of Eq. (3-2) for purely oscillatory flow, but the critical Reynolds number ($Re_{peak} = u_{peak}d/\nu$, where $u_{peak} = u_{mean} + u_{osc}$) is now based on the peak cross-sectional average velocity. Nerem and Seed (1972) found the constant in Eq. (3-3) to be 250 for the descending aorta, which suggests that if Womersley number is higher than 10, the critical Re for this pulsatile flow is higher than 2500. Below this value, the flow remains as laminar, which seems more stable than the steady flow in the straight tube with critical Re of 2300.

Peacock et al. (1998) correlated the critical peak Reynolds number with the Womersley number and the Strouhal number, which can be described as the following equation:

$$Re_{peak(critical)} = 169\alpha^{0.83} St^{-0.27} \quad (3-4)$$

Substituting the physiological range of α and St for the human coronary arteries and aorta into Eq. (3-4), Peacock et al. (1998) provided the critical peak Reynolds numbers as shown in Table 3-2.

Table 3-2 Physiological ranges of dimensionless groups
(taken from Peacock et al., 1998)

Dimensionless group	Re_{mean}	α	St	$Re_{\text{peak(critical)}}$
Human aorta				
Rest	1200	19	0.02	5500
Exercise	4850	30	0.01	9800
Left main coronary				
Rest	180	3	0.008	1650
Exercise	750	3	0.005	2650

In fact, actual coronary peak Reynolds number ranges from 550(at rest) to 2250(at exercise) (Peacock et al., 1998), which is far below the critical values. Therefore their flow waveforms are unlikely to be disturbed if assuming the coronary arteries as the straight tubes. Meanwhile under the pulsatile flow condition adapted in the present study as stated in Chapters 5 and 7 respectively, the peak Re values of aorta are lower than the critical peak Re value (5500) of Table 3-2 and thus supports the assumption of laminar flow.

Furthermore, most in-vivo measurements proved the flow characteristics of aorta and arteries as undisturbed flow, though some disturbances were detected (Seed and Wood, 1971; Stein and Sabbah, 1976). Disturbances were also not found in the in-vitro experiments as described in Chapter 6.

Accordingly, the assumption of laminar flow is acceptable for the present study.

3.1.3 Rigid Wall and “No Slip” Condition at the Wall

Arterial walls are viscoelastic inhomogeneous multi-layered tissues, which are composed mainly of collagen, elastin fibers and SMCs. When a blood vessel is subject to pressure, it undergoes deformation and stresses in the circumferential direction, longitudinal deformation and increasing radial deformation. In the bypass operation, if a vein graft (such as saphenous vein) is used to act as an arterial, it will be exposed to arterial pressure and subject to pulsatile deformations and pulsatile stresses in all the three directions on top of those earlier mentioned static deformations. These may be different from those normally encountered by the vein when it is in its normal anatomic location and is perfused by venous pressure and venous flow. Figure 3-2 provides an overall view of the parameters that are altered when a vein is exposed to arterial pressure and flow. Among these parameters, radial deformation is considered to be a main factor. As an indicator, compliance is a measure of blood vessel dispensability and may be defined as the fractional increase in diameter per unit change in pressure.

The effect of compliance mismatch and distensibility of walls on the flow of end-to-side anastomosis are investigated by researchers. It has been proposed that compliant grafts may provide increased flow, decrease mechanical stresses at anastomoses, prevent the breakdown of anastomotic suture lines and prevent the formation of anastomotic pseudoaneurysms. This proposal was tested by numerical studies of Hofer et al. (1996), Tang et al. (2001) and Leuprecht et al. (2002) and in-vitro studies of Friedman et al. (1992), Kim et al. (1993), Steinman and Ethier (1994) and Rhee and Lee (1998). However, all these results showed that there were no significant differences in the flow fields and WSS magnitude between the compliant and stiff grafts. In the case of end-to-side anastomoses,

the geometry at the anastomosis appears to be more important than the compliance mismatch, which has only played a secondary role.

Figure 3-2 Nine mechanical parameters that are altered by exposing vein grafts to arterial pressure and flow

Furthermore, synthetic grafts and diseased arteries are expected to be relatively stiff, thus partially justifying the rigid wall assumption (Steinman et al., 1993). Therefore, assumption of rigid wall is acceptable in this study.

The assumption of “no slip” condition at the fluid-wall interface, which may be considered as a part of the laminar flow hypothesis, is generally accepted as correct and used to derive the analytical solution. Hydrodynamic experiments in general confirm this assumption, since the true “slippage” has not been demonstrated at any liquid-solid interface (Kaufmann, 1963; Fung, 1984). This point has some degrees of importance as it has occasionally been suggested that some of the anomalous flow properties of the blood vessels may be due to non-wettable properties of their endothelial lining with a

consequent slip at the wall. Even if the endothelium was shown to be non-wettable, the conclusion that slipping would result is unjustifiable. For example, Poiseuille's equation holds for the flow of mercury in a glass tube, so that there must be zero velocity at the wall. The appearance in flowing blood of a narrow but cell-free zone at the walls of the tube has led some workers to treat this lower viscosity zone as a region of "slip". This may be treated conveniently as a mathematical device, but should not be taken as a physical reality (Nichols and O'Rourke, 1990).

3.2 Physical Models

The design of physical models requires some fundamental medical knowledge especially on the actual anastomotic joint in the bypass operation. The surgical operation procedures (Leather et al., 1994 and Doty, 1997) at both proximal and distal anastomoses are illustrated in Figures 3-3 and 3-4 respectively. For the aorta-saphenous vein (proximal) anastomosis, as shown in Figure 3-3a, small openings (4 to 5 mm in diameter) are made into the ascending aorta using an aortic punch. The end of the saphenous vein is cut back longitudinally for a distance of 1 cm. Five suture loops of polypropylene are then placed around the "heel" of the graft and passed through the aortic wall. The traction on both the suture and the vein graft helps to expose the edge of the aortic opening for accurate needle placement. Stitches should include about 3 to 5 mm of the aortic wall for adequate strength of the anastomosis. The suture loops are pulled up to approximate the vein graft. The anastomosis is completed by the placement of stitches in cartwheel fashion around the opening in the aorta. Wide stitches are taken along the lateral edge of the saphenous vein as it is approximated with narrow stitches to the aorta to ensure that the maximum length of saphenous vein is positioned laterally. The completed anastomosis should bulge anteriorly above the aortic wall, achieving a "cobra-head" appearance as seen in Figure 3-3b.

Figure 3-3 Suturing at the proximal anastomosis. (a) stitches around the heel and (b) the completed anastomosis (taken from Doty, 1997)

At the distal anastomosis, the placement of three or four traction stitches on the acute margin of the heart is necessary to expose the distal coronary artery. The coronary artery is incised directly through the epicardium without mobilization. The length of the coronary artery incision should approximate the diameter of the saphenous vein, about 4 to 5 mm. The distal end of the saphenous vein segment is beveled at 30 to 45 degrees, with an adequate length in order to ensure for its course over the surface of the heart. Again five stitches are taken around the “heel” of the graft as described for the proximal anastomosis. Five stitches are taken around the “toe” of the graft and the ends of the sutures are tied precisely with tension to approximate the tissue without causing a purse-string effect. Figure 3-4 provides a better view on the operation procedures.

Figure 3-4 Suturing operations at the distal anastomosis. (a) & (b) showing stitches around the anastomosis and (c) the completed anastomosis (taken from Doty, 1997)

The physical models to represent proximal anastomoses for numerical simulation have the same geometry as the Pyrex glass test models measured through in-vitro experiments, which will be described in Chapter 5. The whole anastomotic joint is also mimicked to be investigated through numerical simulation and will be reported in Chapter 7. All models are designed and fabricated to its true scale based on the medical data provided by a medical surgeon from the National Heart Centre of Singapore.

3.3 Governing Equations (Mathematics Models)

For all flows, conservation equations for mass and momentum are used as governing equations. In this section, the conservation equations for laminar flow are presented.

$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x_i} (\rho u_i) = S_m \quad (3-5)$$

Equation (3-5) is the general form of the mass conservation equation and is valid for incompressible as well as compressible flows. Where ρ is the density of fluid, t is the time and u_i is the velocity in i direction. The source S_m is the mass added to the continuous

phase from the dispersed second phase (e.g., due to vaporization of liquid droplets) and any other mass sources.

Conservation of momentum in the i direction of an inertial (non-accelerating) reference frame is described by Eq. (3-6).

$$\frac{\partial}{\partial t}(\rho u_i) + \frac{\partial}{\partial x_j}(\rho u_i u_j) = -\frac{\partial p}{\partial x_i} + \frac{\partial \tau_{ij}}{\partial x_j} + \rho g_i + F_i \quad (3-6)$$

where p is the static pressure, τ_{ij} is the stress tensor (described below), ρg_i and F_i are the gravitational body force and external body force (e.g., that arise from interaction with the dispersed phase) in the i direction, respectively. F_i also contains other model-dependent source terms such as porous-media. In addition, the stress tensor is given by

$$\tau_{ij} = \left[\mu \left(\frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} \right) \right] - \frac{2}{3} \mu \frac{\partial u_l}{\partial x_l} \delta_{ij} \quad (3-7)$$

where μ is the molecular viscosity and the second term on the right hand side is the effect of volume dilation. δ_{ij} is the Kronecker Delta, which equals to 1 for $i=j$ and 0 for $i \neq j$.

With the assumption of laminar flow, Newtonian homogeneous and incompressible fluid, furthermore, by ignoring the terms of mass source, gravity and external body forces, the continuity and momentum conservation equations can be simplified under (i) steady flow, Mass Conservation Equation:

$$\frac{\partial}{\partial x_i}(u_i) = 0 \quad (3-8)$$

Momentum Conservation Equation:

$$\rho u_j \frac{\partial u_i}{\partial x_j} = -\frac{\partial p}{\partial x_i} + \frac{\partial \tau_{ij}}{\partial x_j} \quad (3-9)$$

and (ii) pulsatile flow.

Mass Conservation Equation:

$$\frac{\partial}{\partial x_i}(u_i) = 0 \quad (3-10)$$

Momentum Conservation Equation:

$$\rho \left(\frac{\partial u_i}{\partial t} + u_j \frac{\partial u_i}{\partial x_j} \right) = -\frac{\partial p}{\partial x_i} + \frac{\partial \tau_{ij}}{\partial x_j} \quad (3-11)$$

3.4 Boundary Conditions

In this project, the inlet and outlet boundary conditions were selected in a manner to match physiological conditions as closely as possible with the available data and facilitate numerical computation, which will be explained in detail at Chapters 5 and 7. No slip condition was assumed for all walls. Symmetry boundary conditions were used, which implied that there was zero normal velocity and zero normal gradients of all variables at the symmetry plane. In general, axial velocity at the inlet was assumed as fully developed steady and pulsatile flow, whose velocity profile was the same as Eq. (3-12) and Eq. (3-14).

3.4.1 Steady Flow

In the steady flow cases, inlet axial flow was assumed to be a parabolic flow profile corresponding to a fully developed Hagen-Poiseuille flow of an incompressible fluid flowing through a circular tube, i.e.

$$u = 2\bar{u} \left[1 - \left(\frac{r}{R} \right)^2 \right] \quad (3-12)$$

where $\bar{u}$ is the average velocity and R is the radius of the inlet.

3.4.2 Pulsatile Flow

Under pulsatile flow condition, the inlet axial velocity profile was assumed to be a Womersley solution (Womersley, 1955), which was derived as a fully developed pulsatile flow in the straight circular tube as described in Appendix A. To generate the time varying inlet velocity profiles, flow rate information over the cycle was used to compute a complex Fourier series as shown in Eq. (3-13). The transient velocity profiles were then computed using Eq. (3-14). Note that $\text{Real}\{\}$ in Eq. (3-14) represented the real part of a complex expression.

$$Q(t) \approx \sum_{n=-N}^{n=N} B_n e^{in\omega t} \quad (3-13)$$

$$u(r,t) = \frac{2B_0}{\pi R^2} \left[1 - \left(\frac{r}{R} \right)^2 \right] + 2 * \text{Real} \left\{ \sum_{n=1}^N \left\{ \frac{B_n}{\pi R^2} \left[\frac{1 - \frac{J_0(i^{3/2}\alpha r/R)}{J_0(i^{3/2}\alpha)}}{1 - \frac{2J_1(\alpha i^{3/2})}{\alpha i^{3/2} J_0(\alpha i^{3/2})}} \right] \right\} e^{in\omega t} \right\} \quad (3-14)$$

Figure 3-5 displays velocity profile of a sinusoidal input flow waveform (average velocity equals to $A (1 + \sin \omega t)$) at different time interval within period T of 0.2s, where A is equal to 13.5cm/s). Note that the radial velocity variation is not, in general, parabolic and in fact reverses in direction close to the wall as can be observed at $t/T=0.625$ in Figure 3-5, even though the total volume flow rate always remain positive. The boundary layer of reversed flow close to the wall is an important characteristic of pulsatile flow. This also illustrates that even for a straight section of artery with positive volume flow rate, there is always some time in the cardiac cycle where the viscous traction forces are opposite to the dominant flow direction.

Figure 3-5 Womersley solutions for pulsatile flow in a long straight tube

Ling et al. (1968) confirmed the predicted waveforms in a rigid tube subjected to a sinusoidal pressure gradient by using a thin film anemometer. The results of their test, which carried out at two values of α , 1 and 10, are shown in Figure 3-6. The close agreement of theory and experiment in these tests also shows that blood behaves as a Newtonian fluid within the range of α relevant to animals and human beings.

Figure 3-6 (a) Predicted and experimental waveforms of velocity in a rigid tube at an α of 10 obtained in dog blood (Δ) and in glycerin and water ($\circ$). (b) Predicted (-) and experimental ($\circ$) velocity profiles in a rigid tube at an α of 1.0 in glycerin (taken from Ling et al., 1968)

The Womersley equations have also been tested experimentally in rigid tubes by Linfor and Ryan (1965) and Kunz and Coulter (1967), over a wide range of values for α . In the comparison of using blood as the medium, they found a very close agreement between the theoretical and measured flows.

In summary, the Womersley equation is almost certainly as close or even closer to a practical approximation as Poiseuille's equation is for steady flow in arteries. The result holds true for the blood flow in both the aorta and pulmonary artery (Nichols and O'Rourke, 1990). Therefore the function of the velocity profile, which was expressed in Eq. (3-14), was implemented as a user defined function for the inlet condition of pulsatile flow within the Fluent, a commercial CFD package in this study. Thus, given a node on the boundary where a Womersley velocity function is prescribed, as well as the Fourier coefficients of the volume flow rate function, period, and fluid properties, the velocity at that node would be computed and prescribed. The detailed information about the flow rate waveform will be illustrated in Chapters 5 and 7.

3.5 Numerical Calculation Method

In this study, the numerical simulation was conducted by using a commercial CFD package, which was FLUENT (Version 5.5). FLUENT provides two numerical methods: segregated solver and coupled solver. Using either method, FLUENT will solve the governing integral equations for the conservation of mass and momentum, and (when appropriate) for energy and other scalars such as turbulence and chemical species. In both cases, a control-volume-based technique is used that consists of:

- Division of the domain into discrete control volumes using computational grids.

- Integration of the governing equations on the individual control volumes to construct algebraic equations for the discrete dependent variables (“unknowns”) such as velocities, pressure, temperature, and conserved scalars.
- Linearization of the discretized equations and solutions of the resultant linear equation system to yield updated values of the dependent variables.

The two numerical methods employ a similar discretization process (finite-volume), but the approach used to linearize and solve the discretized equations is different. In this study, segregated solver is chosen for the fluid, which is incompressible and has low Mach number; mesh (computational grids) building and general solution methods are described in the following sub-sections.

3.5.1 Mesh Generation

As stated before, the first step of simulation procedures is to generate grids for the flow geometry. FLUENT can use grids comprise of tetrahedral, hexahedral, pyramid, or wedge cells (or a combination of these) in three dimensions. The choice of mesh type will depend on the application and the consideration of following issues:

- Setup time

Many flow problems solved in engineering practice involve complex geometry. The creation of structured or block-structured grids (consisting of quadrilateral or hexahedral elements) for such problems can be extremely time-consuming, if not impossible. Setup time for complex geometry is, therefore, the major motivation for using unstructured grids employing triangular or tetrahedral cells.

- Computational expense

When geometry is complex or the range of length scales of the flow is large, a triangular or tetrahedral mesh can often be created with far fewer cells than the

equivalent meshes consisting of quadrilateral or hexahedral elements, because a triangular or tetrahedral mesh allows higher skewness than the structured quadrilateral and hexahedral meshes. Unstructured triangular and tetrahedral meshes offer many advantages for moderately complex geometry. However, quadrilateral and hexahedral elements are also economical in some situations for they permit a much larger aspect ratio than triangular and tetrahedral cells. To relatively simple geometry, in which the flow conforms well to the shape of the geometry, such as a long thin duct, high-aspect-ratio quadrilateral or hexahedral cells may be a better choice.

- Numerical diffusion

A dominant source of error in multi-dimensional situations is numerical diffusion, also termed false diffusion. Note that the term “false diffusion” is used because it is not a real diffusion phenomenon, yet its effect on a flow calculation is analogous to that of increasing the diffusion coefficient in a real situation. All practical numerical schemes for solving fluid flow contain a finite amount of numerical diffusion, which arises from truncation errors that are consequences of representing the fluid flow equations in discrete form. Higher order discretization scheme used in FLUENT can help in reducing the effects of numerical diffusion on the solution. Note that the amount of numerical diffusion is inversely related to the resolution of the mesh. One way of dealing with numerical diffusion is to refine the mesh. Furthermore, numerical diffusion is minimized when the flow is aligned with the mesh.

Moreover, in regions where solution is expected to be complicated, especially the region near the sharp or the abrupt features, a greater nodal density is required in order to provide a given level of approximation and hence accuracy. An efficient way is to refine only at areas where the geometry or solution is expected to be more complex (rapid

variation) or at regions of interest where greater accuracy is required. To report grid refinement studies, grid convergence index (GCI) proposed by Roache (1994, 1998) was calculated. The GCI in terms of relative error was given by Eq. (3-15).

$$GCI^{fine} = F_s |\varepsilon| / (r^p - 1) \quad (3-15)$$

Where p is the order of the numerical method; error $\varepsilon = (f_2 - f_1) / f_1$, f_1 and f_2 are the solutions on fine and coarse grids respectively; as unstructured grids were used, the grid refinement ratio $r = (N_1 / N_2)^{1/D}$, N_1 and N_2 are numbers of elements on fine and coarse grids respectively, and D is the dimensionality of problem. Safety factor F_s was chosen as 3 as recommended by Roache (1994, 1998) for normal applications. Thus, when the solution is within the asymptotic range, the GCI could be used as a worst-case estimation of the solution error to the given problem. Note that the global GCI was not calculated in this study although Cadafalch et al. (2002) took volume weighted average value of local GCI as the estimator of the global GCI. This is due to the difficulty of interpolation for three-dimensional unstructured grids and no integral refinement ratio r used in present study.

Based on the above idea, the proximal anastomosis models and the complete anastomosis model were meshed and described in Chapters 5 and 7 respectively. Since mesh quality plays a significant role in the accuracy and stability of the numerical computation. The attributions associated with mesh quality such as smoothness (a measure changes in cell volume between adjacent cells), skewness (which can be defined as the difference between the cells shape and the shape of an equilateral cell of equivalent volume, highly skewed cells can decrease accuracy and destabilize the solution) and face ratio (which is a measure of the stretching of cells) are examined, before read into Fluent as meshes. Grid

independency test was also carried out and illustrated in Chapters 5 and 7 correspondingly.

3.5.2 Solving Governing Equations

This is an overview of solution procedures for Fluent. In this study, segregated solver was used to solve the governing equations sequentially (i.e., segregated from one another). Because the governing equations are non-linear (and coupled), several iterations of the solution loop must be performed before a converged solution is obtained. Each iteration consists of the steps illustrated in Figure 3-7 and outlined below:

1. Fluid properties are updated, based on the current solution. (If the calculation has just begun, the fluid properties will be updated based on the initialized solution.)
2. The u , v and w momentum equations are each solved in turn using current values for pressure and face mass fluxes, in order to update the velocity field.
3. Since the velocities obtained in Step 1 may not satisfy the continuity equation locally, a “Poisson-type” equation for pressure correction is derived from the continuity equation and the linearized momentum equations. This pressure correction equation is then solved to obtain the necessary corrections to the pressure, velocity fields and the face mass fluxes such that continuity is satisfied.
4. When interphase coupling is to be included, the source terms in the appropriate continuous phase equations may be updated with a discrete phase trajectory calculation.
5. A check for convergence of the equation set is made.

Figure 3-7 Overview of the segregated solution method

Second-order upwind scheme was used for discretization, which provided the same accuracy as the Quick scheme for this study after some trials. In addition, first-order upwind scheme was not used for discretization in this study due to its lower accuracy as a result of numerical diffusion.

Pressure-velocity coupling was achieved by deriving an equation for pressure from the discrete continuity equation. FLUENT provides three pressure-velocity coupling algorithms: SIMPLE, SIMPLEC, and PISO to solve this problem. All these algorithms use a relationship between velocity and pressure corrections to enforce mass conservation and to obtain the pressure field. In this study, SIMPLEC was found to have a better convergence rate with relax factor 0.3-0.5 and 1 for momentum and pressure equations respectively.

The fully implicit scheme was used for the pulsatile flow study of this project, so as to avoid Courant stability restriction on the time-step size. However, in order to fully exploit

the transient phenomena, it is necessary to set at least one order of magnitude smaller than the smallest time constant in the system being modeled. For time-periodic calculations, the choosing of time step shall be based on the time scale of the periodicity. Smaller time step needs less iteration times of one loop whereas the time steps used in one period increase. Better time step must reduce the whole computation time and express the flow field alteration clearly. In this study, time step size was tried out individually, and preferential time step was acquired after some trials as stated in both Chapters 5 and 7. To eliminate the start-up effect of the transient flow, the computation was carried out over at least two and a half periods (more than 48 hours CPU time). The results presented here were solutions obtained after more than one cycle. Although it may be better to run for more pulse, it is in fact not necessary as the velocity changes less than 0.01% from the second to the third pulse.

At the end of each iteration, the residual sum for each conserved variable is computed and stored, thus recording the convergence history. The criterion of convergence is explained as following.

As it is known, after discretization, the conservation equation for a general variable at a cell P can be written as

$$a_P \Phi_P = \sum_{nb} a_{nb} \Phi_{nb} + b \quad (3-16)$$

Here a_P and Φ_P are the coefficient and variable value respectively at the center of cell, a_{nb} and Φ_{nb} are the influential coefficients and the variable values respectively for neighboring cells. Meanwhile b is the contribution of the constant part of the source term S_c in $S = S_c + S_P \Phi$ (S , S_P and Φ are the source term in the governing equations, coefficient and variable respectively) and of the boundary conditions. The residual R^Φ computed by

FLUENT's segregated solver is the imbalance in Eq. (3-16) summed over all the computational cells P . This is referred to as the “unscaled” residual. It may be written as

$$R^\Phi = \sum_{cells P} \left| \sum_{nb} a_{nb} \Phi_{nb} + b - a_P \Phi_P \right| \quad (3-17)$$

In general, it is difficult to judge convergence by examining the residuals defined by Eq. (3-17), since no scaling is employed. This is especially true in enclosed flows such as natural convection in a room where there is no inlet flow rate, which can be used to compare the residual. FLUENT scales the residual using a scaling factor representative of the flow rate through the domain. This “scaled” residual is defined as

$$R_s^\Phi = \frac{\sum_{cells P} \left| \sum_{nb} a_{nb} \Phi_{nb} + b - a_P \Phi_P \right|}{\sum_{cells P} |a_P \Phi_P|} \quad (3-18)$$

For the momentum equations the denominator term $a_P \Phi_P$ is replaced by $a_P V_p$, where V_p is the magnitude of the velocity at cell P . The scaled residual is a more appropriate indicator of convergence for most problems; hence it is used as a criterion in this project.

The convergence criteria set for velocity and pressure were 10^{-5} in steady flow and 5×10^{-5} in pulsatile flow of this study. All the calculations were done on a workstation (SGI Origin 2000) with the operating system SGI IRIX and the convergence history was monitored during the iterations. For example, the convergence history for the 45° forward facing proximal anastomosis model at $Re_G=169$ and the complete anastomosis model under steady flow condition are shown in Figures 3-8 and 3-9 respectively. From the figures, it can be found that there are certain oscillations in the residual at first 4 steps. But after that, the residual drop fast to the convergence criteria (in these cases as 10^{-5}). Further reducing the convergence criteria to 10^{-6} is found to have more iterations and do not show obvious decrease of residues; the residuals have stabilized and do not change

after certain iterations (as shown in Figure 3-8). In these two situations, the calculation is stable and satisfies the convergence criteria of 10^{-5} , since the calculation is approaching the physical solution as calculation goes on. During this study, all calculations show the similar residual histories, thus they are stable. No artificial viscosity was used in the simulation. To enhance numerical stability, the under-relaxation parameters can be modified.

Figure 3-8 Convergence history for 45° forward facing proximal anastomosis model at $Re_G=169$

Figure 3-9 Convergence history for the complete anastomosis model at steady flow condition

3.5.3 Post-processing

When the computation is converged, the resultant data can be stored or exported as other format file that can be used for the next step post-processing, such as Tecplot. Moreover, Fluent also provides the graph tools to draw the vector and contour graphics successfully, animation and other advanced post-processing is also approved. In this study, velocity vector and profiles are done with Tecplot.

As there is strong biological evidence that hemodynamic parameters (HPs) encapsulate “disturbed flow” that may trigger a cascade of abnormal biological processes leading to intimal thickening and/or thrombi formation, sufficiently high and sustained HP values can be employed to determine susceptible sites for the onset of blood vessel diseases (Kleinstreuer et al., 2001) and is investigated in this project. Historically, the most frequently employed indicator of disturbed flow has been the WSS. For laminar flow, the WSS is defined by the normal velocity gradient at the wall and is calculated using the relation: $\tau_w = \mu(\partial u / \partial n)|_{wall}$, where $\partial u / \partial n|_{wall}$ is the normal velocity gradient at the wall.

Then, the time-averaged WSS is defined as:

$$WSS = \frac{1}{T} \int_0^T |\tau_w| dt \quad (3-19)$$

Employing the wall shear stress gradient concept to represent locally disturbed flow, the non-dimensional time-averaged WSSG is defined as (Buchanan et al. 2003):

$$WSSG = \frac{1}{T} \frac{D_G}{\tau_G} \int_0^T \sqrt{\left(\frac{\partial \tau_x}{\partial x}\right)^2 + \left(\frac{\partial \tau_y}{\partial y}\right)^2 + \left(\frac{\partial \tau_z}{\partial z}\right)^2} dt \quad (3-20)$$

Here, T , D_G , τ_G represent the period, diameter of graft and Poiseuille type WSS at the graft corresponding to the mean flow rate in the graft respectively.

Another HP employed is OSI, which was calculated as following (He and Ku, 1996):

$$OSI = \frac{1}{2} \left(1 - \frac{\left| \int_0^T \tau_w dt \right|}{\int_0^T |\tau_w| dt} \right) \quad (3-21)$$

This is a measure of the temporal and spatial variation of the local WSS. In general, the OSI varies between 0 and 0.5. Near separation and reattachment points, the OSI values are 0.5, while regions that experience no reverse flow have OSI equal to zero.

Since segmental averages of HPs, especially WSSG was found to show a statistically significant correlation with the intimal white blood cell (WBC) densities (Buchanan et al., 1999), the segmental averages of time-averaged WSS, WSSG and OSI were also computed individually according to Eq. (3-22):

$$\langle HP \rangle = \frac{\int_{segment} HP dA_{surface}}{\int_{segment} dA_{surface}} \quad (3-22)$$

By means of Tecplot, MATLAB and C programs, the HPs of time-averaged WSS, WSSG, OSI and segmental averages of these HPs are thoroughly investigated in this project.

3.6 Numerical Validation

Computational fluid dynamics offers much more versatility and resolution than in-vitro or in-vivo method, yet computations must be validated carefully to estimate the accuracy of result. The accuracy of solutions cannot be determined exactly but can only be estimated by comparing with some other available data.

First, prior to producing the last results, various aspects of the numerical model were tested. It included: grid independency, advection models, time-step size and effects of boundary condition location. The tests were carried out and the predicted velocity profiles of symmetry plane was used as an indicator of the effect of the various changes, which will be described in Chapters 5 and 7 for proximal and whole anastomoses respectively.

A sequence of solution procedure using finer and coarser meshes to check if the solution converges, as the meshes get finer. Convergence towards some fixed values provides some level of confidence about the solution obtained. Note that it is not necessary to uniformly refine the mesh throughout the domain. Instead, an efficient way is to refine only at areas where the geometry or solution is expected to be complicated (rapid variation) or at regions of interest where greater accuracy is required. This is known as local mesh refinement. It is very important to pay attention to the function of adapting the mesh, which is provided by Fluent. This means that it can adapt the mesh in the location of higher velocity or pressure gradient, yet place relatively more cells in the critical regions. However, for convergence, the largest volume within the domain must be as small as possible. This means that every volume has to be refined, therefore local mesh refinement is effective only up to a certain point.

Moreover, in all predictions presented, the advection terms were modeled using a second-order accurate higher upwind scheme (HUW). Two other advection models were tested prior to this selection. It was found that a third-order accurate scheme of quadratic upwind interpolation of convective kinematics (QUICK) scheme gave results that were not significantly different from those predicted using second-order HUW. However the first-order accurate higher upwind scheme (HUW) did produce small difference in the velocity distribution, which may be due to the false diffusion errors associated with the lower-order discretion scheme.

The time differential was fully implicit, so as to avoid Courant stability restriction on the time-step size. However in the pulsatile flow condition, the convergence rate and accuracy still have some relationship with the time step size. In this simulation, different time step was used and preferential time step was acquired after some trials as stated in both Chapters 5 and 7.

The effect of the location of the outlet boundary on the resulting flow field was checked by extending the length of the outlets to 10 and 15 times of the aorta diameter respectively for both steady and pulsatile flow conditions. The velocity distributions were found to be unaffected by this change.

Secondly, comparing the solution with results from experiments or solutions from some other independent analysis will also give some hints on the possible errors. A way of increasing the level of confidence is to apply the solution procedure to other similar problems with known solutions, i.e. test problems. If the solution obtained for the test problems are accurate, then the solution to the actual problem can be assumed correct too.

Analytical solutions to the Navier-Stokes equations are possible only in a few select cases with very special geometry and boundary conditions. Fortunately, a canonical solution for pulsatile flow does exist: the Womersley solution for fully developed pulsatile flow in a straight circular tube. This analytical solution is essential in assessing the accuracy of numerical methods and examining such important issues as spatial and temporal discretization errors.

In this study, a circular artery with a length of 3 cm and radius of 0.2 cm, which is subject to uniform inlet flow, is used for computation validation. The inlet velocity is uniform in space and periodic in time. The time variation is described by a sinusoidal function $u(t) = \bar{u}[1 + \sin(2\pi/T)]$ with mean velocity $\bar{u} = 13.5 \text{ cm/s}$, and period, T of 0.2s. The fluid has a kinematics viscosity of 0.04 poise, which results in a mean Reynolds number of 135 and Womersley number of 5.6. Axis-symmetry was exploited and a half model constructed. The model was discretized into 65,098 nodes and 59,640 hexahedral elements.

As it can be seen in Figure 3-10, the flow fully developed in a length equivalent to approximately ten times of radius from the inlet as evidenced by the axial velocity distribution of symmetry plane which does not vary with axial position thereafter.

Figure 3-10 Instantaneous axial velocity contours along the symmetry plane of a long straight artery

The Womersley solution for fully developed pulsatile flow valid at the outlet of the artery was compared with the computed axial velocity results at that position.

First the outflow volume is monitored to compare with the inflow volume to verify that incompressibility and continuity are exactly satisfied. As observed in Figures 3-11 and 3-12, the outlet volume flow rate does indeed match the inflow volume flow rate.

Figure 3-11 Inlet mass flow rate for a long straight artery

Figure 3-12 Outlet mass flow rate for a long straight artery

As observed in Figure 3-13, the numerical simulation solution resolves the theoretical velocity profile well with differences observed primarily along the centerline of the vessel in the first half of the cardiac cycle where the numerical results deviate the exact solution a little. It is worth reiterating that the volume flow rate is exactly the same for the analytical and numerical solutions, despite some minor differences of velocity distribution in Figure 3-13. It should be noted that the level of discretization used for this example resulted in approximately 20 nodal points across the diameter, and a maximum error of less than 4.07%. As exact solution is known for this problem, it should be possible to further improve the agreement between the numerical simulation results and the Womersley solution with a finer mesh.

Besides the above validation, independent verification of the simulation results via in-vitro experiment result was also done for all the proximal anastomoses. The detailed information could be referred to Chapter 6 for PIV Experimental Results and Discussion.

Figure 3-13 Comparison of the computed and analytical velocity profiles at various time intervals in the cardiac cycle for the flow in a long straight artery

CHAPTER 4

PIV MEASUREMENT METHODOLOGY

In this project, PIV is used to study the flow field of proximal anastomosis models in order to validate the numerical simulation results. The experimental arrangement and PIV techniques are discussed in this Chapter.

4.1 Experimental Arrangement

4.1.1 General Description of Test Rig

Figure 4-1 shows a schematic drawing of the constructed experimental test rig. Working fluid is delivered from the sump tank to the head tank by a centrifugal pump (JJC-200). A control valve (6) is placed just after the outlet of the head tank to regulate the main flow rate. A needle control valve (1), located at the downstream of the control valve (6), is used to provide a more accurate control on the flow rate into the test section. The whole flow rate can be monitored by an electromagnetic flow meter (EMF. 1) (Endtress Promag A model), which has an accuracy of 0.05%. In order to minimize the flow disturbance into the test model, a 5:1 contraction cone with a honeycomb structure and flow straighteners is placed just before the entrance into the test model.

As the test models mimic the proximal anastomoses, the flow will bifurcate at the joint, where some of the main flow will be diverted into the “bypass graft”. Flow control valves (2) and (3) is placed at the end of aorta and graft respectively in order to control the pressure drop within the test models and flow rate into the graft, measured by another electromagnetic flow meter (EMF. 2). Output signals from both two flow meters can be

connected to an oscilloscope (Tektronix TDS 210 model) so as to provide visual inspection on the flow cycle when the inlet flow involves pulsating characteristics. The bifurcated flows emerge again at the sump tank located below the head tank. Within the head tank, an overflow drainage system is built to allow excessive fluid to flow back into the sump tank, which ensure desired hydraulic pressure under steady flow condition.

In the case of pulsatile flow condition, a special designed pump system is used to generate pulsatile flow characteristics. Firstly the main flow from the head tank is allowed to fill up the whole circuit, including the piston tube and backpressure tank. Then the control valve (5) is closed and the pump system starts to work. A special designed cam, which is attached to a 0.5 horsepower (375W) DC motor, is used to activate the piston for creating required waveform and a control circuit provides external triggering signal to synchronize the PIV system for capturing the images of velocity flow fields in the test models with respect to the phase of the pulsatile flow. Details of the cam and control circuit will be described in Sections 4.1.3 and 4.1.4.

At the visualization section, the Nd: YAG laser emits two laser pulses to illuminate the cross-sectional plane of test model, which is immersed in the transparent tank of liquid. The CCD camera, mounted vertically above the test model, will instantaneously capture the two digital images at a time interval of a few mini-seconds. These images will be processed to obtain the velocity vectors of the flow fields. As for the case of the pulsatile flow, an additional triggering mechanism is required to activate the CCD camera. Details about triggering device are described in Section 4.1.4.

Figure 4-1 Schematic drawing of the experimental arrangement

4.1.2 Working Fluid

One consideration required to be noted for the working fluid is that it should satisfy the refractive index matching rule. As in PIV, when a laser sheet is directed to these curvature surfaces (such as glass tube), part of the laser light will be refracted at the wall. This will result in strong random reflection near the wall and will cause a dropout in acquiring vectors at the near wall regions. In order to minimize the glaring effect at the near wall of the glass tube model, the test section will be immersed into a transparent rectangular tank filled with the same working fluid inside the test model, but without seeding particles. At the same time, the working fluid shall have the same refractive index as the material of the test model and the flat surface of the rectangular tank.

The other consideration about the working fluid is to match the fluid properties with that of the blood. The use of real blood is expensive and is associated with a risk of infection from blood born pathogens. The necessity for a cheap, safe and easy to prepare blood analogue fluid is of constant concern. In addition, as blood is opaque, it cannot be measured by means of PIV. In general, the viscosity of the solution is the most important factor, which will greatly affect the behaviors of the flow and thus should be similar if not exactly the same as the blood.

In this project, a mixture of ammonium thiocyanate, glycerin and water was used as the blood analogue, where the ammonium thiocyanate was used to adjust the refractive index of the solution to match that of Pyrex glass, which was the material of test model and the flat surface of the transparent tank, and the glycerin was used to achieve the same viscosity as the real blood. With reference to Yip (1999), the working liquid, which was

mixed in various proportions of ammonium thiocyanate, glycerin and water, was test and the resultant refractive index and the viscosity were shown in Figure 4-2.

Figure 4-2 The effects of varying X percentage of aqueous ammonium thiocyanate solution, NH₄SCN with (100-X) percentage of glycerine on the refractive indices and dynamic viscosity of the mixture

To achieve the refractive index of the Pyrex glass (1.47-1.49) and the viscosity of blood ($3.8\text{-}5.8 \times 10^{-3} \text{Pa}\cdot\text{s}$), the working fluid involved mixing 30% of glycerin with 70% of aqueous ammonium thiocyanate (NH₄SCN) solution by volume. The aqueous ammonium thiocyanate solution was made up of equal parts of ammonium thiocyanate salt and distilled water by weight. The refractive indices and the dynamic viscosity of the working fluid were measured using a commercial refractometer (model ATAGO 3T) and a controlled rate rheometer (model Contraves low shear 40) respectively. The working fluid was measured to have the refractive index and dynamic viscosity (μ) of 1.47 and 0.00408Pa·s at 22°C respectively.

Dynamic viscosities were measured with a commercial viscometer (Advanced Rheometric Expansion system with a double Couette geometry) and the linear relationship between the applied shear stress and the corresponding rate of shear strain

exhibited by the working fluid indicated that it is the Newtonian fluid. Generally the viscosity of liquids decreases with the increasing of temperature. The accuracy of the fluid temperature was important because too much changes of the viscosity would cause the steady flow or unsteady flow profiles skewed. During the experiment period, a mercury thermometer was placed in the sump tank to monitor the temperature of fluid, which normally varies within the range of $\pm 0.5^\circ\text{C}$ ($22 \pm 0.5^\circ\text{C}$). This is because the test rig is placed in a well-controlled air-conditioned room. Since the temperature difference was marginal, the viscosity is thus treated as a constant during the experiment.

4.1.3 Flow Waveform Generator for Physiological Flow

Various researchers have investigated the physiological characteristics of blood flow through direct measurement techniques on both animal and human beings, which involve using electromagnetic, ultrasonic blood flow meters (Nichols and O'Rourke, 1990), Doppler ultrasonic velocimeter (Deplano and Siouffi, 1999; Gaupp et al., 1999) and Magnetic Resonance Imaging (MRI) (Moore et al., 1994) to measure flow rate in the blood vessels. The physiological waveform applied in the study was a simplified version of a set of flow wave measurements reported by Nichols and O'Rourke (1990). This set of recordings as shown in Figure 4-3 was conducted on the ascending aorta of patients, using multiple pressure sensors and the Millar cathode-mounted electromagnetic flow velocity probes.

Figure 4-3 Typical physiological flow waveform in a human body (taken from Nichols and O'Rourke, 1990)

As the physiological flow waveform is complex, the present cam design to achieve the experimental waveform is based on some of the major characteristics found on the physiological waveform, which includes the frequency and the Peak Reynolds number. Figure 4-4 shows the constructed cam device used to generate pulsatile flow waveform in the experiment. It consists of four main items: cam plate, bearing roller, stationary and moving plates and piston with piston pipe.

Figure 4-4 The cam device

The working mechanism of cam system to generate the physiological flow waveform is illustrated in Figure 4-5. The designed cam is mounted onto a shaft of a 375W motor. One bearing roller located at one end of the plunger is always kept in contact with the cam through the use of two compression springs.

Figure 4-5 Schematic design of the cam

As shown in Figure 4-5(a), during the forward stroke, the rotation of the cam will further compress the spring and moves the plunger in the piston forward in order to push the fluid within the piston tube towards the test section (positive displacement). During this stage, the force applied to push the piston forward is basically due to a higher torque that is produced by the motor as compared to the spring force. The magnitude of fluid flow in the test model ($Q(t)$) is dependent solely on the piston motion and can be estimated by the following relation,

$$Q(t) = A \times V(t) \quad (4-1)$$

whereby A is the cross sectional area of the piston and $V(t)$ is the instantaneous linear velocity of the plunger in the piston. As the cross sectional area of the piston remains constant across its stroke length, the factor varying the magnitude of the flow will depend

on the speed of the stroke which is determined by the cam profile and the rotational speed of the cam.

During the reverse stroke, the spring being compressed will push the roller to maintain the contact with the cam, thus bringing the piston back towards its original location. At this stage, a check valve (just before control valve (2) in Figure 4-1) is placed at the end of the main flow pipeline to block a major amount of reverse flow from the main pipeline. Instead, working fluid in the backpressure tank, through the secondary flow pipeline, is allowed to fill up the piston tube as it retracts. In order to control the magnitude of the reverse flow rate at the test model, the control valve (4) in Figure 4-1 is preset experimentally before the measurements to achieve the targeted fluid flow. This results in the flow within the system to oscillate and achieve the pulsatile mean velocity waveform as shown in Figure 4-6.

Figure 4-6 The pulsatile velocity waveform

4.1.4 Triggering Device

An external triggering device is built to provide input Transistor-Transistor-Logic (TTL) signal (5V) for activating the PIV system under pulstaile flow measurements. The function of this triggering device is to synchronize the PIV system for capturing the images of velocity flow fields in the test model with respect to the phase of the flow generated by the cam. However, as the triggering device is not commercially available, an in-house electronic circuit was constructed to achieve the objective. Figure 4-7 shows the constructed triggering mechanism consisting of the following items: i) A through beam Hybrid Fibre Optic Sensors, ii) A 24 V Power Supply, iii) BJT (Bipolar Junction Transistor) to TTL output converter.

Figure 4-7 Constructed external triggering device for the PIV system

In the experiment, a disc is attached to one of the twin shafts of the motor and marked with a thin black strip stretching from the center and outwards to the circumference. The optical sensors are placed in between the disc and as the disc rotates, the sensors upon locating the strip (light beam is blocked), will emit the signal to the PIV synchronization unit via the BJT to TTL output converter. As the PIV synchronization unit only accept 5

volts TTL signal, the output converter is required as a device to step down the output voltage (24V) of the sensors to 5 volts. Figure 4-8 shows the electronic diagram of the output converter.

Figure 4-8 Electronic diagram of the output converter

4.2 PIV Technique

4.2.1 Basic Theory of PIV Measurement

Particle Image Velocimetry (PIV) is a powerful measurement technique that yields instantaneous realizations of velocities within a cross-sectional plane of the flow. It was developed in the early 1980's and is now routinely used by the experimental fluid-mechanics community to measure the instantaneous two-dimensional velocity fields in a wide variety of complex flows. Traditional point-wise velocity measurement techniques such as hot-wire and LDA are not able to reveal information about the instantaneous spatial structure of the flow. However, PIV is a whole-flow-field technique providing instantaneous velocity vector measurements in a cross-section of the flow field. The use of modern CCD cameras and dedicated computing hardware, results in real-time velocity maps. Figure 4-9 provided a schematic drawing for the PIV principles.

Figure 4-9 Basic principles of PIV

In PIV, the velocity vectors are derived from sub-sections of the target area of the particle-seeded flow by measuring the movement of particles between two light pulses:

$\bar{V} = \frac{\Delta \bar{x}}{\Delta t}$. The flow is illuminated in the target area with a light sheet. The digital camera

lens takes the particle images in the target area into a CCD array, which is able to capture each light pulse in separate image frames. Once a sequence of two light pulses is recorded, the images are divided into small subsections called interrogation areas (IAs). The interrogation areas from each image frame, I1 and I2, are cross-correlated with each other, pixel by pixel. The correlation produces a signal peak, identifying the common particle displacement, X . An accurate measure of the displacement - and thus also the velocity - is achieved with sub-pixel interpolation. A velocity vector map over the whole target area is obtained by repeating the cross-correlation for each interrogation area over

the two image frames captured by the CCD camera. The process to acquire velocity vector is shown in Figure 4-10.

Figure 4-10 The process to acquire velocity vector. Note that the correlation of the two interrogation areas, I_1 and I_2 , results in the particle displacement X , represented by a signal peak in the correlation $C(X)$

PIV technique is thus non-intrusive and can measure the velocities of micron-sized particles following the flow. With sequences of velocity vector maps, statistics, vorticity and other relevant data are available. In addition, PIV system has three basic components: a flow tracer, an illumination source and an imaging system. These independent components offer significant experimental flexibility, allowing application of the technique to a wide range of flow configurations (e.g., low-speed water flow to supersonic air flow). In this application, a Q-switched, pulsed Nd: YAG laser produced a sheet of light to illuminate the cross-sectional plane of the flow medium. A CCD camera was used to capture two consecutive images of the scatter passing through the test section. A wealth of information on the scattering particles' velocities was recorded and processed by the FlowMap processor to achieve a complete two-dimensional velocity vector fields.

The PIV system actually measures the velocity of particles suspended in the flow. To be considered as the actual velocity probes, the seeding particles are thus important and shall satisfy the following criteria: (1) able to follow the motion of the fluid exactly; (2) do not

alter the flow; (3) do not interact with each other. As stated in Melling (1997), the choice of optimal diameter for the seeding particles is a compromise between an adequate tracer response of the particles in the fluid, requiring small diameter and a high signal-to-noise ratio (SNR) of the scattered light signal, necessitating large diameters. Detailed discussion about the optimal choice of the diameter of seeding particle was illustrated in Section 4.2.3.1.

In addition, as PIV utilizes a correlation method to statistically determine the average particle displacement within a small interrogation region, through a series of Monte-Carlo simulations, Keane and Adrian (1990) recommended the following criteria for optimal PIV analysis:

- The number of particle pairs per interrogation region should be greater than 10.
- The particles should be displaced a distance of approximately $\frac{1}{4}$ of the interrogation region width
- The out-of-plane displacement should be less than $\frac{1}{4}$ of the laser sheet thickness;
- The particle displacement should not vary more than 5% across the interrogation region.

4.2.2 Description of FlowMap PIV System

The PIV system used in the present investigation is the Dantec FlowMap PIV system (Dantec Measurement Technology, Denmark). It consists of illumination system, CCD camera, FlowMap Processor and a PC, as shown in Figure 4-11.

Figure 4-11 Architecture of the FlowMap PIV instrumentation (taken from Dantec, 1996)

4.2.2.1 Illumination System

A double cavity pulsed Nd: YAG laser system, capable of emitting 400mJ of infra-red light (with a wavelength of 1064nm) to produce green output pulses (with the wavelength of 532nm) is chosen as the energy source to produce a stroboscopic light sheet.

In moderately fast water flow seeded with micron particles, only pulsed lasers have sufficient energy to record particle images. In order to generate these short bursts of laser pulses, Q-switching the lasing cavity will result the energy to be emitted in 6-10 ns bursts as opposed to pulses of 250 μ s, the duration of the exciting lamp in the lasing cavity. Communication lines between the pulsed laser and the synchronization unit in the PIV FlowMap processor are required for user control of the data acquisition process (Figure 4-12). The synchronization unit will instruct the laser cavities when to fire their flash lamps and when to allow their Q-switches to emit laser radiation, as shown in Figure 4-12.

Figure 4-12 Communication signals between the synchronization units in the processor and a double cavity laser system (taken from Dantec, 2002)

4.2.2.2 CCD Camera

The CCD camera used in the FlowMap PIV system is 80C77 HiSense MkII camera. It is a cross-correlation camera and contains a high-performance progressive scan interline CCD chip, which has 1344×1024 light sensitive cells and an equal number of storage cells. The specifications of CCD camera were listed in Table 4-1.

Table 4-1 Specifications of CCD Camera

Dimensions (L×W×H)	Camera Housing 135×65×65mm
Lens mount	C-mount
CCD type	Progressive scan interline, Sony ER150
Active pixels	1344 by 1024 pixel
Camera bit resolution	12-bit
Pixel pitch	$6.45 \times 6.45 \mu\text{m}$
Dynamic range	1800:1
Readout noise	10 electrons r.m.s
Pixel clock rate	14.7MHz
Max. single-frame rate*	12.2
Pixel binning	Yes(Note: max frame rate increases with binning)
Pulse interval range*	0.3 μs and up
Double-frame rate*	Up to 5.6Hz

Note: * means restrictions may apply in actual operation mode

When the camera is used with the FlowMap system, the camera is driven in the so-called Asynchronous reset mode. In this mode, the FlowMap processor was acted as the master

clock, driving both camera and illumination system, ensuring that camera and laser were always synchronized. During a PIV recording sequence, the first laser pulse is timed to expose the first frame, which is transferred from the light sensitive cells to the storage cells immediately after the laser pulse. The second laser pulse is then fired to expose the second frame. The storage cells now contain the first frame and the light sensitive cells the second. These two frames are then transferred sequentially to the video output for acquisition and cross-correlation calculation by the FlowMap processor. This sequence is shown in Figure 4-13.

Figure 4-13 Timing sequence for recording of a series of three PIV images (taken from Dantec, 2002)

4.2.2.3 FlowMap Processor

FlowMap Processor is the core member of the FlowMap system, which comprises the following modules:

- Correlator Unit, which aims at determining the vector maps(s) from the incoming image maps;
- Input buffer board, which allows continuous operations such as reading image from a CCD camera, storing image maps in a memory area, sending images to PC etc., to be carried out simultaneously so as to process the real-time vector at the correlator unit.

- Synchronization unit, which provides physical communication links between the processor and other elements in the PIV system such as illumination devices and camera as well as the user's devices.

4.2.2.4 FlowManager Software

FlowManager software can be run on the PC as an ordinary MS-Windows application, which controls the whole process of PIV measurement, and also provides analysis optional for validating raw vector maps, obtaining derived quantities such as streamlines. The communication between PC and the FlowMap processor is via a FlowMap System Hub installed in the FlowMap Processor through TCP/IP communication link.

The FlowManager software acted during the whole measurement sequence, such as controlling the necessary synchronization sequence to acquire data; providing an interface for the human user and storing the recorded data etc. The actual measurement sequence is initiated by the occurrence of a trigger event, which can be an external TTL input to the processor, or originated from the PC. After the trigger event, the timing signals will be sent to the illumination system and the CCD camera. The timing signals were used to control the camera shutter to make sure that the CCD sensor is only exposed to the light from the illumination system, since ambient light will reduce the signal-to-noise ratio. Then two successive images were transferred to the FlowMap processor and stored in the database of FlowManager software. Once the particle images were acquired, the instantaneous particle-displacement fields can be calculated using the cross-correlation routines within the FlowManager software. The image maps were divided into interrogation areas of rectangular shape and the length of each side of a rectangle is a number of pixels expressed in powers of 2: 16, 32, 64 or 128. Subsequently, post-processing validation methods including peak height validation and velocity range

validation would be applied on the raw vector map. Furthermore, calculations were adopted to derive other information from the vector maps such as streamline and vorticity. Finally the data were ready for printing and exporting in numerical format.

4.2.3 Parameters for PIV Measurement

The accuracy of the PIV measurement mainly depends on several parameters, including laser light intensity (controlled by Q-Switch delay time), time separation between pulses, pulse duration, the coefficient of magnification and F-number of the CCD camera, interrogation size, particle properties and seeding density etc.

The following parameters are always set as default values, which were obtained by trial and error in this application, as listed in Table 4-2.

Table 4-2 Parameters for PIV measurement

Items	Values
Q-switch delay	110-400 μs
F-number (F)	4.8-11
Particle diameter	20 μm
Interrogation size	32×32 pixels
Overlap	25 %
Pixel size	6.45×6.45 μm

Some other parameters such as the pulse duration ($t_{pulseduration}$) and separation ($t_{separation}$) should be decided by some factors including the flow conditions of the application, the diameter of particle image (d_{image}) and the interrogation size etc. Here detailed discussion about the $t_{pulseduration}$, $t_{separation}$ and d_{image} will be carried out respectively.

4.2.3.1 Diameter of the Particle Image

The choice of optimal diameter for seeding particles is a compromise between an adequate tracer response of the particles in the fluid, requiring small diameters and a high

signal-to-noise ratio (SNR) of the scattered light signal, necessitating large diameters (Melling, 1997). In general, the camera images of seeding particles should have a diameter of at least 1 pixel, optimum 2 pixels (Stanislas et al., 2003). The size of particle image depends on the following factors: the magnification coefficient (M); the particle geometric diameter (d_{geo}) and the point response function (PRF) of the lens, which can be expressed as the diffraction limited spot size (d_s).

- Magnification coefficient (M)

The value represents the ratio of the active area of the CCD camera to the specific area of the model to be studied. Since the specific area of the model is $24 \times 18 \text{ mm}^2$ and the active area of camera is $8.7 \times 6.6 \text{ mm}^2$:

$$M = \frac{6.6}{18} = 0.36 \quad (4-2)$$

- Particle geometric diameter (d_{geo})

The diameter of the geometry image equals to the magnification coefficient multiplied by the diameter of the particle:

$$d_{geo} = M \times d_{particle} \quad (4-3)$$

- Point Response Function (PRF) of the lens

The diffraction of a point image creates a spot of the diameter (d_s) given by

$$d_s = 2.44(M + 1)F\lambda \quad (4-4)$$

where $F = f/D_A$ is the F-number calculated from the focal length of the camera lens (f) and the diameter of the camera aperture (D_A), and λ is the wavelength of the laser sheet (532nm).

- Particle Image Diameter (d_{image})

$$d_{image} = \sqrt{d_{geo}^2 + d_s^2} \quad (4-5)$$

Typically for $F=5.6$, $\lambda=532\text{nm}$, $M=0.36$ and $d_{\text{particle}}=20\mu\text{m}$, it can be found that $d_{\text{geo}}=7.2\mu\text{m}$ and $d_s=9.9\mu\text{m}$, hence $d_{\text{image}}=12.24\mu\text{m}$. Thus the camera images of seeding particles have a diameter near optimum ($d_{\text{image}}/d_{\text{pitch}}=12.24/6.45=1.9\approx 2$). Therefore the seeding used in this investigation is polyamid seeding particles (PSP-20, Dantec Measurement Technology) with mean diameter of $20\mu\text{m}$.

4.2.3.2 Pulse Duration and Separation

The pulse duration ($t_{\text{pulseduration}}$) refers to the time whereby the laser light sheet will be projected onto the test models under investigation. For a good PIV measurement, the duration of the light pulses should never exceed the time, which the particle image takes to move half a particle image diameter, since this will cause streaking.

$$t_{\text{pulseduration}} < \frac{d_{\text{image}}}{2 \times V_{\text{particle}} \times M} \quad (4-6)$$

where V_{particle} is the velocity of the particle. For $d_{\text{image}}=12.24\mu\text{m}$, $V_{\text{particle}}=0.1\text{m/s}$ and $M=0.36$, $t_{\text{pulseduration}}$ should be less than 0.17 ms . It is naturally satisfied since the PIV is capable of generating a pulse duration of 10ns . Therefore the streaking effects can be neglected.

The time between pulses ($t_{\text{separation}}$) also plays an important role in the measurement. Dynamic range of measured velocity is dependent on the interrogation area size and the time between pulses. At first, the time between the light pulses should be long enough to let the particle image move a few particle image diameters (or a few pixels for autocorrelation). Generally the time that the particle image moves 3.5 particle image diameters is the common criterion.

$$t_{separation} > \frac{3.5 \times d_{image}}{V_{particle} \times M} \quad (4-7)$$

At the same time, the maximum particle image displacement on the CCD chip should be less than a quarter of the interrogation size $l_{interrogation}$.

$$t_{separation} < \frac{l_{interrogation}}{4 \times M \times V_{particle}} = \frac{N_{int} d_{pitch}}{4 \times M \times V_{particle}} \quad (4-8)$$

As the interrogation size used in the experiment is 32×32 pixels (i.e. $N_{int}=32$) and applying an average velocity of 0.1 m/s with the rest of the above-calculated values, the time between pulses worked out to be as follows:

$$1.19\text{ms} < t_{separation} < 1.43\text{ms}.$$

It should be noted that, for unsteady flow measurement, there is a special limitation on the pulse separation. Usually, the estimation of fluid velocity from PIV measurement assumes no acceleration of the seeding particle during the flight from the first image-captured position to the second image-captured position: the velocity magnitude and direction are constant. The measured velocity would be given by

$$V_{measured}(t) = \frac{1}{t_{separation}} \int_t^{t+t_{separation}} V_{particle}(t) dt \quad (4-9)$$

For unsteady flow, the velocity of the particle may vary with both time and space position. This will put some serious restrictions on the pulse separation. In general, the larger the $t_{separation}$, the larger the discrepancy can be found in the measured velocity due to the acceleration and deceleration of the particle in the flow.

4.2.4 Verifying the Input Flow Conditions

Before measuring, it is necessary to quantify the accuracy of the velocity plots obtained from the PIV measurement. In this application, one straight glass tube, which has the same inner diameter as the models, was used to take the verification. For steady flow, the

verification was mainly focused on the accuracy of the velocity plots. Under pulsatile flow condition, the waveform obtained and the synchronization between the waveform phase shift and the trigger signals to PIV system would be paid much more attention.

4.2.4.1 Steady Flow

Under steady flow condition, the verification can be achieved by comparing the measurements of the flow rate from the electromagnetic flowmeter and by integrating the velocity profile obtained from the velocity plots. PIV measurements were carried out on a straight glass tube of inner diameter 20 mm and of length 120 mm. The glass tube is similar to the rest of the test models except there is no bifurcation section. The images from the PIV were processed and the velocity vector maps were generated. In this case, the average flow rate indicated on the electromagnetic flow meter was 0.06 m³/hr. Theoretically, the velocity profile for the fully developed steady flow in tube should be the Hagen-Poiseuille solution:

$$u = 2\bar{u} \left[1 - \left(\frac{r}{R} \right)^2 \right] \quad (4-10)$$

where $\bar{u}$ is the average velocity and R is the radius of the inlet.

In the PIV experiment, extra assistant techniques, such as the prolonged tube circuit between the test section and the head tank, the honeycomb contraction structure and flow straighteners just before the test section etc., were used to ensure that the flow into the test section was fully developed. The measured velocity contours and vectors plotted in Figure 4-14 proved that the flow was fully developed as evidenced by the axial velocity distributions of symmetry plane, which do not vary much with the axial position. Note that in the figure, the contour represented the axial velocity magnitude. From the figure, it

can be observed that the velocity profile is parabolic in shape and will be further discussed in Figure 4-15.

Figure 4-14 Velocity contour and vector for the straight tube

To verify the measured flow rate, the average flow rate value was calculated from the velocity profile, using Eq. (4-11).

$$\bar{Q} = \int_0^r u(r) 2\pi r dr \quad (4-11)$$

whereby $\bar{Q}$ is the average flow rate, $u(r)$ is the local velocity with respect to radius of the tube and dr is the small increment in length of the cross-sectional ring along the radial direction. Based on the velocity values obtained from the vector plots at the two planes, the average flow rate is computed numerically at plane 1 ($x/D = 1$) and plane 2 ($x/D = 2$), where x represents the axial distance from the inlet to the measured plane and D is the inner diameter of the tube, was $0.0562 \text{ m}^3/\text{hr}$ and $0.0560 \text{ m}^3/\text{hr}$ respectively. The discrepancies between the values attained by the PIV measurements and flow meter recording were within 6.7%. The small discrepancy could be due to the disturbance of background noise, wall reflection and the accuracy of positioning the illuminating laser sheet at the measuring plane as well as the accuracy of the flow meter.

Similarly, the normalized velocities were calculated at the two planes (X_1 ($x/D = 1$) and X_2 ($x/D = 2$)) and the comparison with the normalized theoretical velocity solution was shown in Figure 4-15. From the figure, it is found that the experimental results on the velocity distributions agree well with the theoretical Hagen-Poiseuille solution for circular pipe flow with a maximum error of 4.1%, thus the accuracy of the velocity plots obtained from PIV measurements is acceptable.

Figure 4-15 Comparison of normalized velocity profiles

4.2.4.2 Pulsatile Flow

As described in Section 4.1.3, the pulsatile flow input applied in the experiment is produced through the designed cam device. As the input flow is relatively more complex than the steady flow, the verification of the input flow condition and the results obtained from the PIV measurement is important and thus discussed in this section.

A straight tube of 20 mm in diameter is used as a test model in the system to verify the characteristics of pulsatile flow waveform. The cam mechanism was activated and after a few cycles of the pulsed flow, the pulsatile flow rate waveform is captured on a real-time

oscilloscope via the electromagnetic flow meter attached to the inlet of the straight tube. The pulsatile flow rate waveform (in terms of voltage and time) obtained directly from the oscilloscope is shown in Figure 4-16.

Figure 4-16 Pulsatile flow rate waveform obtained from oscilloscope

Based on the setting of the electromagnetic flow meter, the range of 0 to 4.84 volts represents the flow rate ranging from 0 to 1 m³/h. Figure 4-17 compares the pulsatile velocity waveform from the experiment with the physiological waveform from Nichols and O'Rourke (1990). From Figure 4-17, it is observed that the experimental pulsed waveform has a slightly higher peak than that from literature. The pulsed waveform achieved the highest peak Re of 5430 at the phase angle of 105 degree and experienced the maximum reverse flow with Re = 865 at the phase angle of 231 degree. Note the Re is determined based on the 20mm diameter of aorta. The pulsed waveform has a second peak at the phase angle of 321 degree, which has a Reynolds number of 667. It is comparable with that of Nichols and O'Rourke (1990) which has the first peak Re = 4900 and second peak Re = 647 at phase angles of 84 and 300 degrees respectively. The

average mean velocity of the pulsed waveform is estimated as 27.4 cm/s and the corresponding flow rate of 4.84 liters/min. Due to the limitations in the cam mechanism, it is only able to run the pulsatile experiment at 0.8 Hz or below. Therefore, the period of each pulsed cycle is set at 1.25 second (0.8 Hz) and the Womersley number calculated is 12.2.

Figure 4-17 Comparison of the present experimental velocity waveform—○— with those of Nichols and O'Rourke (1990).....

In addition, during the experiment in conducting pulsatile flow cases, triggering signal is required to send from the cam mechanism to the PIV synchronization system. The function of the signal is to activate the PIV system. The trigger device was described in Section 4.1.4. However, as the cam mechanism is located quite a distance away from the measurement region, a phase shift in the flow is detected. A time lag was found by comparing the waveform obtained from the Electromagnetic flow meter (EMF. 1) and the flow waveform evaluated from the PIV measurement at the test section. The flow in the test model is 0.25s lagged behind from the flow generated at the cam piston. In the

experiments, the initial triggering signal is thus set 0.25s in advance. The flow waveform and velocity vectors discussed in the test region were thus identical in Chapter 6.

4.2.5 Derivation of WSS

Although a number of important implications regarding mechanisms of normal cellular activity and its disruption were established, a standard technical basis for fluid shear measurement has not been established. While some studies have used techniques capable of direct shear measurement, most approaches employ a more versatile, although less direct, approach based on the detection of flow velocities in the vicinity of the vessel wall. The assumption behind these techniques is that all measured velocities are obtained from within the viscous boundary layer so that the derived fluid shear rates are representative of those acting on the wall. A curve is then fitted to those data to obtain a near-wall velocity profile and the slope of the curve at the wall is determined as a measure of velocity gradient or shear rate (Fatemi and Rittgers, 1994). The primary sources of error in wall shear rate (WSR) estimation are velocity measurement error and curve fitting approximation error. Walsh et al. (2003) found that the estimated WSS distributions from LDA experimental results were highly depended on the curve-fitting method used to calculate the WSR. Therefore in this study, the curve-fitting method was carefully checked before processing the experimental data to obtain the WSS values.

In order to determine the shear rate estimation scheme under different flow conditions, a global protocol was devised for both steady and pulsatile flows. A power series polynomial of the form: $u(\xi) = a_0 + a_1\xi + a_2\xi^2 + a_3\xi^3 + \dots + a_n\xi^n$ was used for velocity

$$\begin{matrix} 1 \leq n \leq 8 \\ n \leq N-1 \end{matrix}$$

approximation using the measured discrete point velocities, where ξ is the local normal distance to the wall. The parameters n and N signify the degree of the polynomial

approximation and number of points, including the non-slip point at the wall, used in the approximation, respectively. When N is greater than $n+1$, the approximation became a least square regression of first or higher order based on the selected n . Wall shear rate is estimated by differentiating the above power series with respect to ξ at $\xi=0$ and always equals to the coefficient of the first term, a_1 , as higher order terms will be zero at the wall.

$$\frac{du(\xi)}{d\xi} = a_1 + 2a_2\xi + 3a_3\xi^2 + \dots + na_n\xi^{n-1} \quad (4-12)$$

$$\left. \frac{du(\xi)}{d\xi} \right|_{\xi=0} = a_1 \quad (4-13)$$

The upper limit of n was decided by the boundary layer thickness as to how far from the wall the measurement points can be involved for WSS calculation. Under steady flow condition, it can be estimated by $\delta = \sqrt{\frac{\nu x}{u_\infty}}$ (Schlichting and Gersten, 2000), where ν is kinematic viscosity of the fluid, x is the distance along the wall from the starting point of the boundary and u_∞ is the free-stream velocity. For pulsatile flow, the boundary layer thickness δ can be estimated by $\delta=R/\alpha$ (Fung, 1984). Here, R and α represent the radius of tube and Womersley number respectively.

As investigated by Fatemi and Rittgers (1994), the approximation error for WSR estimation depends not only on the number of points and order of the curve fitting, but also on the distance of the first point from the wall and the increment between the subsequent points in the radial direction in LDA measurements. However for PIV measurements, the distance of the first point from the wall and the increment between the subsequent points cannot be manually controlled, which was decided by the particle distribution density. Smaller particles and interrogation size with high resolution CCD

camera can be used to improve the resolution. In this study, particles of 20 μ m diameter and interrogation size of 32 $\times$ 32 pixels were used with a high resolution CCD camera (pixel size 6.45 $\times$ 6.45 μ m), which could provide convincing results. In order to check the number of points and order of the curve fitting suitable for this study, the WSR at two locations ($x/D=1$ and $x/D=2$) in a straight tube under steady flow measurement was investigated and presented as follows.

PIV measurements were carried out on a straight glass tube of internal diameter 20mm and length 120mm. The flow rate was 0.06m³/hr. As the glass tube had long enough entrance (50cm) in the experimental arrangement, the flow within the tube was fully developed as shown by the measured parabolic velocity profiles. Detailed velocity distributions at these two locations were validated and presented in Section 4.2.4.1. The boundary layer was around 1.24mm in this case. As the increment between subsequent experimental points was 0.25mm, the maximum number of points within viscosity boundary layer was 5. Table 4-3 shows the calculated WSR according to the different degree of the polynomial approximation (n) and number of experimental points used for curve-fitting (N). As the theoretical WSR was 20, a linear approximation with three experimental points and a second-degree polynomial curve-fit with five experimental points were shown to produce more accurate estimation of the WSR. Therefore in this study, a linear approximation with three experimental points was implemented to calculate all the WSS for both steady and pulsatile flow conditions, because the fifth experimental point was outside the viscosity boundary layer under pulsatile flow condition.

Table 4-3 Calculated WSR at two locations with different n and N

Location	N	2	3		4			5			
A	n	1	1	2	1	2	3	1	2	3	4
($x/D=1$)	a_1	32.5	18.75	46.25	17	28.25	59.58	17.25	20.82	42.32	72.08
Location	N	2	3		4			5			
B	n	1	1	2	1	2	3	1	2	3	4
($x/D=2$)	a_1	25	20	30	18	25.5	33.33	18	20.86	31.61	34.58

4.2.6 Experimental Procedure

In the first phase of research work, flow measurement is performed on the proximal models using steady flow inlet conditions. This includes varying the anastomotic angles of 45° forward facing, 90° and 45° backward facing. The first part of the experiment is to investigate the fixed flow rate condition at the bypass graft. Reynolds numbers of 100, 169 and 250 (based on the graft diameter) were selected to represent the range of flow rate in the present investigation. During the experiment, the flow control valve (1) before the contraction cone (Figure 4-1) is fully opened and the flow is basically driven by the static pressure from the reservoir. The flow control valve (3) at the bypass route is also opened. The control valve (2) is initially closed to throttle the flow into the bypass and is slowly opened to meet the experimental conditions. The second part of the experiment involves applying the condition of different resistance (flow rate ratio) at the graft with a fixed inlet flow condition (flow rate is 0.3m³/hr) at the aorta. This is achieved by adjusting the opening of the control valve (3) (as shown in Figure 4-1) to simulate the resistance level at the graft. In this case, four different conditions with respect to the opening of the valve (55%, 75%, 85% and 95%) were set.

In the second phase of the experiment, pulsatile flow condition is applied to the test model to simulate the physiological flow condition. The fluid from the reservoir tank is initially allowed to fill up the entire system so as to remove the entrapped air present in the piston, pipes and joints etc. After the system is fully filled, the motor with the cam attached is turned on. The cam is allowed to rotate a few cycles (allow the system to reach the steady state) before a signal is sent to the PIV system to start the measurement.

In addition, during the steady flow measurement, the system is allowed to stabilize at each preset condition before the two laser pulses were fired onto the test models in the transparent tank. The two respective images were instantaneously captured by the CCD camera and for each condition at least 10 sets of images were captured for analysis so as to ensure the repeatability of the results. At pulsatile flow measurement, a fixed time interval (125ms) between two recordings was used and 10 recordings were collected within one cycle (one image set is one recording). Each measurement was repeated 10 times to ensure the repeatability and accuracy of the results.

With the process of experiments, the model can be removed and replaced easily by another model through the use of a flexible silicone tube coupling. The central axis of the new model is realigned with the laser sheet in order to ensure the velocity vector fields obtained truly reflect the central plane velocity of the fluid. This is achieved through the help of the clamp holder for adjusting the position of the test model and comparing the laser marks reflected on the Kodak burn paper upon firing the laser.

CHAPTER 5

SIMULATION RESULTS AND DISCUSSION FOR PROXIMAL ANASTOMOSIS MODELS

In this chapter, discussions on the numerical simulation results obtained for the proximal anastomosis models are presented. Finding out the details of the hemodynamics at the proximal side are necessary for venturing into the complete anastomotic system, which includes both proximal and distal ends. The areas of interest include both steady and pulsatile flow. The purpose of conducting investigation on the steady state condition is to provide fundamental knowledge and understanding on some of the phenomenon that may occur if the anastomosis model is subjected to the pulsatile flow.

5.1 Brief Introduction of Simulation Conditions

The simulation method and sequence were carried out as described in Chapter 3. However detailed information about simulation conditions for the proximal anastomosis models were characterized in this section.

5.1.1 Physical Models for Mimicking Proximal Anastomosis

The physical models used in numerical simulation had the same geometry as the Pyrex glass test models used in PIV experiments, which were designed to represent the proximal anastomosis based on clinical data of Asian patients from the National Heart Centre of Singapore. Internal diameter of the aorta and graft were 20mm and 6mm respectively. Schematic views of models with forward and backward facing grafts were shown in Figures 5-1 (a) and (b) respectively. Note that in the study, three models, namely 45°

forward facing, 45° backward facing and 90° anastomotic joints were investigated for comparisons.

(a) Forward facing graft

(b) Backward facing graft

Figure 5-1 Schematic designs of the proximal anastomotic models with 45°
(a) forward and (b) backward facing graft

5.1.2 Building Meshes and Mesh Independency Tests

To optimize the computational time and memory, only one symmetric half of models were built and meshed. With the compromise of set-up time, computational cost and numerical accuracy, tetrahedral cells were used in the joint, while hexahedral elements were used for other parts as shown in Figure 5-2. A total of 45,451 nodes and 77,736 elements were used for each model. Mesh density near the wall was larger than elsewhere

to get more accurate WSS. Present grid density was found to be sufficient after successively mesh independency tests as shown in Figures 5-3 and 5-4.

Figure 5-2 (a) Whole view (b) inlet cross-sectional view and (c) front view of grids for 45° forward facing model

A sequence of solution procedure with finer and coarser meshes was used to check if the solution converges, as the meshes get finer. Convergence towards some fixed values provides some confidences about the solution obtained. Figure 5-3 shows the x -velocity profiles along three different locations (A, B and C) at the symmetry plane of 45° forward facing model under the steady flow condition. It can be observed that present grid density (45,451 nodes with 77,726 elements) was found to be sufficient after successively refining the grid from one containing about 15,676 nodes with 32,403 elements. Further

refinement to meshes with 70,764 nodes and 156,292 elements did not produce any significant change in velocity distribution with the maximum difference of 0.2%.

Figure 5-3 Grid independency test at $Re_G=169$ (a) three different locations A, B and C at symmetry plane and x-velocity profiles at locations A (b), B (c) and C (d) for different grid sizes

Furthermore, GCI of 45° forward facing proximal anastomosis model was investigated. The labels to represent the four mesh schemes were tabulated in Table 5-1. GCI for x-velocity along line E (as shown in Figure 5-4(a)) on the symmetry plane was shown in Figure 5-4(b). In this case, p equals to 2, D equals to 3. GCI_{12} , GCI_{23} and GCI_{34} represents the grid convergence index calculated from grids 1 to 2, 2 to 3 and 3 to 4 respectively. As GCI_{12} and GCI_{23} were the same order of magnitude, suggesting almost asymptotic behavior of the solution with increasing refinement of the grid. In addition, the maximum of GCI_{23} was already less than 8%, which was within the acceptance for engineering calculation. Thus meshes 2 (45,451 nodes, 77,726 elements) was selected due to its higher credibility and less computational expense.

Table 5-1 Different meshes for 45° forward facing proximal anastomosis model

Label for different meshes	Number of nodes	Number of elements
4	15,672	32,403
3	31,392	41,233
2	45,451	77,726
1	70,764	156,292

Figure 5-4 (a) Location E at symmetry plane (b) calculated GCIs at location E for x -velocity

Similar meshes and grid independency implement tests were implemented for 45° backward facing and 90° anastomotic models.

5.1.3 Boundary Conditions

5.1.3.1 Steady Flow

As stated in Section 3.4.1, no slip condition was assumed for all walls and symmetry boundary conditions were used for all symmetry planes. The axial velocity at the inlet

was assumed as fully developed steady flow with the same velocity profile as Eq. (3-12). As the compliance at the end of the aorta differs from patient to patient, depending on the size of the heart, there is a need to verify this parameter because different compliance at the end of aorta could affect the hemodynamics of the implanted graft. The Reynolds number based on the 6mm diameter graft for the mean flow rate of saphenous vein aortocoronary graft is around 169. Therefore, in the first phase, Reynolds number of 100, 169 and 250 were selected for grafts as the representative of flow characteristics in the test model with different compliance at the exit of the aorta. The flow rate at the inlet, Re of aorta and the flow ratio between the two outlets (of graft and aorta) and aorta inlet with fixed Re of graft are shown in Table 5-2. In the second phase, the inlet flow rate was fixed, while the flow rate in graft was different to mimic the resistance effect of graft. This resistance reference could be used to represent the level of stenosis or blockage in the graft or arteries, which could result in the failure of the graft (Nielsen et al, 1996). The flow rate ratio between two outlets (of graft and aorta) and aorta inlet with prefixed inlet flow rate is shown in Table 5-3.

Table 5-2 Inlet flow rate, Re of aorta and flow ratio between two outlets and aorta inlet with fixed Re of graft

	Inlet Flow Rate (m ³ /hr)			Re of Aorta			Flow Rate Ratio at the Outlets of Graft and Aorta			
Re of graft	100	169	250	100	169	250		100	169	250
90°	0.193	0.185	0.172	441.3	423.0	393.3	graft	0.034	0.060	0.095
							aorta	0.966	0.94	0.905
45° Forward	0.195	0.1873	0.1715	445.8	428.2	392.6	graft	0.0336	0.0592	0.0956
							aorta	0.9664	0.9408	0.9044
45° Backward	0.195	0.1844	0.1789	445.8	421.6	409.0	graft	0.0336	0.0601	0.0917
							aorta	0.9664	0.9399	0.9083

Table 5-3 Flow ratio between two outlets and aorta inlet with prefixed inlet flow rate ($0.3 \text{ m}^3/\text{hr}$)

Flow Rate Ratio		45° Forward	90°	45° Backward
55%	Graft	0.0293	0.0307	0.0293
	Aorta	0.9707	0.9693	0.9707
75%	Graft	0.0387	0.0400	0.0380
	Aorta	0.9613	0.9600	0.9620
85%	Graft	0.0447	0.0473	0.0433
	Aorta	0.9553	0.9527	0.9567
95%	Graft	0.0507	0.0533	0.0507
	Aorta	0.9493	0.9467	0.9493

Note: The first column shows the opening percentage of the valve at the end of graft during PIV experiments, larger value means a larger graft flow rate and lower graft resistance.

For the outlet boundary conditions, the flow rate ratio between two outlet branches and the inlet was used and the exit flow was assumed to be a fully developed condition. Therefore the lengths of the specified branches had been checked to satisfy the fully developed flow condition before presenting the results.

5.1.3.2 Pulsaile Flow

As described in Section 3.4.2, a transient Womersley solution was implemented as the time varying inlet velocity profile based on a standard input flow rate waveform, which was applied for all the configurations both in the numerical simulation and PIV experiments. The waveform as shown in Figure 5-5 was characterized by a first peak Reynolds number of 5430, a second peak Reynolds number of 667, a mean Reynolds number of 1293, and a Womersley number of 12.2.

Figure 5-5 Comparison of pulsatile waveform for simulation and PIV experiment, —○—; and Nichols and O'Rourke (1990),

Furthermore, the outlets were assumed to have zero gauge pressure to be consistent with the PIV experiment. During the calculation, this pressure will be used as the static pressure of the fluid at the outlet plane; all other variables will be extrapolated from the interior of the domain. In addition, $1/25$ (0.05s) of the period ($T=1.25$ s) was selected as the preferential time step after some trials.

5.2 Hemodynamics in Proximal Anastomosis Models for Steady Flow

The two areas of interest in this section would be: 1) to find out the hemodynamics of proximal anastomosis with different anastomotic angles and flow rate condition (or Re) at the graft; 2) to find out the effect of graft resistance at different anastomotic angles with a fixed flow rate at the inlet. In addition, both flow characteristics and WSS distributions will be discussed in following sections.

5.2.1 Flow Characteristics

5.2.1.1 Basic Flow Characteristics of Different Reynolds Numbers at the Graft

Numerical simulation was conducted over the proximal anastomotic models, with graft Reynolds numbers of 100, 169 and 250 according to the clinical data. Figures 5-6 (a) and (b) show the streamlines with velocity magnitude contour (in different degree of darkness) at the center planes of $Re_G=100$ and $Re_G=250$ respectively.

As shown in Figure 5-6 (a), when $Re_G = 100$, the main flow from the aorta maintained its flow path upon reaching the joint at the heel, and only part of the flow was diverting into the graft. Due to the relative high momentum, the diverted flow slightly overshot the curve of the heel and formed a low velocity region near the graft inner wall, which spanned almost one graft diameter in length as indicated by the darkness in color of velocity magnitude. Along the graft outer wall, the deviated main flow approached the curved surface, and then bifurcated into two streams, with the formation of a stagnation point at the toe. The deflected flow near the toe entered the graft at an angle larger than 45° , the grafting angle. At the location of about 3mm away from the stagnation point, another low velocity region of about 3mm in length was observed. The reason was that the impinging on the graft outer wall resulted in the lost of flow momentum there. The flow, however, aligned back to the graft axis at further downstream.

At $Re_G=250$, the deviated flow in graft as shown in Figure 5-6 (b) had higher velocity than the earlier case. The size of the low velocity region at the heel became smaller and the flow streamline skewed more towards the inner wall as compared to the cases of $Re_G=100$ and 169 (not shown here). It was also observed that the streamlines in the graft had a better alignment with the graft axis and a larger portion of fluid was deviated from

the main aorta flow when comparing with other cases. Similar phenomena can be found for 45° backward facing and 90° anastomotic models.

Figure 5-6 Streamlines with velocity magnitude (m/s) contour at the symmetry plane in the 45° forward facing anastomosis model (a) $Re_G=100$ and (b) $Re_G=250$

5.2.1.2 Effect of Anastomosis Angles on the Flow Characteristics when $Re_G=\text{constant}$

Different anastomotic angle is believed to be one of the reasons in generating distinct flow characteristics of anastomosis. Figures 5-7 (a), (b) and (c) show the velocity vector and streamline maps at center planes for proximal anastomosis models of 45° forward facing, 90° and 45° backward facing at graft Reynolds number of 100 respectively. Comparing the forward facing graft models of 45° and 90° anastomotic angles, the

velocity vectors exhibited two low velocity regions. One of them occurred near the heel along the graft inner wall and the other along the graft outer wall just after the toe. It was observed that as the anastomotic angle became larger, the size of the low velocity region at the heel decreased along the inner wall. The low velocity region at the toe, which was formed due to the change in flow direction after impinging on the outer wall surface, was also observed to decay in size and move further upstream as the anastomotic angle increased. At a smaller anastomotic angle, the flow decelerated sharply upon entering the graft and accelerated thereafter. The deceleration and acceleration, at a larger anastomotic angle, was however not as dramatic as compared to the flow in a smaller anastomotic angle model.

Similarly, the comparison of the models in the 90° and 45° backward facing grafts are demonstrated in Figures 5-7 (b) and (c) respectively. A stagnation point was observed at the toe region where the flow bifurcated. The low velocity region formed at the heel was due to the change in the flow direction. As the anastomotic angle decreased from 90° to 45° (backward facing graft), this low velocity region was observed to decrease in size along the inner wall of graft. It was also noticed that at smaller anastomotic angles, the flow upon entering the graft tended to follow more closely to the geometry of the graft at further downstream.

Based on the velocity vector distributions obtained from the numerical simulation, the low velocity regions were observed to occur at the heel and toe of the anastomotic model. These regions are believed to experience low shear stress, which are ideal sites for thrombosis formation (Binns et al., 1989). These low velocity regions will also be prone to fat deposition and result in the formation of intimal hyperplasia at the joint, blocking

the re-routed blood flow into the graft. Detailed results on the WSS will be presented in Section 5.2.2.

(a) 45° forward facing graft model

(b) 90° graft model

(c) 45° backward facing graft model

Figure 5-7 Velocity vectors and streamlines at the center plane when $Re_G=100$ for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models

5.2.1.3 Effect of Graft Resistance on the Flow Characteristics at Constant Inlet Flow Rate Q_{inlet}

As the area of interest is around toe, heel and suture line, which are more prone to fat deposition and result in the formation of intimal hyperplasia, Figures 5-8 shows the enlarged views of velocity vectors and streamlines at center planes of 45° forward facing anastomotic models with different resistance configurations. The preset inlet flow rate at the aorta was $0.3\text{m}^3/\text{hr}$ and the resistance effect at the graft was simulated by 55%, 75%, 85% and 95% opening of the valve at the end of graft during PIV experiments. The corresponding flow rate information was indicated in Table 5-3. Note that the resistance is inversely proportioned to the flow rate as $R=P/Q$, where P and Q are the time averaged pressure drop and flow rate respectively. Therefore the larger valve opening represented the larger graft flow rate and the smaller graft resistance.

As demonstrated in Table 5-3, the flow rate increased in graft as the opening of valve became bigger. From (a) to (d) of Figure 5-8, it was observed that the low velocity region at the heel of the anastomotic joint decreased in size with the increase of graft flow rate. It was also noticed that at larger flow rate, the flow in the aorta skewed less towards the outer wall of the graft before entering the graft, and the flow aligned back to the graft axis at relative shorter downstream distance. Furthermore, larger flow rate of graft was corresponding to larger velocity at the downstream of the stagnation point along the outer wall, which meant the lashing stress at the toe of graft was higher. The low velocity region and high lashing stress region were associated with low and high WSS respectively; these effects will be further discussed in Section 5.2.2. The same trend can also be found for 90° and 45° backward facing anastomotic models as illustrated in Appendix B.

(a) 55% valve opening

(b) 75% valve opening

(c) 85% valve opening

(d) 95% valve opening

Figure 5-8 Velocity vectors and streamlines of 45° forward facing graft model with different resistance configurations: (a) 55%, (b) 75%, (c) 85% and (d) 95% of valve opening

5.2.2 WSS Distribution

It was believed that the development of intimal hyperplasia at the suture joint was closely related to low WSS (Rittgers et al., 1978; Binns et al., 1989), high or unidirectional shears (Fry, 1969; Friedman et al., 1992). Therefore the calculation of WSS for anastomotic models was conducted. In the laminar flow, WSS is defined by the normal velocity gradient at the wall and is calculated using the relation: $\tau_w = \mu(\partial u / \partial n)|_{wall}$, where $\partial u / \partial n|_{wall}$ is the normal velocity gradient at the wall and $\mu(=0.00408 \text{ N}\cdot\text{s}/\text{m}^2)$ is the viscosity of blood. To obtain the accurate velocity gradient at the wall, grids near the wall must be sufficiently fine to accurately represent the flow in the boundary layer. Based on the boundary layer theory, Schlichting and Gersten (2000) proposed guidelines (see Eq.

(5-1)) for the appropriate placement of near-wall nodes in laminar flow, which is based on the Blasius solution for laminar flow over a flat plate at zero incidence.

$$y_P \sqrt{\frac{u_\infty}{\nu x}} \leq 1 \quad (5-1)$$

where y_P = distance to the wall from the adjacent cell centroid;

u_∞ = free-stream velocity;

ν = kinematic viscosity of the fluid;

x = distance along the wall from the starting point of the boundary layer .

In this study, the velocity is smaller than 0.6m/s and the kinematic viscosity of the fluid equals to $3.87 \times 10^{-6} \text{m}^2/\text{s}$. Therefore if the length of x is chosen as 2mm, the maximum distance to the wall from the most adjacent cell centroid is 0.12mm according to Eq. (5-1). In the present investigation, nevertheless, all the nearest meshes had a distance less than 0.1mm from the wall, which satisfied this criterion. Furthermore, along the radial directions of graft and aorta, the meshes were arranged according to an exponential distribution, so more meshes were allocated near the wall. With such high-density meshes near the wall, the calculated WSS was justified. The WSS distribution contours are shown in the following sections.

5.2.2.1 Basic Characteristics of WSS Distribution

Figure 5-9 shows the WSS distribution of 45° forward facing graft model when $Re_G=169$.

Note that a schematic view indicating the region of interest is placed at the lower left corner of the figure. First of all, the WSS of the aorta and graft is above 0.4 Pa in most of the regions except at the anastomosis. With μ was taken as $4.08 \times 10^{-3} \text{Pa}\cdot\text{s}$, the shear rate was above 98s^{-1} in most of the wall surface, which is consistent with the earlier assumption of Newtonian fluid. Furthermore, distinguishable WSSG can be found around the heel, toe and suture line. Along the inner wall, a low WSS region was found at the

downstream of the heel, which was corresponding to the low velocity region discussed in Section 5.2.2.1. Along the suture line and near the heel, the WSS was higher than the mean value (1.4Pa), which may be due to the sharp change of velocity induced by the complicated anastomosis geometry. At the outer wall, the wall surface was split into two high WSS regions at the stagnation point. The reason for these high WSS zones is the highly skew velocity near the stagnation point. Due to the loosing of momentum upon impinging the wall at the downstream of stagnation point, the low velocity fluid was found at the further downstream along the outer wall and a low WSS region was formed as shown in Figure 5-9. In addition, there was a low WSS region near the suture line at the aorta wall, which was due to the diversion of flow from the aorta into graft.

Figure 5-9 WSS distribution at the anastomosis region ($Re_G=169$)

5.2.2.2 Effects of Anastomosis Angles on the WSS Distributions when $Re_G=100$

Figure 5-10 shows the WSS distributions near the joint of 45° forward facing, 90° and 45° backward facing graft models when $Re_G=100$. From the figure, it can be observed that the

WSS distribution characteristics for all the three models were similar. High WSS region can be found at the regions of the heel, upstream of the stagnation point and downstream of the stagnation point separately. Two low WSS regions could be found at the downstream of the heel and near the anastomosis on the aorta. However the low WSS region at the further downstream along the outer wall shown earlier in Figure 5-9 was not observed in Figure 5-10. The reason was that when $Re_G=100$, little fluid was diverted into the graft, the decrease of momentum upon impinging the graft outer wall was thus not serious enough to form a low WSS region there. In addition, comparing Figures 5-10 (a), (b) and (c), it can be observed that the low WSS region at the downstream of the heel was reduced in size with the increasing of anastomosis angle if the 45° backward facing is treated as 135° forward facing. At the same time, the low WSS region near the anastomosis at the aorta was also reduced in size with the increasing of anastomosis angle.

According to the low shear stress theory proposed by Caro and co-workers (1971), atherosclerosis usually developed in regions of the artery exposed to a low level of average shear stress as the ECs did not receive a sufficient amount of nutrients and simultaneously waste products tended to accumulate on the cell surface, which led to the necrosis of cells at low shear rates. Therefore larger anastomosis angle may be favor in improving the graft patency rate for reducing the low WSS regions in size. Same conclusion can be made for proximal anastomosis model when $Re_G=169$ or 250 .

(a) 45° forward facing model

(b) 90° facing model

(c) 45° backward facing model

Figure 5-10 WSS distributions near the joint for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models at $Re_G=100$

5.2.2.3 Effect of Graft Resistance on the WSS Distribution

Figures 5-11 and 5-12 show respectively the WSS distribution along the inner and outer walls of 45° forward facing, 90° and 45° backward facing graft models. The non-dimensional X/D_G is used to represent the spatial location of the WSS computed where D_G is the diameter of the graft (6mm). The annotation, X_1 and X_2 are the points selected approximately at the end of the straight aortic wall and are going along the direction of the inner and the outer walls of the graft respectively.

From Figure 5-11 (a), it was observed that along the inner wall, the WSS was increasing from a nearly constant value (0.43Pa) along the aorta wall and reached its peak at $X_1/D_G=0$. Then it began to decrease when the flow entered the graft near the heel, which corresponded to the low velocity region. When the flow passed over this region, the velocity along the wall increased steeply because the fluid skewed to the outer wall had

restored the flow direction to the graft axis, which was shown by the increasing WSS. At further downstream along the graft inner wall, the WSS achieved a new asymptotic value, which was represented by a horizontal line. As shown in the figure, different distributions illustrated the influence of different graft resistance. The curve with higher value was the one having lower graft resistance with higher graft flow rate. From the figure it can be seen that the trend of WSS distributions for different graft resistance was similar. However, the lower graft resistance, which represented higher graft flow rate, resulted in the higher WSS values to some extent. In addition, it can be observed that the influence of graft resistance to the WSS within the aorta part along the inner wall ($X_1/D_G \leq 0$) was less than that of the downstream part ($X_1/D_G \geq 0$). This may not be unexpected as the flow rate in the aorta is constant until the flow approaches the graft. Furthermore, the flow rate of graft was much smaller than that of aorta. The changes of flow rate in graft had smaller influence on its upstream than downstream.

Similar WSS distributions along the inner wall can be found at Figure 5-11 (b) and (c) for the 90° and 45° backward facing graft models respectively. The same asymptotic WSS values for the aorta and graft were observed for different models regardless of graft resistance. This was due to the same flow rate condition for different models under the same graft resistance. However some differences can be observed for the three models. Firstly, the spatial distance for the low velocity region was reduced with the increasing of grafting angle. For 45° forward grafting model, the distance between the two apexes of WSS curve was $2.4 D_G$, while it was 1.2 and $1.0 D_G$ for 90° and 45° backward facing graft models respectively. As the low shear stress was believed to be an ideal site for thrombosis formation (Binns et al., 1989), 45° backward facing graft models would result in better graft patency rate in this aspect. Secondly, the variation range of WSS

magnitudes was different for these three models. For the case of largest graft resistance (the lowest graft flow rate, 55% valve opening), the WSS along the inner wall of 45° forward facing graft models, varied from 0.012Pa to 1.055Pa, while those of 90° and 45° backward facing graft models changed from 0.014Pa to 1.178Pa and from 0.092Pa to 1.150Pa respectively. The 45° backward facing graft models had the smallest variation range of WSS (0.058Pa) as compared with those of 90° model (1.164Pa) and 45° forward facing graft model (1.043Pa). The smallest variation range of WSS should reduce the growth of intimal hyperplasia at the anastomosis and thus prevented the graft conduit from stenosis based on the safe-bandwidth theory (Kleinstreuer et al, 1991). Therefore the 45° backward facing model may merit the graft patency rate than other models studied due to its smallest variation range of WSS along the inner wall.

Figure 5-12 (a) shows the WSS distributions along the outer wall of the 45° forward facing graft model. The WSS magnitude (absolute value) was increasing from a nearly constant value ($|-0.71\text{Pa}|=0.71\text{Pa}$) along the X_2 direction and reached its maximum at $X_2/D_G=0.29$. Then it began to decrease and reached zero at $X_2/D_G=0.475$, where the WSS changed the sign and continued to increase until reaching another peak value at $X_2/D_G=0.8$. At further downstream along the graft outer wall, the WSS achieved a new asymptotic value, which was represented by a nearly horizontal line. As shown in the figure, the lower graft resistance, which represented higher graft flow rate, resulted in the higher WSS values to some extent, although the trend of WSS distributions for different graft resistance was similar. In addition, it can be observed that the influence of graft resistance on the WSS within the aorta part along the outer wall ($X_2/D_G \leq 0$) was much lesser than that of the downstream part ($X_2/D_G \geq 0$). The reason was that the flow rate of graft was much smaller than that of aorta and the changes of flow rate in graft had little

influence for the aorta downstream. From Figure 5-12 (a), it can be observed that the stagnation point, which has zero WSS, was fixed in location regardless of the graft resistance, which may induce the aggregation of red blood cells.

Similar WSS distribution trend along the outer wall can be found in Figures 5-12 (b) and (c) for the 90° and 45° backward facing graft models respectively. The same asymptotic WSS values for the aorta were observed for different models regardless of graft resistance. This was due to the same flow rate condition for different models under the same graft resistance. The variation range of WSS was quite different for these three models. For the largest graft resistance (the lowest graft flow rate, 55% valve opening), the WSS along the outer wall of 45° forward facing graft models, varied from -2.685Pa to 3.296Pa, while those of 90° and 45° backward facing graft models changed from -2.26Pa to 3.183Pa and from -2.961Pa to 1.954Pa respectively. The 45° backward facing graft models had the smallest variation range of WSS (4.915Pa) in contrast to 90° (5.443Pa) and 45° forward facing (5.981Pa) graft models with the lowest peak WSS magnitude (2.961Pa). It can also be observed that the WSS distributions of 45° backward facing graft model had a more gentle and smaller variation in contrast to the other two models. In addition, the WSS along the downstream of graft outer wall generally had a higher magnitude than the values of the graft inner wall, which indicated the flow path of the fluid was skewed more towards the outer wall.

In general, the graft resistance had some influences on the WSS magnitude. Lower graft resistance resulted in higher WSS due to the higher flow rate in graft. The anastomosis angle was also observed to influence the WSS distributions along the inner and outer walls. Among them, 45° backward facing graft model may be the best due to its smallest

low WSS region at the heel and the smallest variation ranges of WSS along both inner and outer walls respectively.

Figure 5-11 WSS distributions along the inner wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models under different graft resistance

Figure 5-12 WSS distributions along the outer wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models under different graft resistance

5.2.3 Comparisons with Other Published Works

Since there were little published works available on the proximal anastomosis, the studies of bifurcation were used to give some clue about the WSS distribution along the wall for validating the present results. Shipkowitz et al. (1998) studied the local shear stress in abdominal aortic branches under steady flow condition by means of numerical simulation. The schematic illustration of the model is shown in Figure 5-13. Blood enters the thoracic aorta, and then split into the left and right renal, as well as further flowing into the left and right iliac. Although the flow has more outlets than the present model, the WSS distribution along the superior and the inferior walls of left renal really provided some useful information as shown in Figure 5-14 (a) and (b) respectively.

In Figure 5-14, the abscissas, which lie along the axial (Z) direction, were normalized by the diameter of the aorta (D), while the ordinates were normalized by Poiseuille WSS (τ_p). Labels on the curves in Figure 5-14 are the Reynolds numbers based on the thoracic aorta. Comparing Figure 5-14 (a) with the present WSS distribution along the inner wall of 45° forward facing anastomosis model shown earlier in Figure 5-11 (a), similar trend was found when recalling that the abscissas started from zero in Figure 5-14 (a). Both inner walls experienced a low WSS region before restored to an asymptotic value at further downstream. Similarly, the WSS distribution along the left inferior wall as shown in Figure 5-14 (b) had the same trend as that of the present 45° forward facing anastomosis model along the graft outer wall as illustrated in Figure 5-12 (a). Note that only absolute values of WSS are shown in Figure 5-14. The WSS magnitude decreased to the stagnation point before increasing to a peak. After that, the WSS decreased to achieve an asymptotic value. This has shown that the present numerical simulation results are reliable.

Figure 5-13 Schematic illustration of the abdominal aortic model used in Shipkowitz et al. (1998)

Figure 5-14 Distribution of WSS along the superior and inferior wall of the left renal (a) superior wall (b) inferior wall (taken from Shipkowitz et al., 1998)

Moreover, Yamaguchi and Kohtoh (1994) investigated the WSS distribution in daughter tube through 45° branch model according to the relationship between WSS and electric current. The set-up information is schematically illustrated in Figure 5-15. The flow pattern was visualized by dye stream. Resultant flow visualization and WSS distribution are demonstrated in Figures 5-16 and 5-17 respectively.

Similar pathline was found when comparing Figure 5-16 with Figure 5-6, which showed the ability of numerical simulation to indicate the correct velocity field. Due to the relative high momentum, the diverted flow into graft slightly overshoot the curve of the heel. The flow, however, aligned back to the graft axis at further downstream. The inner wall of their model can be presented by the line from B_0 to B_{40} , while the outer wall was presented through F_{27} - F_1 - E_1 - E_{20} as shown in Figure 5-15 (b). Along the inner wall, the WSS as shown in Figure 5-15 decreased when entering the low velocity region before increasing to the asymptotic value, which had the similar trend to that of the WSS distribution along the inner wall of the present 45° forward facing anastomosis model as shown in Figure 5-11 (a). Note that only the absolute values of WSS was shown in Figure 5-17. Therefore, the WSS distributions along the outer wall of the present 45° forward facing anastomosis model as shown earlier in Figure 5-12 (a) had the same trend with their experimental results shown in Figure 5-17. The only difference was that Yamaguchi and Kohtoh (1994) did not find the stagnation point with zero WSS. That was due to the lack of experimental points between E_1 and F_1 in their measurements.

In view of the above, numerical simulation can provide detailed and reliable flow fields and the WSS distribution of steady flow. The pulsatile flow results will be presented and discussed in the next section.

Figure 5-15 Sketch of system information

Figure 5-16 Flow visualization at even flow ratio

5.3 Hemodynamics in Proximal Anastomosis Models for Pulsatile Flow

5.3.1 Flow Characteristics

As stated in Section 5.1.3.2, the Womersley solution based on the waveform of Figure 5-5 was implemented as inlet axis velocity for proximal anastomosis models during numerical simulation. The inlet volume flow rate can be obtained by integrating the inlet velocity when monitoring numerical iterations. Figure 5-18 shows the mean inlet velocity waveform, which was derived from volume flow rate by dividing it with inlet cross-sectional area. Note that the period of the cycle used in both experiments and numerical simulation is 1.25s. As simulation results at the second period were presented to avoid the influence of initial condition, the figure was plotted from 360 to 720 degree in phase angle. In addition, Figure 5-18 was exactly the same as Figure 5-5, which partly demonstrated the accuracy of user-defined program compiled to determine the inlet axis velocity. Also shown in the figure are seven indicated time intervals within a cycle at which velocity maps and WSS distributions were computed and presented as follows.

Figure 5-18 Location of time intervals selected for presenting the flow characteristics

5.3.1.1 Flow Characteristics at the Center Plane

Figure 5-19 shows velocity vector maps obtained for the center plane of the 45° forward facing graft model at different phases as indicated in Figure 5-18. Note that a full period was 1.25s and the timing shown was after one complete cycle. At $t_1=1.35s$ as observed in Figure 5-19 (a), main flow from the aorta maintained its flow path upon reaching the heel; only part of flow diverted into graft. Along the graft outer wall, deviated main flow approached the curved surface, and then bifurcated into two streams with the formation of a stagnation point at the toe. The velocity magnitude was generally small as the inlet flow just began to accelerate. Note that only flow field at the joint region is shown here as the location has high tendency in forming mitogens, activating platelets and etc., which lead to the graft failure eventually.

At peak flow rate ($t_2=1.6s$), a recirculation region with 10 mm (about $1.67 D_G$) length was observed along the graft inner wall as shown in Figure 5-19 (b). This was similar to flow structures noted by Hughes and How (1995) under steady flow conditions, where Reynolds number was 306 and 76% of the inlet fluid flowed downstream through the mother tube. The recirculation region was three-dimensional in nature. To study the three-dimensional flow in detail, two cross-sectional planes of the graft indicated as A and B in Figure 5-19 (b) were extracted, which were 13mm and 15mm from the centerline of aorta respectively. The flows in planes A and B are shown in Figure 5-20 (a) and will be discussed later. Since flow dynamics at deceleration phases were more diverse than other time intervals, more results were presented for deceleration phases. When flow just began to decelerate, such as $t_3=1.7s$ shown in Figure 5-19 (c), the recirculation region near the inner wall distended into the graft center region and occupied more space than those of previous time phase. After that, when $t_4=1.8s$, a remarkable phenomenon was observed as shown in Figure 5-19 (d) - a vortex was found at approximately the center of the joint,

which induced some fluid in the graft to reverse its flow direction near the graft inner wall. The existence of vortex combined with reversed flow near the heel reduced the effective flow flux of graft. With the advancing of time, the vortex center moved upward into the aorta and shifted towards the toe, which induced more fluid in graft to flow back into the aorta as shown in Figure 5-19 (e), when $t_5=1.85s$. At $t_6=2.1s$, the net inlet flow was in the reversed direction dominated by backflow from graft as shown in Figure 5-19 (f). Such phenomenon was also reported in the velocity vector plots at net reversed flow rate by Buchanan et al (1999) for a rabbit aorto-celiac junction. For $t_7=2.4s$ as demonstrated in Figure 5-19 (g), backflow in graft disappeared, thus fluid moved towards the downstream of the aorta when some fluids were channeled into graft with small velocity magnitude.

(a) Time (t_1) at 1.35s

(b) Time (t_2) at 1.6s

(c) Time (t_3) at 1.7s

(d) Time (t_4) at 1.8s

(e) Time (t_5) at 1.85s

Figure 5-19 Velocity vectors at center plane in 45° forward facing graft model at different phases: (a) $t_1=1.35s$; (b) $t_2=1.6s$; (c) $t_3=1.7s$; (d) $t_4=1.8s$; (e) $t_5=1.85s$; (f) $t_6=2.1$; (g) $t_7=2.4s$

Similar trend of flow characteristics at the center plane can be found for 90° and 45° backward facing graft models as illustrated in Appendix C.

5.3.1.2 Flow Characteristics of Cross-sectional Planes at Peak Flow Phase

Since the velocity field at peak flow rate was rather complex than other time intervals, Figures 5-20 (a), (b) and (c) show the velocity vectors (and corresponding streamlines) in both center plane and planes A and B of 45° forward facing, 90° and 45° backward facing grafts respectively. Note that the origin of x , y and z Cartesian coordinate was set at the center of the inlet cross-sectional plane. Only half of the x - z planes are shown, as models are symmetrical with respect to the x -axis. From figures, it was confirmed that at peak flow rate, flow separation region could be found along the graft inner wall immediately downstream of the heel, which was represented by the flow recirculation for 45° forward facing graft and diverged streamlines from a point for the 90° and 45° backward facing grafts. The nodal points viewed as sources in Figures 5-20 (b) and (c) were the attachment points of three dimensional flow separation (Filippone, 2004). In addition, anastomosis angle was observed to affect the separation region near the heel. With the increase of anastomosis angle from 45° to 135° (viz. 45° backward facing graft), the flow separation region not only reduced in size, but also more restricted to the region close to the inner wall (See Figure 5-22 later). Similar trend was also reported by Hughes and How (1995), when the downstream of mother tube was partially occluded.

A pair of vortex was found at both planes A and B of the 90° (and 45° backward facing) grafts as shown in Figure 5-20 (b) (and Figure 5-20 (c)). For the 90° anastomotic model, the extension of vortex increased from 3.5mm (0.58D_G) at plane A to 5.0mm (0.82D_G) at plane B in x -axis when the cross-sectional area decreased from plane A to plane B. For the 45° backward facing anastomotic model, the vortex reduced in length when moving

from plane A to plane B due to an increase in cross-sectional area. Since the presence of vortex in graft would increase contact between blood and the thrombogenic graft surface, which may result in platelet activation (Hughes and How, 1995), increasing the cross-sectional area caused vortex size reduction and thus may be in favor of graft patency. In addition, it should be noted that the vortex center for 90° graft was closer to the wall than that of 45° backward facing graft. The vortex center of 45° backward facing graft even moved far away from the wall when shifting cross-sectional plane A to plane B, which may reduce the probability of pathological changes.

Figure 5-20 Distributions of velocity vectors with streamline plots in symmetry and horizontal sectional planes A and B at peak flow rate $t_2=1.6s$ for (a) 45° forward facing, (b) 90° and (c) 45° backward facing grafts

To further explore flow structures at peak flow phase, Figures 5-21 (a), (b) and (c) show the cross-sectional flow cut at the center plane of graft for 45° forward, 90° and 45° backward facing models respectively. Note that x' is the coordinate along the graft axis. It can be observed that due to the resolving of velocity into components parallel to the cutting plane, the velocity at aorta sections of 45° forward and 45° backward facing models were in direction downward towards the graft and upward towards the bed of aorta respectively. For 90° model as it is a perpendicular cut, the velocity component at the plane of aorta section were basically very small with those near the graft had shown the velocity components started to flow into the graft. The flow in graft for all three models were in the direction parallel to the graft axis, these observations are quite different from the flow visualization, Figure 7 (center plane of the graft) of Hughes and How (1995), in which the flow within graft is inclined at an angle to the graft axis for their 30° proximal anastomosis. The discrepancy may be due to their low Reynolds number (600) and fully occluded mother tube downstream. Although as demonstrated in Figure 5-20, there were vortices at cross-sectional planes A and B of the 45° backward facing and 90° models as observed by Hughes and How (1995).

Figure 5-21 Velocity distributions at the cross-sectional plane cutting along graft axis of (a) 45° forward facing (b) 90° and (c) 45° backward facing models for $t_2=1.6s$

5.3.2 Hemodynamic Parameters Distribution

As there is strong biological evidence that hemodynamic wall parameters (HPs) encapsulate “disturbed flow” that may trigger a cascade of abnormal biological processes leading to intimal thickening and/or thrombi formation, sufficiently high and sustained HP values can be employed to determine susceptible sites for the onset of blood vessel diseases (Kleinstreuer et al., 2001). Historically, the most frequently employed indicators of disturbed flow have been the WSS, time-averaged WSS, WSSG, OSI and the newly proposed segmental averages of above HPs. Therefore, in this study, all these indicators were investigated and discussed in detail sequentially.

5.3.2.1 Transient WSS Distributions near the Anastomosis Joint

Figures 5-22 and 5-23 show WSS distributions at different time intervals along the graft inner and outer walls near the anastomosis joint of three models respectively. Normalized axial distance, X/D_G represents the spatial location of WSS computed. The annotation, X_1 and X_2 are the points selected approximately at the end of straight aortic wall and are going along the direction of graft inner and outer walls respectively. In addition, the WSS distributions along outer wall at $t_2=1.6s$ and $t_3=1.7s$ for all models are particularly presented in Figure 5-23 (d) for clarity as a result of its higher variations than other time intervals. Note that 45F, 90 and 45B represent 45° forward facing, 90° and 45° backward facing anastomotic models respectively.

Along the inner wall of 45° forward facing anastomotic joint as shown in Figure 5-22 (a), at $t_1=1.35s$, the WSS increased when accessing the heel, then it decreased once entering the low velocity region ($0.15 \leq X_1/D_G \leq 1.25$). After passing this region, the fluid accelerated slightly, which was shown by increasing WSS, until reaching the developed flow condition. When the inlet flow rate increased to the peak from t_1 to t_2 , the WSS level

reached to its maximum of 11.6Pa as well. Corresponding to the flow recirculation formed near the heel at $t_2=1.6s$, WSS was negative in the region ($0.5 \leq X_1/D_G \leq 2.2$). When flow just began to decelerate at $t_3=1.7s$, the flow characteristics and WSS distribution kept the pattern of peak flow. However, the maximum WSS decreased to 5.4 Pa and the recirculation region near the heel was increased in size ($0.35 \leq X_1/D_G \leq 2.85$). At $t_4=1.8s$ and $t_5=1.85s$, WSS remains negative along the inner wall on account of the backflow in graft and the vortex formed upstream of the aorta. At $t_6=2.1s$, WSS was basically less negative than those at t_4 and t_5 . Complex flow condition at aorta upstream resulted in the variation of WSS signs there. The WSS came back to positive only when $t_7=2.4s$. At that time, WSS varied slightly along the inner wall but maintained positive value.

Similar trend can be found for other two models in Figure 5-22 (b) and (c). Note that the two zero WSS points along graft inner wall at peak flow phase corresponded to the separation and attachment points sequentially. The length between them decreased from $1.7D_G$ for 45° forward facing graft ($0.5 \leq X_1/D_G \leq 2.2$) through $1D_G$ for 90° graft ($0.7 \leq X_1/D_G \leq 1.7$) to $0.4D_G$ for 45° backward facing graft ($0.8 \leq X_1/D_G \leq 1.2$), which demonstrated that flow separation region at peak flow phase decreased in size with increase of anastomosis angle.

Along the outer wall of 45° forward facing anastomosis, in the accelerating stage (t_1) the WSS (as shown in Figure 5-23 (a)) varied tremendously from $-1.52Pa$ to $1.25Pa$ for $0.18 \leq X_2/D_G \leq 0.96$ and changed sign at stagnation point ($X_2/D_G=0.65$). At peak flow phase ($t_2=1.6s$), the WSS magnitude level also attained its maximum as shown in Figure 5-23(d). When flow just began to decelerate ($t_3=1.7s$), the WSS maintained the same pattern as that of peak flow. However the maximum WSS was reduced and the stagnation

point moved upward a little towards the aorta ($X_2/D_G=0.5$). Once entering into late deceleration phase at $t_4=1.8s$, the WSS was negative before accessing the stagnation point as demonstrated in Figure 5-23 (a), then it became negative again at further downstream, as a result of vortex formed in the joint and the backflow in graft. At $t_5=1.85s$, because of the vortex formed at aorta downstream, the WSS became positive at the beginning of X_2 . Then it changed to negative downstream, which was different from those of early time intervals in virtue of flow reverses from graft back to the aorta. Same trend can be observed for $t_6=2.1s$, however, the WSS magnitude decreased for lower inlet flow rate. At $t_7=2.4s$, the variations of WSS were similar to those of $t_1=1.35s$ with a much smaller magnitude.

Same trend of WSS distributions can be found for the other two models as shown in Figures 5-23 (b), (c) and (d). It was evident from the findings that 90° graft had the largest variation range of instantaneous WSS at both inner wall ($-5.1Pa \leq \tau_w \leq 15.4Pa$) and outer wall ($-22.2Pa \leq \tau_w \leq 21.3Pa$). The stagnation point with zero WSS was found along the outer wall with small shifting, which would reduce the risk of red blood cells aggregation.

Figure 5-22 WSS distributions along the inner wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing anastomotic models at different time intervals

(a)

(b)

(c)

Figure 5-23 WSS distributions along the outer wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing anastomotic models at different time intervals and (d) at peak ($t_2=1.6s$) and earlier deceleration phases ($t_3=1.7s$)

5.3.2.2 Time-averaged WSS, WSSG and OSI Distributions and Segmental Average of Them

In the study of Buchanan et al. (1999), the comparisons between hemodynamic parameters with the animal experimental intimal WBC density, LDL permeability, lesion growth data were explored. The results show that the segmental averages of time-averaged WSSG significantly correlated with WBC densities. The highest LDL permeability and the largest sites of elevated permeability are associated with regions of elevated time-averaged WSSG, although an elevated WSSG is not associated with all sites of elevated permeability. Early and continued atherosclerotic lesion growth occurred lateral to the branch orifice is associated with regions of low time-averaged WSS and an elevated oscillatory component. However the early atherosclerotic lesion growth occurred distal to the branch orifice is in an area of high time-averaged WSS and low OSI. Using these criteria as reference, the comparisons of HP distributions among different models

could reveal more physiological information as shown in Figure 5-24 and Tables 5-4 and 5-5.

Figures 5-24 (a), (b) and (c) show the surface contour plots of time-averaged WSS, WSSG and OSI for a complete period obtained using Eqs. (3-18), (3-19) and (3-20) respectively for all three models. The first, second and third row of Figure 5-24 represent the results for 45° forward facing, 90° and 45° backward facing models respectively. From the first column, it can be observed that the time-averaged WSS at the heel, toe and the region downstream of the toe was higher than other places for all three models. In addition, the region of high time-averaged WSS at the heel of the 45° backward facing model was the smallest among the three models. Note that for ease of comparison, the contour plots of time-averaged WSS, WSSG and OSI for all three models adopt the same darkness code within the same range of limits. Three low time-averaged WSS regions could be found for 45° forward facing model and 90° facing model near the center region of anastomosis on the aortic wall side, downstream of the heel along the graft inner wall and the region further downstream of the graft inner wall, while only two low time-averaged WSS regions were found for 45° backward facing model near the center region of anastomosis on the aortic wall side and the region further downstream of the graft inner wall respectively. Among the three models, 45° forward facing model has the largest size of the low time-averaged WSS region just downstream of the heel. The reason is that 45° forward facing model experienced the highest reverse flow at the peak flow and deceleration phases, as indicated by elevated OSI shown in Figure 5-24 (c).

The distribution of time-averaged WSSG as demonstrated in Figure 5-24 (b) were quite similar among the three models. Three high time-averaged WSSG regions distributed at

the heel and the toe as well as downstream of the toe respectively. The magnitude of time-averaged WSSG for 90° model was larger than those of other two models as shown by its darkness in color. In addition, the spatial distribution of OSI for the 45° forward facing model was a little different from others. A low OSI region was observed downstream of the heel, which corresponded to the low time-averaged WSS region. However, there was also some common ground among the three models such as two low OSI regions existed at the toe and the region downstream of the toe and high OSI region demonstrated at the further downstream of the heel. Detailed quantitative data are tabulated in Tables 5-4 and 5-5.

As listed in Table 5-4, the OSI indicated relatively high values for all three models because the flow was highly dependent on the present input pulse with reverse flow. However, the time-averaged WSS variation range of the 45° backward facing model was the smallest, which has the highest minimum time-averaged WSS (1.17Pa) and the lowest maximum time-averaged WSS (4.94Pa). Bearing in mind that early and continued atherosclerotic lesion growth is associated with regions of either low time-averaged WSS with an elevated oscillatory component or high time-averaged WSS with low OSI. The smallest variation range of time-averaged WSS should have reduced the growth of intimal hyperplasia at the anastomosis and thus prevented the graft conduit from stenosis. This was consistent with the “safe-bandwidth theory” (Kleinstreue et al., 1991) - which postulated that both low and high shear stresses contribute to the growth of plaque formation and assumed a “safe-bandwidth” of the WSS (within the low and high limits). As the “safe-bandwidth” theory had been proven useful in determining some susceptible sites and growth patterns of atherosclerotic lesions, the 45° backward facing model would merit the graft patency rate than other models studied due to its smallest variation range

of time-averaged WSS. In addition, the maximum time-averaged WSSG for 45° backward facing model were the smallest among three models and the minimum time-averaged WSSG for 45° backward facing model was in the second position among three models, which was just marginally larger than that of 90° model. Because high time-averaged WSSG is believed to associate with elevated LDL permeability (Buchanan et al., 1999) and intimal hyperplasia (Lei et al., 1995), 45° backward facing model was the best among three models in this aspect.

To have a more complete picture of time-averaged WSS, WSSG and OSI distributions, besides the extreme values of these HPs presented in Table 5-4, Table 5-5 shows the segmental average of HPs calculated by Eq. (3-21) on two surfaces at the joint, which is above and below the anastomosis line, named as A' and B' respectively. From the table, it could be observed that the segmental average of time-averaged WSS for surface A' has not much discrepancy among the three models, while 45° backward facing model had the lowest segmental average of time-averaged WSS for surface B' and the lowest segmental average of time-averaged WSSG for both surface A' and B'. Since segmental averages of time-averaged WSSG significantly correlated with WBC densities as demonstrated by Buchanan and coworkers (1999), these findings further support that 45° backward facing model merits the high patency of graft. To synthesize the effect of different HPs, Kleinstreuer et al. (2001) proposed a composite severity parameter (SP), which was

defined as $SP = average(HP_{norm}) = \frac{\sum_{n=1}^N HP_{norm}}{N}$, where HP_{norm} was the HP normalized by

its maximum value, N was the number of HPs used. In Table 5-5, SP_1 synthesized the effects of time-averaged WSS, WSSG and OSI (N=3), while SP_2 ignored the influence of OSI (N=2) since its segmental average was not varying much among three models as

listed in Table 5-5. Significant differences in SP_2 values were found especially for surface B'. The SP_2 for 45° backward facing model was the lowest among the three models. As a result, it is expected that the 45° backward facing model will have less potential for stenosis and would result in improving the graft patency rate as mentioned earlier.

Figure 5-24 Contours of HPs (a) time-averaged WSS, (b) time-averaged WSSG and (c) OSI on the surface of 45° forward facing, 90° and 45° backward facing models

Table 5-4 Comparison of HP Range between different models

	45° F	90°	45° B
Min. Time-averaged WSS (Pa)	1.098	0.968	1.17
Max. Time-averaged WSS (Pa)	5.42	5.678	4.94
Min. Time-averaged WSSG	6.59	5.53	5.58
Max. Time-averaged WSSG	89.74	78.49	71.52
Min. OSI	0.021	0.013	0.021
Max OSI	0.498	0.498	0.498

Note: 45° F, 90° and 45° B represent 45° forward facing, 90° and 45° backward facing models respectively.

Table 5-5 Comparison of <HP> between different models

	Sketch Maps	Location	Area (mm ²)	<WSS> (Pa)	<WSSG>	<OSI>	SP ₁	SP ₂
45°F		A'	1034.48	2.06	28.37	0.24	0.67	0.54
		B'	67.60	2.73	41.77	0.18	0.73	0.75
90°		A'	872.68	2.02	31.47	0.23	0.66	0.56
		B'	87.50	2.76	56.56	0.14	0.76	0.87
45°B		A'	1034.48	2.07	28.37	0.24	0.67	0.54
		B'	67.60	2.50	38.73	0.17	0.68	0.69

5.3.3 Comparisons with Other Published Works

To further validate the numerical results, some comparisons between the present simulation results and other published works were carried out and presented in this section.

Figure 5-25 shows the WSS variations within a complete pulsatile cycle at the heel ($X_1/D_G=-0.2$) and the toe ($X_2/D_G=-0.2$) of 45° forward facing anastomosis. From the figure, it could be observed that the WSS varied in a relatively sinusoidal manner. The peak WSS at the heel led those at the toe by about 14.4 degree, and the magnitude of WSS at the toe was higher than those of heel at most time phases as demonstrated in Figure 5-25. All these results followed the similar trend of the photochromic tracer study obtained by Ojha et al. (1993), although quantitative comparison was difficult due to the different flow ratio, graft diameter and flow waveform used.

Figure 5-25 WSS variations on the heel ($X_1/D_G=-0.2$) and toe ($X_2/D_G=-0.2$)

Besides the instantaneous WSS distributions along graft inner and outer walls, Figure 5-26 shows the surface contour plots of time-averaged WSS, WSSG and OSI calculated by Eqs. (3-18), (3-19) and (3-20) respectively for 90° facing model. To facilitate the comparison with the results of Buchanan et al. (1999) for a rabbit aorto-celiac junction,

the 90° facing model was inverted in the figure and white arrows represented flow directions. The surface contour plots of each HP are presented in two separate figures for comprehensive viewing, viz. Figure 5-26 (a) and (b) for time-averaged WSS, (c) and (d) for time-averaged WSSG and (e) and (f) for OSI. The high time-averaged WSS regions were seen on both heel and toe and the region downstream of the toe with a locally decreasing at the stagnation region. These high time-averaged WSS regions experienced less reverse flow as shown by the low OSI values in Figure 5-26 (e). There were also two significant areas with low time-averaged WSS, near the middle of anastomosis at the aorta wall as indicated in Figure 5-26 (a) and along the graft inner wall as demonstrated in Figure 5-26 (b). These low time-averaged WSS regions were regions of flow separation through the whole cycle as indicated by elevated OSI values at the same locations as shown in Figures 5-26 (e) and (f). In addition, high time-averaged WSSG regions were associated with the high time-averaged WSS regions near the toe and heel as observed in Figure 5-26 (c). Comparing Figure 5-26 with Figure 4 of Buchanan et al. (1999), a good agreement can be found except that the low time-averaged WSS region at the lateral to the celiac opening of their model had much larger size than those of the present model, and their OSI distributions along the aorta wall had more obvious variations. This is due to the large diameter ratio (3.33) between the aorta and graft in the present study as comparing to their much smaller diameter ratio (1.64), which should induce more flow from the aorta to the branch.

Figure 5-26 Contours of hemodynamic parameters on the surface of 90° facing model: (a) and (b) time-averaged WSS; (c) and (d) time-averaged WSSG; (e) and (f) OSI

5.4 A Summary for This Chapter

In this chapter, numerical simulation study provided a comprehensive view of the flow fields in three proximal anastomotic models (i.e. 45° forward, 90° and 45° backward facing grafts) under both steady and pulsatile flow conditions. The investigation of steady flow revealed the basic flow characteristics of proximal anastomosis. The flow rate of aorta, graft and the grafting angle were found to correlate with flow characteristics and WSS distributions of the proximal anastomosis. The 45° backward facing graft was found to be better than the other two models in terms of graft patency rate due to its relative small variation range of WSS and small low velocity region near the heel.

Under the pulsatile flow condition, at peak flow phase, flow separation was found along the graft inner wall just after the heel and decreased in size with the increase of grafting angle. At the same time a pair of vortex was found at the graft cross-sectional planes A and B of 45° backward facing and 90° grafts. The location of stagnation point at the outer graft wall near the toe was not fixed but has small variation for all three models within the physiological cycle. The existence of flow separation, vortex and the small shifting of stagnating locations may accelerate the formation of IH.

In addition, high fluctuations (range of -22 Pa to 21Pa) and oscillations of instantaneous WSS were found around the proximal anastomotic joint. Low time-averaged WSS with elevated OSI was observed near the middle of anastomosis at the aorta wall and along the graft inner wall respectively, while high time-averaged WSS with low OSI was found at the toe and the heel as well as downstream of the toe. Both of these regions are correlated to early atherosclerotic lesion growth (Buchanan et al., 1999). Moreover, elevated time-

averaged WSSG, which corresponds to the elevated LDL permeability (Buchanan et al., 1999), was found near the anastomosis.

Among the three models studied, 45° backward facing model is the best as the vortex formed at the graft cross-sectional planes for the peak flow rate moved away from the wall when moving downstream and it had the smallest flow separation region along the graft inner wall at the same time. In addition, its variation range of time-averaged WSS together with segmental average of time-averaged WSSG was the lowest. The lowest composite SP_2 value further affirmed the superiority of 45° backward facing model.

In general, 45° backward facing model would provide the best graft patency rate among the three models. In addition, increasing the graft cross-sectional area may improve the graft patency rate by reducing the vortex size. This coincides with the simulation of proximal anastomosis under steady flow condition. All these findings would be useful in the study of the complete bypass model, which included the flow from aorta through the graft to the coronary artery and would be reported in Chapter 7.

CHAPTER 6

EXPERIMENTAL RESULTS AND DISCUSSION FOR PROXIMAL ANASTOMOSIS MODELS

In this chapter, discussions on the experimental results obtained for proximal anastomosis models are presented. The experimental results not only help in exploring the hemodynamics of proximal anastomosis, but also supply a validation basis for numerical simulation. It is well-known that computational fluid dynamics offers much more versatility and resolution than in-vitro or in-vivo methods, yet computations must be validated by careful comparison with experimental data. To facilitate the comparison, PIV experimental conditions are the same as those of numerical simulation described in Section 5.1 under both steady and pulsatile flow conditions. The experimental methodology was described earlier in Chapter 4.

6.1 Hemodynamics in Proximal Anastomosis Models for Steady Flow

The investigation on steady flow condition is to provide fundamental knowledge and understanding on some of the phenomenon that may occur under pulsatile flow conditions. Three models namely 45° forward facing, 90° and 45° backward facing proximal anastomosis models were studied separately and two parts of experiments were carried out. For the first part, Reynolds number of 100, 169 and 250 were selected for grafts as the representative of flow characteristics in the test model with different compliance at the exit of the aorta. In the second part, the inlet flow rate was fixed, while the flow rate in graft was different to mimic the resistance effect of graft.

6.1.1 Flow Characteristics

During PIV experiments, the particle images were captured with selected time between pulses and other parameters for PIV measurements as described in Section 4.2.3. Through cross-correlation, velocity vectors can be obtained. Detailed theory for PIV measurement can be found in Section 4.2. The following velocity maps were captured in the center plane of three models separately.

6.1.1.1 Basic Flow Characteristics of Different Reynolds Number at the Graft

Figures 6-1 (a), (b) and (c) show the velocity vectors at the center plane of 45° forward facing proximal anastomosis model for $Re_G=100$, 169 and 250 respectively.

When $Re_G = 100$, the main flow from aorta maintained its flow path upon reaching the joint at the heel, and only part of the flow was diverting into graft. Due to the relative high momentum, the diverted flow slightly overshot the curve of the heel and formed a low velocity region near the graft inner wall, which spanned almost one graft diameter in length as indicated by the small magnitude of velocity vector, which was short in length. Along the graft outer wall, the deviated main flow approached the curved surface, and then bifurcated into two streams, with the formation of a stagnation point at the toe. The deflected flow near the toe entered the graft at an angle larger than the grafting angle. The flow, however, aligned back to the graft axis at further downstream.

With the increase of Re_G , it can be observed that the deviated flow in graft had higher velocity as it had longer velocity vectors. The size of the low velocity region at the heel became smaller and the flow in graft skewed more towards the inner wall. It was also observed that the velocity vectors in graft had a better alignment with the graft axis with

higher Re_G . Similar phenomena can be found for 90° and 45° backward facing proximal anastomotic models.

(c)

Figure 6-1 Velocity vectors in the center plane of 45° forward facing proximal anastomosis model at (a) $Re_G=100$, (b) $Re_G=169$ and (c) $Re_G=250$

6.1.1.2 Effect of Anastomosis Angles on the Flow Characteristics when $Re_G=\text{constant}$

Different anastomotic angle is believed to be one of the parameters in generating distinct flow characteristics of anastomosis. Figures 6-2 (a), (b) and (c) show the velocity vectors at center planes of 45° forward facing, 90° and 45° backward facing proximal anastomosis models at graft Reynolds number of 100 respectively. It was observed that as the anastomotic angle increased from 45° through 90° to 135° (viz. 45° backward facing), the size of the low velocity region at the heel decreased along the inner wall. At a smaller anastomotic angle, the flow decelerated sharply upon the entrance into graft and accelerated thereafter. The deceleration and acceleration, at a larger anastomotic angle, were however not as dramatic as compared to the flow in a smaller anastomotic angle

model. It was also noticed that at smaller anastomotic angles, the flow upon entering the graft tended to follow more closely to the geometry of the graft at further downstream.

Based on the velocity vector distributions obtained from PIV experiments, the low velocity region was observed to occur at the heel. It was shown to experience low shear stress, which is an ideal site for thrombosis formation (Binns et al., 1989). The low velocity region will also be prone to fat deposition and result in the formation of IH at the joint, blocking the re-routed blood flow into the graft. Detailed results on the WSS will be presented in Section 6.1.2.

(a) 45° forward facing graft model

(b) 90° graft model

(c) 45° backward facing graft model

Figure 6-2 Velocity vectors at the center plane when $Re_G=100$ for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models

6.1.1.3 Effect of Graft Resistance on the Flow Characteristics at Constant Inlet Flow Rate Q_{inlet}

Figure 6-3 shows the velocity vectors at center plane of 45° forward facing anastomotic model with different resistance configurations by varying the valve opening. The preset inlet flow rate at the aorta was 0.3m³/hr and the resistance effect at the graft was simulated by 55%, 75%, 85% and 95% opening of the valve at the end of graft during PIV experiments. The larger the valve opening represented the larger graft flow rate and thus smaller graft resistance. Flow rate increased in graft as the opening of valve became bigger. From (a) to (d) of Figure 6-3, it was observed that the low velocity region at the heel of the anastomotic joint decreased in size with the increase of graft flow rate. It was also noticed that at larger graft flow rate, the flow in aorta skewed less towards the graft outer wall before entering the graft, and the flow aligned back to the graft axis at relative shorter downstream distance. The low velocity region was associated with low WSS and would be discussed in Section 6.1.2. The same trend can also be found for 90° and 45° backward facing anastomotic models as illustrated in Appendix D.

(b) 75% valve opening

(c) 85% valve opening

Figure 6-3 Velocity vectors of 45° forward facing proximal anastomosis model with different resistance configurations: (a) 55%, (b) 75%, (c) 85% and (d) 95% of valve opening

6.1.2 WSS Distribution

This study stems from an interest in the role of WSS with initiation and progression of vascular diseases such as atherosclerosis, thrombosis and IH.

Figures 6-4 and 6-5 show WSS distributions derived from measured velocity vectors along the inner and outer walls of 45° forward facing, 90° and 45° backward facing graft models respectively. The ratio of X/D_G is used to represent the spatial location of the WSS calculated, where D_G is graft diameter (6mm). The annotation, X_1 and X_2 are the points selected approximately at the end of the straight aortic wall and are going along the direction of graft inner and outer walls respectively.

From Figure 6-4 (a), it was observed that along the inner wall, WSS increased until reaching its peak at $X_1/D_G=0.0$ of 45° forward facing proximal anastomosis model. Then

it began to decrease, which corresponded to the low velocity region. When the flow passed over this region ($0.0 \leq X_1/D_G \leq 1.25$), the velocity near inner wall increased quickly because the fluid skewed to graft outer wall restored to the original velocity direction and flowed along graft inner wall, which was shown by increasing WSS. As shown in the figure, the curve with higher percentage value was the one having lower graft resistance and higher graft flow rate. From the figure it can be seen that the WSS distribution patterns for different graft resistance were similar. However, the lower graft resistance, which represented higher graft flow rate, resulted in higher WSS values. In addition, the influence of graft resistance to the WSS within the aorta part along the inner wall ($X_1/D_G \leq 0.0$) was less than that of the downstream part ($X_1/D_G \geq 0.0$). The reason was that the flow rate of graft was much smaller than that of aorta. The changes of flow rate in graft had little influence at its upstream than downstream.

Similar WSS distributions along the inner wall can be found in Figures 6-4 (b) and (c) for 90° and 45° backward facing graft models respectively. The WSS increased initially in the aorta wall region and reached its peak, after that it decreased along the graft inner wall to be consistent with the low velocity region observed from velocity vectors. Finally, the WSS increased as the velocity downstream had higher values near the wall. Meanwhile the spatial distance for low WSS region reduced with the increase of grafting angle. Because the low shear stress was believed to be an ideal site for thrombosis formation (Binns et al., 1989), 45° backward facing graft models would result in better graft patency rate for its smallest low WSS region along graft inner wall. As an example, the region with WSS lower than 0.4Pa along the graft inner wall was $1.71D_G$ ($0.63 \leq X_1/D_G \leq 2.34$), $1.34D_G$ ($0.44 \leq X_1/D_G \leq 1.78$) and $0.92D_G$ ($0.58 \leq X_1/D_G \leq 1.50$) for 45° forward facing, 90°

and 45° backward facing proximal anastomosis models respectively, when the valve opening was 55%.

Figure 6-5 (a) shows WSS distribution along the outer wall of 45° forward facing graft model. The WSS magnitude (absolute value) increased along the X_2 direction and reached its maximum near $X_2/D_G=0.0$. Then it began to decrease and reached zero value at $X_2/D_G=0.5$, where the WSS changed sign and continued to increase. As shown in the figure, lower graft resistance, which represented higher graft flow rate, resulted in higher WSS values to some degree, although the trend of WSS distributions for different graft resistance was similar. In addition, it can be observed that the influence of graft resistance on the WSS within aorta part along graft outer wall ($X_2/D_G \leq 0.0$) was less than that of downstream part ($X_2/D_G \geq 0.0$). The reason was that the flow rate of graft was much smaller than that of aorta. The changes of flow rate in graft had little influence for aorta downstream. Furthermore, zero WSS point represented the stagnation point. From Figure 6-5 (a), it can be observed that the stagnation point was fixed in location regardless of graft resistance, which may induce the aggregation of red blood cells. Similar WSS distribution trend along graft outer wall can be found at Figures 6-5 (b) and (c) for 90° and 45° backward facing graft models respectively.

In general, graft resistance had some influence on WSS magnitude. Lower graft resistance resulted in higher WSS due to higher flow rate in graft. In addition, anastomosis angle was also observed to influence the WSS distributions along graft inner and outer walls. Among them, 45° backward facing graft model would be the best due to its smallest low WSS region at the heel. All these findings were in line with the observations from numerical simulation.

Figure 6-4 WSS distributions along the inner wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models under different graft resistance

Figure 6-5 WSS distributions along the outer wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models under different graft resistance

6.1.3 Comparisons with Numerical Simulation Results

As described in the literature review, the comparison of numerical results with experimental data has either not been conducted or been conducted in a simplified model using a flow visualization method (Steinman et al., 1993; Hofer et al., 1996; Cole et al., 2002c) or LDA measurements (Lei et al., 2001 and Bertolotti et al., 2001). Although PIV method was recently implemented for hemodynamics investigation (Bates et al., 2001; Heise et al., 2004) due to its high temporal resolution, the comparison between numerical simulation results and PIV measurements has not been performed until now. Therefore, in this study, comparisons between the numerical results and PIV measurements in proximal anastomoses were carried out to verify the validity of numerical simulation.

6.1.3.1 Comparisons of Velocity Distributions

Figure 6-6 shows the experimental velocity profiles at center plane in contrast to numerical simulation results at three locations (viz. AA, BB and CC) within the graft of 45° forward facing proximal anastomosis model under different resistance configurations. A fair match between numerical and experimental data can be found in Figure 6-6 (a), and in general the following phenomena were observed both in simulation and experimental results.

At location AA, the velocity skewed towards the graft outer wall and higher velocity can be found near the graft outer wall. Low velocity was found near the graft inner wall as fluid there was within the low velocity region. When fluid moved from location AA to BB and further downstream to location CC, the peak of velocity profile moved from graft outer wall to the center of graft, and the velocity near the graft inner wall increased gradually at the same time.

The same velocity profile patterns can be found for the simulation and experimental results, although the experimental profiles slightly overshoot the velocity of simulation results near the wall and had relatively lower peak value at the locations of AA, BB and CC. This agrees with the observations of Fatemi and Rittgers (1994) that the experimental velocities always overestimated the theoretical values for near-wall measurements because of wall reflection. In addition, Walsh et al. (2003) also found that the maximum velocity of the experimental profiles was smaller than the corresponding data for the numerical results when investigating the hemodynamics of distal anastomosis by means of LDA measurements.

In general, the overall comparison of PIV measurements and numerical simulation was quite convincing for the velocity profiles. Despite mean error between the numerical and experimental data ranged from 12 to 47 percent. Note that the error was defined as $\frac{f_N - f_E}{f_E} \times 100\%$, where f_N and f_E represented the data for numerical simulation and PIV experiment respectively. This error was acceptable as Lei et al. (2001) and Bertolotti et al. (2001) also reported the error ranged from 1 to 40 percent by means of LDA measurements. Therefore PIV measurement was capable to provide the same order of accuracy as LDA measurements and could validate the simulation results, although numerical simulation with enough mesh density was capable of providing more convincing results. The discrepancy between the simulation and experimental results could be due to the disturbance of background noise, wall reflection and the accuracy of positioning the measuring plane in the PIV techniques as well as the accuracy of the flowmeter.

Same conclusion can be made for the PIV measurements of 90° and 45° backward facing proximal anastomosis models as shown in Figures 6-7 and 6-8 respectively.

Figure 6-6 Comparison of velocity profiles between simulation and experimental results at three locations for 45° forward facing proximal anastomosis model under different resistance configuration: (a) 55% valve opening; (b) 75% valve opening; (c) 85% valve opening and (d) 95% valve opening

Figure 6-7 Comparison of velocity profiles between simulation and experimental results at three locations for 90° proximal anastomosis model under different resistance configuration: (a) 55% valve opening; (b) 75% valve opening; (c) 85% valve opening and (d) 95% valve opening

Figure 6-8 Comparison of velocity profiles between simulation and experimental results at three locations for 45° backward facing proximal anastomosis model under different resistance configuration: (a) 55% valve opening; (b) 75% valve opening; (c) 85% valve opening and (d) 95% valve opening

6.1.3.2 Comparisons of WSS Distributions

Figures 6-9 and 6-10 show the comparisons between numerical and experimental WSS distributions along graft inner and outer walls of 45° forward, 90° and 45° backward facing proximal anastomoses respectively.

From Figure 6-9, it can be observed that the WSS distribution patterns derived from numerical simulation have the similar trend with those of PIV experiments, although the WSS values obtained from measurements generally were a little higher than those of simulation, which may be due to the over-estimated near wall velocity. The experimental WSS values within low velocity region were nevertheless smaller than the simulation results for 90° and 45° backward facing proximal anastomoses. The reason was that some particles might accumulate in the low velocity region once there was imperfection in producing smooth surface, which will induce the error into velocity measurements and subsequently the WSS calculation. In addition, the experimental low WSS region for 45° forward facing proximal anastomosis shifted a little from that of simulation on account of slightly difference of inner wall curvature for experimental and simulation models. The manufacture of glass tube may induce small divergence at the connection region. In general, the WSS distribution patterns of numerical simulation along graft inner wall were quite similar with those of PIV measurements as can be found in the 90° and 45° backward facing models as shown in Figures 6-9 (b) and (c) respectively.

Same conclusion can be made for WSS distributions along graft outer walls of three models. Both numerical and experimental results revealed fixed stagnation point along graft outer wall, where WSS changed sign. The simulated WSS distribution for 45° backward facing proximal anastomosis was much close to those of PIV measurements,

while larger discrepancy can be found for 45° forward facing proximal anastomosis model. This may be due to the slight difference of wall curvatures for experimental and simulation models. The manufacture of glass tube may induce tiny waviness for the connection part. In addition, the small WSS apex at the downstream of graft outer wall observed in simulation results of 90° proximal anastomosis model was not found in the measurement results. As velocity there changed greatly both in direction and magnitude, the 0.25mm experimental spatial resolution may not be fine enough to capture the small variations of WSS distribution, especially in the region with greater curvature changes. Whereas numerical simulation may provide more reliable results as the nearest distance of grids to the wall was within 0.1mm and more meshes were put near the wall to capture the small variations of WSS. In general, the WSS distribution patterns of numerical simulation along graft outer walls were in agreement with those of PIV experiments, especially for 90° and 45° backward facing proximal anastomosis models.

To sum up, PIV measurements provided a fair validation of the hemodynamics in proximal anastomosis. Meanwhile numerical simulation could provide the much detailed information in line with those of PIV experiments. The average errors between numerical and experimental data were 33.2%, 27.8% and 27.1% for 45° forward, 90° and 45° backward facing proximal anastomosis models respectively.

Figure 6-9 Comparison of simulation and experimental WSS distributions along the inner wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models under different graft resistance

Figure 6-10 Comparison of simulation and experimental WSS distributions along the outer wall for (a) 45° forward facing (b) 90° and (c) 45° backward facing graft models under different graft resistance

6.2 Hemodynamics in Proximal Anastomosis Models for Pulsatile Flow

6.2.1 Flow Characteristics

PIV measurements were also carried out to investigate pulsatile flow characteristics of proximal anastomoses and validate the numerical simulation results. As the manufactured 45° forward facing proximal anastomosis model had the wall curvature slightly different from that of numerical simulation, only 90° and 45° backward facing proximal anastomosis models were measured under pulsatile flow condition by means of PIV. Figure 6-11 shows five indicated time intervals within a cycle at which measured velocity maps and computed WSS distributions were presented as follows.

Figure 6-11 Location of time intervals selected for presenting the experimental results

Figures 6-12 and 6-13 show measured velocity vector maps for 90° and 45° backward facing proximal anastomosis models at different phases respectively. At $t_a=1.35s$ as observed in Figure 6-12 (a), main flow from the aorta maintained its flow path upon reaching the heel; only part of flow diverted into graft. Along graft outer wall, deviated main flow approached the curved surface, and then bifurcated into two streams with the

formation of a stagnation point at the toe. The velocity magnitude was generally small as the inlet flow just began to accelerate. At peak flow rate ($t_b=1.6s$), a flow separation region was observed along graft inner wall as shown in Figure 6-12 (b). This was similar to flow structures of numerical simulation as shown in Appendix C. Since flow dynamics at deceleration phases were more diverse than other time intervals, more results were presented for deceleration phases. When flow just began to decelerate, at $t_c=1.7s$ as shown in Figure 6-12 (c), the flow separation region near the inner wall evolved into a vortex with the center moved close the graft center. At the late deceleration phase ($t_d=1.85s$), two vortexes were observed at aorta upstream near the heel and downstream near the toe separately. The fluid in graft flowed back into the aorta as shown in Figure 6-12 (d). This was in agreement with numerical simulation results except that the vortex at aorta downstream observed in PIV measurements had smaller region than those of numerical simulation. For $t_e=2.4s$ as demonstrated in Figure 6-12 (e), backflow in graft disappeared, fluid thus moved towards the downstream of the aorta when some fluids were channeled into graft with small velocity magnitude.

Similar flow characteristics at the center plane can be found for 45° backward facing graft model as illustrated in Figure 6-13. Comparisons between PIV measurements (Figures 6-12 and 6-13) and numerical results (in Appendix C) showed reasonably fair agreement. Further detailed comparisons of velocity profiles were demonstrated in Section 6.2.3.1.

(a) Time (t_a) at 1.35s

(b) Time (t_b) at 1.6s

(c) Time (t_c) at 1.7s

(d) Time (t_d) at 1.85s

Figure 6-12 Measured velocity vectors at center plane of 90° proximal anastomosis model at different phases: (a) $t_a=1.35s$; (b) $t_b=1.6s$; (c) $t_c=1.7s$; (d) $t_d=1.85s$; (e) $t_e=2.4s$

(b) Time (t_b) at 1.6s

(c) Time (t_c) at 1.7s

(d) Time (t_d) at 1.85s

(e) Time (t_e) at 2.4s

Figure 6-13 Measured velocity vectors at center plane of 45° backward facing proximal anastomosis model at different phases: (a) $t_a=1.35s$; (b) $t_b=1.6s$; (c) $t_c=1.7s$; (d) $t_d=1.85s$; (e) $t_e=2.4s$

6.2.2 WSS Distributions

Figures 6-14 and 6-15 show experimental WSS distributions at different time intervals along graft inner and outer walls of two models respectively. Normalized axial distance, X/D_G represents the spatial location of WSS computed. The annotation, X_1 and X_2 are the points selected approximately at the end of straight aortic wall and are going along the direction of graft inner and outer walls respectively.

Along the inner wall of 90° proximal anastomotic joint as shown in Figure 6-14 (a), at $t_a=1.35s$, the WSS increased when accessing the heel, then it decreased once entering the low velocity region ($0.37 \leq X_1/D_G \leq 1.5$). When inlet flow rate increased to peak from t_a to t_b , the WSS level reached its maximum to 14Pa. Corresponding to the flow separation region formed near the heel at $t_b=1.6s$, WSS kept negative in the region ($0.57 \leq X_1/D_G \leq 0.82$). When flow just began to decelerate at $t_c=1.7s$, the flow characteristics and WSS distributions had the similar pattern as those of peak flow. However, the maximum WSS decreased to 8Pa and the flow separation region near the heel was increased in size ($0.34 \leq X_1/D_G \leq 1.38$). At $t_d=1.85s$, WSS was all negative along the inner wall on account of the backflow in graft and the vortex formed upstream of the aorta. The WSS came back to positive when $t_e=2.4s$. At that time, WSS varied slightly along the inner wall but maintained positive value. Similar trend can be found for 45° backward facing proximal anastomotic joint as shown in Figure 6-14 (b).

Along the outer wall of 90° proximal anastomosis, in the accelerating stage ($t_a=1.35s$) the WSS, as shown in Figure 6-15 (a), varied from -0.5Pa to 1Pa and changed sign at stagnation point ($X_2/D_G=0.72$). At peak flow phase ($t_b=1.6s$), the WSS magnitude level also attained its maximum of 8.8Pa at $X_2/D_G=1.4$ as shown in Figure 6-15 (a). When flow

just began to decelerate ($t_c=1.7s$), the WSS maintained the same pattern as that of peak flow. However the stagnation point moved upward a little towards the aorta. At late deceleration phase ($t_d=1.85s$), because of the vortex formed at the downstream of aorta, WSS became positive at the beginning of X_2 . Then it changed to negative downstream, which was different from those of early time intervals in virtue of flow reverses from graft back to the aorta. At $t_e=2.4s$, the variations of WSS were similar to those of $t_a=1.35s$.

Same trend of WSS distributions can be found for 45° backward facing proximal anastomosis model as shown in Figure 6-15 (b). They showed reasonably fair agreement with those observed in numerical simulation. Detailed comparisons of experimental and numerical WSS distributions will be presented in Section 6.2.3.2.

Figure 6-14 Experimental WSS distributions along the inner wall for (a) 90° and (b) 45° backward facing anastomotic models at different time intervals

Figure 6-15 Experimental WSS distributions along the outer wall for (a) 90° and (b) 45° backward facing anastomotic models at different time intervals

6.2.3 Comparisons with Numerical Simulation Results

Numerical simulation results for proximal anastomosis models under pulsatile flow condition were validated against PIV experimental data in the same way as that of steady flow. Both velocity profiles and WSS distributions were compared and validated.

6.2.3.1 Comparisons of Velocity Distributions

Shown in Figure 6-16 are experimental and simulated velocity profiles at two locations (viz. AA and BB) within the graft of 90° proximal anastomosis model at different time phase. A basically similar trend can be observed between numerical and experimental results, although differences can be found. For example, at $t_b=1.6s$, as demonstrated in Figure 6-16 (b), the experimental and simulated velocity near the inner wall at BB location had different signs there. The reason was that the flow separation region observed in PIV experiment (as illustrated in Figure 6-12 (b)) was smaller in size than that of numerical simulation shown in Figure C-1 (b) in Appendix C. Due to the same reason, the experimental WSS along the inner wall changed sign from negative to positive earlier than that of simulation at peak flow phase as shown in Figure 6-18 (a) on page 242. In addition, the experimental velocity near the outer wall of location AA at $t_d=1.85s$, as demonstrated in Figure 6-16 (d), had different sign with that of numerical simulation on account of smaller vortex size observed in PIV experiment at the aorta downstream. In like manner, experimental WSS changed sign from positive to negative earlier than that of simulation at $t_d=1.85s$ as observed in Figure 6-19 (a) on page 243. To sum up, the simulated velocity profiles were in agreement with that of PIV experiment qualitatively; the overall difference of 9-46% was observed. In addition, the error range between numerical and experimental data maintained similarity for different time phases. This was different from the study of Lei et al. (2001), who observed that the relative error between numerical and LDA experimental data was smaller (typically around 1-8 percent) during the forward flow phases and much larger (ranged from 1-40 percent) during the reverse flow phase. The discrepancy may be due to the different measuring instrument used. In PIV measurement, it was capable to capture the whole flow field instantaneously, while for LDA measurement, the measured data of a location was the average value of several

cycles at the same location, which rely heavily on the repeatability of test rig and measuring instrumentation.

Similar comparisons of measured and numerical velocity profiles of 45° backward facing proximal anastomosis model were shown in Figure 6-17. Some discrepancies can be observed although the shapes of the velocity profiles were qualitatively similar for both the simulation and experimental results. At $t_b=1.6s$, the experimental velocity near the inner and outer walls of location AA were different from those of simulation. The larger flow separation region observed in PIV experiment (referring to Figure 6-13 (b)) resulted in positive velocity at the inner wall and the stagnation point had also been shifted further downstream along the outer wall as demonstrated by the positive velocity there. Because of the same reason, the experimental WSS changed sign earlier from positive to negative along inner wall as shown in Figure 6-18 (b), while delayed the changing of sign from negative to positive along graft outer wall as seen in Figure 6-19 (d). Similarly as the vortex observed in the graft of PIV experiment occupied larger size than that of numerical simulation, the experimental velocity near graft inner wall at location BB when $t_c=1.7s$ was still positive whereas simulated velocity was negative as demonstrated in Figure 6-17(c). In addition, the measured velocity near the outer wall of location AA at $t_d=1.85s$ as shown in Figure 6-17 (d) had different sign with that of numerical simulation on account of smaller vortex size observed in PIV experiment at the aorta downstream. The difference of the velocity near the outer wall of location AA at $t_e=2.4s$ due to the movement of stagnation point. The experimental stagnation point moved upstream along the outer wall, which can be observed in Figure 6-19 (c). In general, the simulated velocity profiles were qualitatively similar with those of PIV experiment, although at

some specific locations the difference of 8-55% could be observed. The error range between numerical and experimental data maintained similarity for different time phases.

In some cases, experimental profiles slightly overshoot the numerical velocity results near the wall. This agrees with the observations under steady flow condition and those of Fatemi and Rittgers (1994) because of wall reflection, although glaring effect at the near wall was minimized by immersing the test section into a transparent rectangular tank filled with the same working fluid. The overall agreement of PIV measurements and numerical simulation was quite fair for the velocity profiles. The discrepancy between the simulation and experimental results could be due to the slight differences in geometry between the experimental and numerical models especially at the anastomosis, disturbance of background noise, wall reflection and the accuracy of positioning the measuring plane in the PIV techniques as well as the accuracy of cam system used to mimic the pulsatile inlet flow.

Figure 6-16 Comparison of velocity profiles between simulation and experimental results at two locations for 90° proximal anastomosis model at different phases: (a) $t_a=1.35s$; (b) $t_b=1.6s$; (c) $t_c=1.7s$; (d) $t_d=1.85s$; (e) $t_e=2.4s$

Figure 6-17 Comparison of velocity profiles between simulation and experimental results at two locations for 45° backward facing proximal anastomosis model at different phases: (a) $t_a=1.35s$; (b) $t_b=1.6s$; (c) $t_c=1.7s$; (d) $t_d=1.85s$; (e) $t_e=2.4s$

6.2.3.2 Comparisons of WSS Distributions

Figures 6-18 and 6-19 show the comparisons between numerical and experimental WSS distributions along graft inner and outer walls of 90° and 45° backward facing proximal anastomoses respectively. Similar trend can be observed between the simulation and experimental results.

From Figure 6-18, it can be observed that the WSS distribution patterns derived from numerical simulation have shown similar trend with those of PIV experiments, although differences in magnitude still existed. Same conclusion can be made for the WSS distribution along graft outer walls as seen in Figure 6-19. However shifting of stagnation point can be found at $t_c=1.7s$ and $t_d=1.85s$, this was due to the different size of vortex formed near graft inner wall and aorta downstream respectively. In addition, most

experimental WSS along graft outer wall was observed to be smaller than those of numerical simulation. As the velocity along outer wall varied tremendously both in direction and magnitude, the 0.25mm spatial resolution of PIV experiments may not be fine enough to capture the small variation of WSS distribution, especially in the region with curvature changes. Whereas numerical simulation may provide more reliable results as the nearest distance of grids to the wall was within 0.1mm and more meshes were put near the wall to capture the small variations of WSS distribution.

To sum up, the WSS distributions of PIV measurement and numerical simulation were quite similar, although discrepancies can be found quantitatively. Along the graft inner wall, the difference between the numerical and experimental WSS was within 0.5Pa for the acceleration phases ($t_a=1.35s$ and $t_c=2.4s$). Around the peak flow rate ($t_b=1.6s$ and $t_c=1.7s$), the difference became much larger, and the largest difference even could reach 5Pa. While for the deceleration phase ($t_d=1.85s$), the difference was also larger than the acceleration phase due to its relatively complex flow phenomena. Similar conclusions can be made for the numerical and experimental WSS distributions along the graft outer wall.

Figure 6-18 Comparison of simulation and experimental WSS distributions along the inner wall for (a) 90° and (b) 45° backward facing graft models at different phases

(a)

(b)

(c)

Figure 6-19 Comparison of simulation and experimental WSS distributions along the outer wall for (a)&(b) 90° and (c)&(d) 45° backward facing graft models at different time phases

6.3 A Summary for This Chapter

PIV measurements provided a very good physical insight into the hemodynamics of proximal anastomoses under both steady and pulsatile flow conditions. Meanwhile the numerical simulation results were validated against experimental data. A fair match between numerical and experimental data was observed for both velocity vectors and WSS distributions. The overall difference between them ranged from 8 to 54 percent, which was acceptable as Lei et al. (2001) and Bertolotti et al. (2001) also reported the error ranged from 1 to 40 percent by means of LDA measurements. In addition, the error range maintained similarity for different time phases. This was different from the study of Lei et al. (2001), who observed that the relative error between numerical and LDA experimental data was smaller (typically around 1-8 percent) during the forward flow phases and much larger (ranged from 1-40 percent) during the reverse flow phase. The discrepancy may be due to the different measuring instrument used. In PIV measurement, it was capable to capture the transient overall flow field, while for LDA measurement, the

measured data at a location was the average value of several cycles of the same location, which relied heavily on the repeatability of experiment. Therefore PIV measurement was capable to provide quantities as accurate as LDA measurements and numerical simulation could also provide validated information with enough mesh density. The discrepancy between the simulation and experimental results could be due to the slight differences in geometry between the experimental and numerical models especially at the anastomosis, disturbance of background noise, wall reflection and the accuracy of positioning the measuring plane in the PIV techniques as well as the accuracy of flowmeter and cam mechanism used to mimic the pulsatile flow.

CHAPTER 7

SIMULATION RESULTS AND DISCUSSION FOR WHOLE ANASTOMOSIS MODEL

As stated in literature review, earlier studies only reported on subsections of the bypass, especially on distal (end-to-side) anastomosis, except Lee et al. (2001) and Cole et al. (2002b). However Lee et al. (2001) claimed that with a complete bypass, the velocity distribution in the bypass graft was obviously different from that in a simple end-to-side anastomosis and the complete flow fields could consequently be different. In this chapter, numerical simulation results obtained for whole anastomosis model are presented and discussed. Finding out the details of hemodynamics at whole anastomosis are necessary for providing a better insight into the patency rate of CABG, which has source and host arteries different from what Lee et al. (2001) have mimicked. The areas of interest include both steady and pulsatile flows. The purpose of conducting investigation on the steady state condition is to provide fundamental knowledge and understanding on some of the phenomenon that may occur if the anastomosis model is subjected to pulsatile flow condition.

7.1 Brief Introduction of Simulation Conditions

The simulation method and sequence were carried out as described in Chapter 3. Additional and detailed information about simulation condition for the whole anastomosis model were given in this section.

7.1.1 Physical Model for Mimicking CABG

The physical model used in numerical simulation was designed to mimic the complete anastomosis during a CABG operation according to the medical data provided by the National Heart Centre of Singapore. The diameters (and the lengths) of aorta, graft and coronary artery were 25mm, 4mm and 2mm (120mm, 118.7mm and 45mm) respectively. Since the right coronary artery (RCA) bypass graft had higher potential for stenosis and the typical location and course of saphenous vein for RCA bypass graft surgery shown in Figure 7-1 (Galjee et al., 1996) can be assumed approximately in the same plane, the representative model was designed as demonstrated in Figure 7-2. The blood flow into the aorta (Q_1), and then some of them flow through the graft to enrich the coronary artery. As the proximal end of coronary artery usually was occluded within a month after surgery, to investigate the patency rate in a longer time, the proximal end of coronary artery was assumed to be fully occluded ($Q_3=0$).

Figure 7-1
Schematic view of CABG
(taken from Galjee et al., 1996)

Figure 7-2
The designed model
for mimicking CABG

7.1.2 Building Meshes and Mesh Independency Tests

To optimize the computational time and memory, only one symmetric half of model was built and meshed. With the compromise of set-up time, computational cost and numerical accuracy, the proximal anastomosis was divided into three parts, hexahedral elements were used for the front and rear parts of aorta, while tetrahedral cells were used in the joint and other parts including graft and coronary artery as shown in Figure 7-3. Note that the model was slightly rotated for better illustration. A total of 72,537 nodes and 224,208 elements were used for each model. Mesh density near the wall was larger than elsewhere to get more accurate WSS. Present grid density was found to be sufficient after successively mesh independency tests as shown in Figures 7-4 and 7-5.

A sequence of solution procedure with finer and coarser meshes were used to check if the solution converges, as the meshes get finer. Convergence towards some fixed values provides some confidences about the solution obtained. Figure 7-4 shows the velocity profiles along three different locations (A, B and C) at the symmetry plane of the whole anastomosis model under steady flow condition. It can be observed that present grid density (72,537 nodes with 224,208 elements) was found to be sufficient after successively refining the grid from one containing about 54,223 nodes with 161,711 elements. Further refinement to meshes with 101,552 nodes and 336,312 elements did not produce any significant change in velocity distribution with the maximum difference of 0.2%.

Figure 7-3 Grids for whole anastomosis model

Figure 7-4 Grid independency test (a) three locations A, B and C at symmetry plane and velocity profiles at locations (b) A, (c) B and (d) C for different grid sizes

Furthermore, GCI of complete anastomosis model was investigated. The labels to represent the three mesh schemes were tabulated in Table 7-1. GCI for x -velocity along line E (as shown in Figure 7-5(a)) on the symmetry plane was shown in Figure 7-5(b). In this case, p equals to 2, D equals to 3. GCI_{12} and GCI_{23} represent the grid convergence index calculated from grids 1 to 2 and 2 to 3 respectively. As both GCI_{12} and GCI_{23} were the same order of magnitude, suggesting near asymptotic behavior of the solution with increasing refinement of the grid. In addition, the maximum of GCI_{23} was already less than 12%, which was within the acceptance for engineering calculation. Thus meshes 2 (72,537 nodes, 224,208 elements) was selected due to its higher credibility and less computational cost.

Table 7-1 Different meshes for complete anastomosis model

Label for different meshes	Number of nodes	Number of elements
3	54,223	161,711
2	72,537	224,208
1	101,552	336,312

Figure 7-5 (a) Location E at symmetry plane (b) calculated GCIs at location E for x -velocity

7.1.3 Boundary Conditions

Boundary conditions including the no-slip wall condition were selected in a manner to match physiological conditions as closely as possible with the available data and facilitate numerical computations.

7.1.3.1 Pulsatile Flow

To generate the time varying inlet velocity profiles, a transient Womersley solution was implemented. Flow rate information over variable time-steps was used to compute a complex Fourier series approximation of the pressure gradient pulse. The transient velocity profiles were then computed using Womersley solution for Newtonian fluid flow. The widely accepted aortic blood flow waveform (Ganong, 1973) as shown in Figure 7-6 was used as inlet flow waveform. The phase of the cardiac cycle identified by the numbers at the bottom were as follows: 1, aortic systole; 2, isovolumetric ventricular contraction; 3, ventricular ejection; 4, isovolumetric ventricular relaxation; 5, ventricular filling. Note that this waveform was slightly different from those used for numerical simulation and experiments of proximal anastomosis models because previous experimental investigation was limited by the cam mechanism used to produce the pulsatile flow. Also indicated in the figure were time intervals for presenting flow field. The ordinate represented the ratio between transient mean inlet velocity and the maximum mean inlet velocity. Mowat et al. (1983) investigated the peak velocity values of aorta for adults and found that it was related with ages. People aged 30, 40, 50 years old had the peak velocity of 1 m/s, 0.95 m/s and 0.85m/s respectively. As CABG usually conducted for the elderly more than 50 years old, 0.85m/s was selected as the peak velocity. Thus the flow waveform was characterized by a peak Reynolds number of 5495, a mean Reynolds number of 1054, and a Womersley number of 17.8 based on the diameter of aorta.

Figure 7-6 Inlet flow waveform

Although some researchers investigated the flow in graft after CABG surgery, the flow waveforms published were quite different (Galjee et al., 1996; Kajiya et al., 1987; Moran et al., 1971; Lu et al., 2001). However most of the reported flow rate values of graft were quite similar. Mortan et al. (1971) reported flow was greater in left-side grafts, $73 \pm 23 \text{ ml/min}$, than on the right one, $53 \pm 25 \text{ ml/min}$ through in-vivo investigation of 31 grafts in 21 patients. Galjee et al. (1996) observed the flow volume $63 \pm 41 \text{ ml/min}$ for single graft by means of magnetic resonance (MR) spin-echo (SE) and cine gradient-echo (GE) techniques for forty-seven patients with previous histories of coronary artery saphenous vein grafting, while Eckstein et al. (2002) measured $50 \pm 27 \text{ ml/min}$ for single-vein graft through intraoperative flow rate measurement for 43 patients. In addition, Lu et al. (2001) even observed that a patent bypass graft had a flow curve morphologically similar to that of the aorta by means of electron beam tomography (EBT) investigation for 589 CABGs undergone 3 month to more than 5 years ago. Therefore the graft was assumed to have the flow rate of 50 ml/min and the outlets of coronary artery and aorta were assumed to be fully developed with flow rate ratios of $Q_4/Q_1 = 1.04\%$ and $Q_2/Q_1 = 98.96\%$ within the cycle respectively (see Figure 7-2). In addition, times step of 0.01 s was selected as the preferential time step after trials of 0.005 s , 0.01 s , 0.04 s and

adaptive time step sizes. Meanwhile the lengths of aorta and coronary artery outlets had been checked to fulfill the condition of fully developed flow.

7.1.3.2 Steady Flow

As the purpose of conducting investigation on steady state condition was to provide fundamental knowledge and understanding on some of the phenomenon that may occur if the anastomosis model was subject to pulsatile flow, the inlet flow velocity profile was assumed parabola with mean velocity of 0.28m/s under steady flow condition, which corresponds to $Re=1810$ of aorta. In addition, the outlets of coronary artery and aorta were assumed to be fully developed with flow rate ratios of $Q_4/Q_1=1.04\%$ and $Q_2/Q_1=98.96\%$ respectively.

7.2 Hemodynamics in Whole Anastomosis Model for Steady Flow

Since abnormal hemodynamic events often labeled “disturbed flow” play important roles in the regulation of vascular biology and the localization of atherosclerosis, computational simulations were carried out to determine hemodynamic factors which encapsulate disturbed flow and identify local sites in the CABG system which are susceptible to the onset of atherosclerotic lesions.

7.2.1 Flow Characteristics

Figure 7-7 shows the streamlines in the symmetry plane of the whole anastomosis model. For better illustration, the model is rotated. As observed by Lee et al. (2001), the entrance and the exit junctions (proximal and distal anastomoses) of the bypass graft were the two critical locations, where the flows were complicated, and were therefore more vulnerable to plaques. To study the flow characteristics in detail, the velocity vectors in proximal

anastomosis, graft and distal anastomosis were illustrated in Figures 7-8 and 7-9 respectively.

Figure 7-7 Streamlines in the symmetry plane

Figures 7-8 (a) and (b) show the velocity vectors and streamlines in the symmetry plane of proximal anastomosis and graft respectively. When blood flow through the aorta, the deviated main flow approached the curved wall surface at the toe of proximal anastomosis and bifurcated into two streams, which resulted in a stagnation point at the toe and low velocity region near the heel. The flow in the graft was generally parallel to the graft axis, and approximately parabola in shape with the peak flow skewed slightly towards the outer wall.

Figure 7-8 Velocity vectors and streamlines at (a) proximal anastomosis and (b) graft

Figure 7-9 shows the velocity vectors at the symmetry plane of distal anastomosis. The velocity at the entrance of coronary artery skewed toward the toe and demonstrated a strong downwash toward the bed of coronary artery as observed by Lee et al. (2001). The fluid next to the occlusion was almost kept stationary; nevertheless, a weak recirculation existed. The flow pattern obtained near the heel was agreeable to that observed by Ojha et al. (1990, e.g. their Figure 2). Similar flow fields such as the “skewed velocity profile” can also be found in the coronary artery (distal end) for the present study. In addition, a stagnation point can be found on the bed of coronary artery. Well-structured secondary flow pattern was formed and persisted throughout the coronary artery as shown in Figure 7-10. It demonstrated that the flow patterns there were highly three-dimensional as observed by Hughes and How (1996). The boundary-layer separation and flow reversal observed at the toe in the 30° and 45° models of Hughes and How (1996) when Re was larger than 500, were not found in the present study with $Re_G=226$. Since stagnation point, vortex, low velocity regions supposed to correlate with IH (Hughes and How, 1996; Jones et al., 1997), the complex flow characteristics of distal anastomosis was more crucial than those at the proximal anastomosis in terms of graft patency rate.

Figure 7-9 Velocity vectors at symmetry plane of distal anastomosis

Figure 7-10 Velocity vectors and streamlines at locations AA (a) and BB (b) of distal anastomosis

7.2.2 WSS and WSSG Distribution

As low WSS (Rittgers et al., 1978; Binns et al., 1989), high or unidirectional WSS (Fry, 1969; Friedman et al., 1992) and WSSG (Lei et al., 1996; Ojha, 1993) were proposed to correlate with the development of IH at the suture joint, WSS and WSSG of whole anastomosis model were calculated and presented in this section.

Figures 7-11 (a) and (b) show the WSS distributions of whole anastomosis model and at proximal and distal anastomoses respectively. As seen from Figure 7-11 (a), WSS at proximal and distal anastomosis regions was relatively higher than other parts. Although higher WSS was also found in the toe and heel of proximal anastomosis than its surrounding observed at upper right corner of Figure 7-11 (a), the WSS values there were much smaller than those of distal anastomosis. The peak WSS value of proximal anastomosis was 2.99Pa, while the maximum WSS for distal anastomosis was 21.8Pa. To demonstrate the WSS distribution at distal anastomosis in detail, the front view and top view of WSS in distal anastomosis were plotted in Figure 7-11 (b). From the figure, it can

be observed that the WSS at the toe was the highest than other regions; meanwhile the WSS along the coronary artery after the toe was also high. This was in line with the observations of Lee et al. (2001) at the distal anastomosis. The distinguished high WSS at the toe and its downstream of distal anastomosis together with the low WSS at its occlusion end may promote the development of IH and/or atherosclerotic lesions there. This may be the reason that abnormal, progressive thickening of the innermost layer of the artery wall were observed to occur predominantly at the distal anastomosis of a bypass system (Sottiurai et al., 1989).

Figure 7-11 WSS distributions along the whole anastomosis model (a) and its distal anastomosis part (b)

Figures 7-12 (a) and (b) show the WSSG distributions for the whole anastomosis model and its distal part respectively. As observed from Figure 7-12 (a), distinguished high WSSG was observed at the toe of distal anastomosis as was found by Lee et al. (2001). To further demonstrate the WSSG distribution at distal anastomosis, the front and top views of WSSG in distal anastomosis were demonstrated in Figure 7-12 (b). From the figure, it can be observed that the WSSG at the toe was the highest as compared with other regions. This was in line with the observations of Lee et al. (2001) at the distal anastomosis. The distinguished high WSSG at the toe may promote the development of IH and/or atherosclerotic lesions there. This may explain that IH and atherosclerosis was observed to occur more predominantly at the distal anastomosis of a bypass system than at the proximal anastomosis, although atherosclerotic lesions appeared most frequently in bends and junctions of medium to large arteries.

Figure 7-12 WSSG distributions for whole anastomosis model (a) and its distal anastomosis part (b)

7.2.3 Comparisons with Other Published Works

Figure 7-13 shows the WSS distribution obtained by Kute and Vorp (2001) when one end of distal anastomosis was occluded. Although high WSS was observed at the toe of distal anastomosis, a region of high WSS was also observed at the bed of their model, which was different from present results (Figure 7-11 (b)). These may be due to the enlarged junction area of present model, it hence reduced the severity of disturbed flow patterns, especially in the toe region and on the artery bed. Not only the improved flow field of present model will help in improving graft patency rate, the enlarged junction area of

distal anastomosis will provide less restriction to the flow due to the wider opening between graft and artery as concluded by Cole et al. (2002b).

Figure 7-13 WSS of distal anastomosis (Kute and Vorp, 2001)

Figure 7-14 WSS of distal anastomosis part (Chua et al., 2004)

Figure 7-14 shows the WSS distribution of distal anastomosis part for a whole anastomosis model with prominent bulge to simulate the situation when tightening force during the suturing process was too large. Besides the high WSS region observed in the toe and downstream of the coronary artery, a low WSS region was also found inside the bulge, where WSSG would be high. Although the junction area of distal anastomosis was also enlarged, the distinguished bulge aorta would bring problem in terms of graft patency rate.

In conclusion, the high WSS and WSSG found at the toe of distal anastomosis may lead to the graft stenosis. However, reducing the tightening force during the suturing process and having a longer arteriotomy on the coronary artery for the distal anastomosis may aid in enhancing the graft patency rate on account of improved flow field and reduced unfavorable WSS and WSSG regions. Meanwhile, the design of sleeve shall consider the HPs parameters. Increasing the cross-sectional area of anastomosis part, eliminating the graft bulges and smoothening wall curvatures may improve the graft patency rate by reducing the vortex size and reduced the abnormal HPs distributions.

7.3 Hemodynamics in Whole Anastomosis Model for Pulsatile Flow

7.3.1 Flow Characteristics

As “disturbed flow” was believed to trigger a cascade of abnormal biological process leading to intimal thickening and/or thrombi formation (Kleinstreuer et al., 2001), the flow patterns of whole anastomosis model under pulsatile flow condition were investigated carefully. To present them in detail, the flow characteristics of proximal, distal anastomoses and graft were described separately as follows.

7.3.1.1 Flow Characteristics of Proximal Anastomosis

The qualitative or visual indicators of “disturbed flow” are the velocity fields shown in Figure 7-15. The results shown here was after one cycle, but the time indicated was the time within a period ($T=0.8s$) for simplicity in presentation. As observed in Figure 7-15 (a), when flow just began to accelerate ($t_1=0.18s$), part of the main flow from aorta diverted into the graft. Once inlet flow reached its peak at ($t_2=0.24s$), flow separation was observed near the heel of proximal anastomosis as shown in Figure 7-15 (b). Secondary flow at sections AA, BB and CC was observed and amplified in the downstream direction. This was similar to the investigations of Buchanan et al. (1999) for rabbit aorto-celiac junction. From section AA to BB, the vortex observed near the wall was evolved into two vortices and moved close to the middle of graft. When the blood flowed further downstream to section CC, the vortex disappeared in the cross-section. Flow fields during deceleration ($t_3=0.40s$) showed that the flow separation moved further downstream and the secondary flows were typically amplified comparative to the velocity magnitude in symmetry plane due to a steep reduction in inertia. Specifically, secondary flows developed at section AA forming a vortex. This was in line with the simulation of

Buchanan et al. (2003) for renal branches at systolic deceleration phase. In addition, backflow was observed along the inner wall of proximal anastomosis due to the three-dimensional flow separation and flow recirculation at the aorta upstream.

With further deceleration, the flow separation began earlier in the heel region and moved upstream as shown in Figure 7-15 (d) at $t_4=0.41s$. The nodal point viewed as source in the streamlines was the attachment point of three dimensional flow separation (Filippone, 2004). Because of the decrease in inertia, some blood in the graft flowed back to the aorta along the inner wall, which reduced the effective flow rate in graft. Buchanan et al. (1999) also reported the annular effect induced in the aorta proximal to the junction at flow deceleration phase, which resulted in flow reversal along the entire dorsal wall of the aorta. At time level $t_5=0.44s$, the net flow rate was in the reverse direction dominated by the backflow along the inner wall of aorta, however the core of the inlet flow was still positive in the aorta. The reverse flow along the aorta inner wall and the positive core flow of the proximal aorta combined with the flow from graft formed a complex flow pattern at the junction region as shown in Figure 7-15 (e), which was also reported by Buchanan et al. (1999). At $t_6=0.47s$, the flow was accelerating again with a zero net flow rate. Although the flow velocity magnitude was quite small, the flow pattern found in $t_5=0.44s$ still could be observed at the region and evolved into more complicated flow especially at the toe region that a nodal point existed.

In contrast to the earlier investigations of 45° backward facing proximal anastomosis model as demonstrated in Appendix C, similar flow characteristics can be found in most time phases. The flow characteristics of both two models were similar to what had observed in the steady flow condition when the flow just began to accelerate. Flow

separation was found near the heel of the two models at peak flow rate and its size increased with the development of flow deceleration. Obvious difference can be observed after the late deceleration phase, more complex flow can be found at the proximal anastomosis of the whole anastomosis models. This was due to the sharp gradient of the aorta waveform used and the compensatory graft and distal anastomosis part, which influenced the pressure difference and thus the velocity distribution.

In conclusion, it can be observed that the flow field in the junction region of proximal anastomosis was truly “disturbed”, which may trigger a cascade of abnormal biological process leading to intimal thickening and/or thrombi formation (Kleinstreuer et al., 2001).

(a) $t_1 = 0.18s$

(b) $t_2 = 0.24s$

(c) $t_3 = 0.40s$

Figure 7-15 Velocity fields of proximal anastomosis part at different time intervals

7.3.1.2 Flow Characteristics of Graft

Figure 7-16 shows velocity fields in graft at different time intervals. Comparing to the proximal anastomosis, the flow characteristics were quite simple. However, some variations during the flow cycle can also be observed. At acceleration ($t_1=0.18s$) and peak flow phases ($t_2=0.24s$), the flow in the graft was quite smooth and parallel to the wall, and it was approximately parabola in shape. However at the deceleration phase ($t_3=0.40s$), because of the decrease of inertia and the complex flow characteristics at the junction of proximal anastomosis, the blood flow in graft skewed a little towards the outer wall due to the curvature of graft. With the advancing of time ($t_4=0.41s$), some of the blood along graft inner wall reversed the flow direction. This was coincided with the observations of Buchanan et al. (1999) for flow in the celiac branch at the flow deceleration phase. At $t_5=0.44s$, when the net flow rate was in the reverse direction, the flow in graft was dominated by the backflow along the inner and outer walls. However, some blood in the center of graft still flowed forward downstream on account of the vortex formed at the junction of proximal anastomosis. This observation was slightly different from that of Buchanan et al. (1999) for flow in the celiac branch at T_3 . The flow of celiac branch was reported to be fully backward, no positive flow direction can be found. This difference was due to the larger diameter ratio and angle between the celiac branch and aorta of their model. When flow was acceleration again with a zero net flow rate at $t_6=0.47s$, the reverse flow also observed near the graft inner wall and the flow in the center of graft was still complex.

Based on the above observations, it can be concluded that the flow characteristics of graft was less complicated than those of proximal anastomosis, although some disturbances can also be observed.

(a) $t_1=0.18s$

(b) $t_2=0.24s$

(c) $t_3=0.40s$

(d) $t_4=0.41\text{s}$

(e) $t_5=0.44\text{s}$

(f) $t_6=0.47\text{s}$

Figure 7-16 Velocity fields of graft at different time intervals

7.3.1.3 Flow Characteristics of Distal Anastomosis

Figure 7-17 shows the flow field of distal anastomosis. During the systolic acceleration phase ($t_1=0.18s$), the flow features of separation at the heel and a stagnation point on the coronary artery bed opposite the heel of distal anastomosis were observed. A zone of low momentum, recirculating fluid was contained between the junction and the blockage in the coronary artery. Separation was not yet found at the toe and the velocity distribution across the channel downstream from the anastomosis was symmetric. It was apparent that the long arteriotomy on the coronary artery reduced gradually the average velocity of the blood as it approached the distal anastomosis, since the cross-sectional area of the junction became larger. Due to the curved inlet configuration, the core of the highest velocity flow was skewed towards the toe region. At peak flow rate ($t_2=0.24s$), the stagnation point on the bed drifted distally while the recirculation over the heel was enlarged. The flow of graft impacted more strongly on the toe and the coronary artery bed. The skewing of the flow within the distal anastomosis and as the fluid diverted into the coronary artery through the anastomosis generated secondary motions, which were essential to the flow topology and influenced the residence time of blood elements in the vicinity of the junctions. As observed in Figure 7-17 (b) vortex was observed in the cross-sectional planes DD and EE, which made blood stay longer there. During the deceleration phase ($t_3=0.40s$), the recirculatory motion, formerly located at the heel was enlarged in shape and was drawn slightly further downstream as shown in Figure 7-17 (c). The secondary flow was also noticeable at the time phase as shown by persisted vortex in the cross-sectional planes DD and EE. As only half of the symmetrical model was simulated, the other vortex in the opposite half of the cross-section was assumed. In turn, the blood close to the wall of coronary artery was subject to flow circumferentially in opposite directions. It was thus demonstrated that the fluid advanced downstream of the coronary artery along helical paths during this phase of the cardiac cycle. All these observations

were in agreement with those of Cole et al. (2002b) at distal anastomosis of Taylor bypass model.

At later deceleration phase ($t_4=0.41s$), the recirculatory motion close to the heel became more elongated in shape and was drawn downstream near to the center of anastomosis. Some fluid particles departed this region, flowing past the heel and further upstream along the graft wall as reported by Cole et al. (2002b). The secondary flow in the cross-sectional planes DD and EE implied two counter-rotating vortexes situated symmetrically with respect to the y-axis in the Y-Z plane of coronary artery, which reflected the nature of the spiral flow trajectories as seen in Figure 7-17 (d). At $t_5=0.44s$, when the net flow rate was in the reverse direction, the flow in the graft was dominated by the backflow along the inner and outer walls as shown in Figure 7-17 (e). The expanding recirculation progressed towards the interface between the graft and coronary artery, moving close to the toe with the nodal point located close to the center of distal anastomosis. A small flow separation region was observed upstream of the toe when streamlines were viewed to converge to a point. A nodal point, viewed as sink, was separation point of three dimensional flow (Filippone, 2004). When flow was acceleration again with a zero net flow rate at $t_6=0.47s$, the flow patterns became more complex. Recirculation regions occupied the whole regions of coronary artery and the junction of distal anastomosis. Flow separation regions were observed in Figure 7-17 (f) at the toe and upstream of the toe as the streamlines were shown to diverge from a point and converge to a point respectively.

It was clear that the flow conditions at the distal anastomosis might favor the progression of IH at the heel and toe. In the vicinity of the heel, a large, low momentum recirculation

region persisted within the cycle, which augments the residence times of blood there, thus increasing the likelihood of adhesion of platelets and leukocytes to the endothelium and leading to the stimulation of smooth muscle cell proliferation. The flow separation and noticeable secondary flow regions observed near the toe were also susceptible to disease there.

(a) $t_1 = 0.18\text{s}$

(b) $t_2 = 0.24\text{s}$

(c) $t_3 = 0.40\text{s}$

Figure 7-17 Velocity fields of distal anastomosis at different time intervals

7.3.2 Hemodynamic Parameters Distribution

As there is strong biological evidence that hemodynamic parameters (HPs) encapsulate “disturbed flow” which may trigger a cascade of abnormal biological processes leading to intimal thickening and/or thrombi formation, sufficiently high and sustained HP values can be employed to determine susceptible sites for the onset of blood vessel diseases (Kleinstreuer et al., 2001). Historically, the most frequently employed indicators of disturbed flow under pulsatile flow have been the time-averaged WSS, WSSG, OSI and the newly proposed segmental averages of above HPs. Therefore, in this study, all these indicators were investigated and discussed in detail sequentially.

Figures 7-18, 7-19 and 7-20 show the surface contour plots of time-averaged WSS, WSSG and OSI for whole anastomosis model and its proximal and distal anastomoses obtained using Eqs. (3-18), (3-19) and (3-20) respectively. From Figures 7-18 (a), 7-19(a) and 7-20 (a), it can be observed that the distribution of time-averaged WSS, WSSG and OSI had more variations at the proximal and distal anastomoses than the graft regions. For proximal anastomosis, three high time-averaged WSS were observed at the heel, toe and the region downstream of the toe from Figure 7-18 (b), and these regions experienced relatively less reverse flow as shown by the low OSI values in Figure 7-20 (b). There were also two significant areas with low time-averaged WSS, near the middle of anastomosis at the aorta wall and along the graft inner wall as demonstrated in Figure 7-18 (b). These low time-averaged WSS regions were areas of flow separation throughout the whole cycle as indicated by elevated OSI values at the same locations as shown in Figure 7-20 (b). In addition, high time-averaged WSSG regions were associated with the high time-averaged WSS regions near the toe and heel as observed in Figure 7-19 (b). All these observations for the proximal anastomosis part was in agreement with those

observed for the 45° backward facing proximal anastomosis as demonstrated in Figure 5-24. Buchanan et al. (1999 and 2003) also reported the similar HPs distribution for aorto-celiac junction and an abdominal aorta model. Through comparisons between HPs with the animal experimental intimal WBC density, LDL permeability and lesion growth data, they concluded that the early atherosclerotic lesion development corresponds to regions of High-OSI-and-low-WSS and Low-OSI-and-high-WSS combinations. The continued growth of the lesions was likely due to modifications in the permeability as can be related to increases in the WSSG. Therefore, these regions of proximal anastomosis would be more prone to disease.

To the distal anastomosis, high time-averaged WSS regions were observed at the toe and downstream of the coronary artery in Figure 7-18 (c), due to the skewing of the flow through the anastomosis and generated secondary motions there. These regions experienced less reverse flow as shown by low OSI in Figure 7-20 (c). However, low time-averaged WSS were found at the heel and the coronary artery near the occluded end. The large area but low momentum flow recirculating region at the heel had higher OSI values as indicated in Figure 7-20 (c). In addition, high time-averaged WSSG was observed at the toe region. These HPs distributions were similar with the case A of Longest and Kleinstreuer (2003), when one end of the coronary artery was totally occluded. As regions with High-OSI-and-low-WSS and Low-OSI-and-high-WSS combinations were suspected to initiate the atherosclerotic lesion, which were further worsened by modifications in permeability indicated with the increases of WSSG, these regions of distal anastomosis might more prone to disease.

Figure 7-18 Time-averaged WSS contours for (a) whole anastomosis model; (b) proximal anastomosis part and (c) distal anastomosis part

Figure 7-19 Time-averaged WSSG contours for (a) whole anastomosis model; (b) proximal anastomosis part and (c) distal anastomosis part

Figure 7-20 OSI contours for (a) whole anastomosis model; (b) proximal anastomosis part and (c) distal anastomosis part

In conclusion, the susceptible sites of IH and/or atherosclerotic lesion formation in a complete CABG model were the toe, heel, the region downstream of the toe, near the middle of anastomosis at the aorta wall and along the graft inner wall of proximal anastomosis together with the toe, downstream of the coronary artery, the heel and the coronary artery near the occluded end. To quantitatively compare their probability of disease occurrence, segmental averages of HPs calculated using Eq. (3-21) on these surfaces were tabulated in Table 7-2 and Figure 7-21 shows the sketch maps of area investigated.

From the table, it can be observed that the segmental averages of time-averaged WSSG were high at the toe (Region G in Figure 7-21) and its downstream (Region H in Figure 7-21), named as “toe region”, of distal anastomosis. In addition, the suture line region (Region J in Figure 7-21) of distal anastomosis also had high segmental average of time-averaged WSSG. As segmental averages of time-averaged WSSG significantly correlated with WBC densities (Buchanan et al., 1999), these may be the reasons that IH was observed to occur predominantly at the distal anastomosis of a bypass system (Sottiurai et al., 1989) and it was found to be most significant along the suture line of distal anastomosis (Bassiouny et al., 1992; Loth et al., 2002). Meanwhile in these regions, the segmental average of time-averaged WSS was relatively high and the segmental average of time-averaged OSI was relatively low. As region with Low-OSI-and-high-WSS combination was suspected to initiate the atherosclerotic lesion (Buchanan et al., 1999), these regions were further proved to be susceptible sites of atherosclerotic lesion. The smaller junction area of distal anastomosis also restricted the flow if IH was formed, the situation would be worse than those of proximal part. However it was clear that further quantitative histopathological data regarding the development of IH and atherosclerotic

lesion was required for comparison in order to better relate hemodynamic characteristics to sites of potential lesion formations. Once the relationship was well established, the hemodynamic parameter can be widely used for optimization the CABG, especially the sleeve design for the distal anastomosis.

Figure 7-21 Sketch maps of area investigated for segmental averages of HPs

Table 7-2 Comparisons of <HP> for different locations

Name		Labels in maps	Area (mm ²)	<WSS> (Pa)	< WSSG>	<OSI>
Proximal anastomosis	heel	A	4.23	4.48	11.88	0.41
	toe	B	1.59	8.58	20.24	0.36
	part3	C	9.46	3.17	3.24	0.49
	part4	D	25.50	6.56	14.25	0.07
	suture_line	E	12.00	5.06	9.01	0.29
Distal anastomosis	heel	F	0.55	2.92	12.75	0.24
	toe	G	0.55	28.04	147.17	0.02
	part3	H	9.70	14.63	64.24	0.07
	part4	I	6.81	0.85	3.59	0.22
	suture_line	J	3.18	9.20	41.43	0.11

7.4 A Summery for This Chapter

The numerical simulation results obtained for whole anastomosis model under steady and pulsatile flow conditions were presented and described in this chapter. Disturbed flow (flow separation/ reattachment, vortical and secondary flow) was found at proximal and

distal anastomoses, especially at the distal anastomosis. In the vicinity of the heel of distal anastomosis, a large recirculation region with low momentum persisted within the cycle, which augmented the residence times of blood there, and thus increasing the likelihood of adhesion of platelets and leukocytes to the endothelium and leading to the stimulation of smooth muscle cell proliferation. The flow separation and noticeable secondary flow regions observed near the toe of distal anastomosis were also susceptible to disease there.

In addition, quantitative indicators, such as WSS, WSSG and time-averaged WSS, WSSG, OSI were investigated. The results indicated the High-OSI-and-low-WSS and Low-OSI-and-high-WSS regions of proximal and distal anastomoses, especially at the toe and heel regions of distal anastomosis. These regions were suspected to initiate the atherosclerotic lesion and were further worsened by modifications in permeability indicated with the increases of WSSG. The comparisons of segmental average of HPs further proved that IH was more prone to form in the distal anastomosis than the proximal anastomosis, especially along the suture line at the toe and heel of distal anastomosis, which was in line with the in-vivo studies of Bassiouny et al. (1992) and Loth et al. (2002).

Furthermore, reducing the tightening force during the suturing process and having a longer arteriotomy on the coronary artery for the distal anastomosis may aid in improving the graft patency rate on account of smooth flow field and reduced unfavorable WSS and WSSG regions. Meanwhile, the design of sleeve shall consider the HPs parameters. Increasing the cross-sectional area of anastomosis part, eliminating the graft bulges and smoothening wall curvatures would improve the graft patency rate by reducing the vortex size and reduced the abnormal HPs distributions.

CHAPTER 8

CONCLUSIONS AND SUGGESTIONS FOR FUTURE WORK

8.1 Conclusions

Flow structures of the proximal anastomosis were extensively explored by means of numerical simulation in order to establish the conditions of flow at upstream. Three proximal anastomotic models (i.e. 45° forward, 90° and 45° backward facing grafts) were studied under both steady and pulsatile flow conditions. The investigation of steady flow revealed the basic flow characteristics of proximal anastomosis. The flow rate of aorta, graft and the grafting angle were found to correlate with flow characteristics and WSS distributions of the proximal anastomosis. 45° backward facing proximal anastomosis model is recommended to be the best in terms of graft patency rate due to its smallest variation range of WSS and smallest low velocity region near the heel. Under pulsatile flow condition, at peak flow phase, three dimensional flow separation was found along the graft inner wall just after the heel and decreased in size with the increase of grafting angle. The stagnation point was found to shift within a small area along the graft outer wall during the physiological cycle. It was shown that the existence of flow separation, vortex and the small shifting of stagnating locations might accelerate the formation of IH.

In addition, high fluctuations (range of -22 Pa to 21Pa) and oscillations of instantaneous WSS were found around the proximal anastomotic joints. Low time-averaged WSS with elevated OSI was observed near the middle of anastomosis at the aorta wall and along the graft inner wall respectively, while high time-averaged WSS with low OSI was found at

the toe and the heel as well as downstream of the toe. Both of these regions are believed to correlate with early atherosclerotic lesion growth (Buchanan et al., 1999). Moreover, elevated time-averaged WSSG was found near the anastomosis, which implies the elevated LDL permeability there (Buchanan et al., 1999).

In contrast to the other two models, the 45° backward facing model is recognized to have higher patency rate as the vortex formed at graft cross-sectional planes for the peak flow rate moved away from the wall when moving downstream and it had the smallest flow separation region along graft inner wall simultaneously. In addition, 45° backward facing model had the smallest variation range of time-averaged WSS and the lowest segmental average of time-averaged WSSG, which further affirmed its superiority.

PIV measurements were carried out for the proximal anastomosis models in order to validate the numerical simulation results. A fair match between numerical and experimental data was observed in the flow characteristics, the velocity vectors and WSS distributions. The overall difference between them ranged from 8 to 54 percent, which is acceptable as Lei et al. (2001) and Bertolotti et al. (2001) also reported the error ranged from 1 to 40 percent by means of LDA measurements. In addition, the error range maintained similarity for different time phases. This was different from the study of Lei et al. (2001), who observed that the relative error between numerical and LDA experimental data was associated with the time phase. The relative error of their study was small during the forward flow phases (around 1-8 percent) and much larger during the reverse flow phase (ranged from 1-40 percent) (Lei et al., 2001). This discrepancy may attribute to the different measuring instrument used. PIV was capable to capture the transient overall flow field, while LDA measured the velocity at fixed location as the mean value obtained

from the instantaneous samples taken at numerous cycles within the sampling period, which heavily rely on the repeatability of experiment. Therefore it is recommended that PIV measurement can obtain quantities as accurate as LDA and can be used to validate the numerical simulation results. The slight differences in geometry between the experimental and numerical models especially at the anastomosis, disturbance of background noise, wall reflection and the accuracy of positioning the measuring plane in the PIV techniques as well as the accuracy of flowmeter and cam mechanism used to mimic the pulsatile flow have contributed to the discrepancy between numerical and experimental results.

Since the objective of the present project is to enhance the understanding of the stenosis pathophysiological process in CABG and then provide useful information for medical doctors and serve as the basis for the design of biocompatible sleeve device, numerical simulation was implemented for the whole anastomosis model under both steady and pulsatile flow conditions. Disturbed flow (flow separation / reattachment, vortical and secondary flow) was found at proximal and distal anastomoses, especially at the distal anastomosis. In the vicinity of the heel of distal anastomosis, a large recirculation region with low momentum persisted within the cycle, which enhanced the residence times of blood there, thus increasing the likelihood of adhesion of platelets and leukocytes to the endothelium and leading to the stimulation of smooth muscle cell proliferation. The flow separation and secondary flow regions observed near the toe of distal anastomosis also suggested it was a possible location for disease formation.

In addition, quantitative indicators, such as WSS, WSSG and time-averaged WSS, WSSG, OSI were investigated. The results reported the High-OSI-and-low-WSS and

Low-OSI-and-high-WSS combination regions of proximal and distal anastomoses, especially at the toe and heel regions of distal anastomosis. These regions are suspected to initiate the atherosclerotic lesion and might be further worsened by modifications in permeability indicated with the increase of WSSG. The comparisons of segmental average of HPs further proved that IH might be more prone to form at the distal anastomosis than at the proximal anastomosis, especially along the suture line at the toe and heel of distal anastomosis, which is in line with the in-vivo studies of Bassiouny et al. (1992) and Loth et al. (2002).

Further comparisons with other models indicate that reducing the tightening force during the suturing process and having a longer arteriotomy on the coronary artery for the distal anastomosis may aid in enhancing the graft patency rate on account of smoother flow field and reduced unfavorable WSS and WSSG regions. Meanwhile, the design of sleeve should take into the consideration of the HPs obtained. Increasing the cross-sectional area of anastomosis part, eliminating the graft bulges and smoothening wall curvatures may improve the graft patency rate by reducing the vortex size and the abnormal HPs distributions.

8.2 Suggestions for Future Work

Although present simulation and experimental works have successfully investigated the complex hemodynamics of proximal anastomosis and the complete CABG model and provided useful information for the medical doctors and sleeve design, there are still areas of interest for further study. As an extension to the current work, the followings are suggested:

1. A new complete anastomosis model with different percentage of stenosed coronary artery is necessarily to be investigated for exploring the short-term patency rate as the

residual flow through the stenosis is not negligible at least two weeks after grafting (Bertolotti and Deplano, 2000). The calculated stenosis influence length based on right coronary artery waveform as presented in Appendix E is 59.2mm, which is much longer than the distance used by surgeons. Note that surgeons usually suture the graft just distal to the stenosis or within 3cm from the site of stenosis. This has suggested that the influence of stenosis cannot be ignored. The investigations can aim at answering the questions of surgeons about the suitability of their choices in term of graft patency rate, e.g. the decision in conducting the bypass surgery, that is whether or not to do the bypass surgery for mid stenosed coronary artery, and selecting the location for anastomosis, that is whether to place the graft just beyond the stenosis to take advantage of the jet from the partly occluded coronary artery or on the contrary keep a distance from the stenosis in order to dissociate competitive flows. In short, the optimal distance to place the graft away from the stenosed coronary artery should be determined.

2. A realistic CABG model could be fabricated employing casting techniques, using e.g. porcine heart with coronary bypass. This casting technique can be used to fabricate a master replica. It may be resolved 2-dimensionally by means of Computed Tomography (CT), and then a 3-D reconstruction can be made using appropriate CAD/CAM software. This data can then be utilized for further modification and modeling. In addition, the flow waveforms of aorta, graft and the downstream of coronary artery could be obtained through Magnetic Resonance Imaging or flow sensors in-vivo, which could provide the first hand physiological information. The numerical simulation based on the above information could derive more realistic

physiological information for the CABG. To couple the influence of compliance effect, the fluid-structure coupling calculation must also be considered in the future.

3. Quantitative data regarding the histopathological development of IH as well as refined correlations for adhesive molecule expression, endothelial cell activation and expression of thrombogenic compounds, platelet-wall interactions, red blood cell induced dispersion and platelet activation shall be obtained through in-vivo experiment, therefore the comparisons with numerical simulation results will have better correlation with the hemodynamic characteristics at the site of potential lesion formations.

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APPENDIX A - The Derivation of Womersley Solution

Analytical solutions to the Navier-Stokes equations are possible in only a few selected cases with very special geometry and boundary conditions. These solutions are essential for making the assumption of the inlet velocity profile and the validation of numerical methods. Moreover, most of these analytical solutions require the assumption of steady flow conditions and are thus of no use in addressing time dependent issues for transient problems such as blood flow. Fortunately, a canonical solution for pulsatile flow does exist, that is the Womersley solution (Womersley, 1955) for fully developed pulsatile flow in a straight circular tube.

Consider a long circular tube, which is subject to a time varying flow rate at inlet and a constant but arbitrary pressure over the outflow boundary. With a sufficient distance from the inlet (which depends on the geometric and flow parameters), the radial and circumferential components of velocity vanish, the only non-zero component of the velocity vectors is in the axial direction and is denoted as u . Using cylindrical polar coordinates, and taking the problem to be axis-symmetric (ie. $u=u(r, x, t)$, $p=p(r, x, t)$), the continuity equation reduces to

$$\frac{\partial u}{\partial x} = 0 \quad (\text{A-1})$$

The Navier-Stokes equations become

$$\rho \frac{\partial u}{\partial t} = -\frac{\partial p}{\partial x} + \frac{\mu}{r} \frac{\partial}{\partial r} \left(r \frac{\partial u}{\partial r} \right) \quad (\text{A-2})$$

$$0 = -\frac{\partial p}{\partial r} \quad (\text{A-3})$$

The above equations imply that

$$u = u(r, t), \quad p = p(x, t) \quad (\text{A-4})$$

Therefore rearrange Eq. (A-2) into

$$\frac{\mu}{r} \frac{\partial}{\partial r} \left(r \frac{\partial u}{\partial r} \right) - \rho \frac{\partial u}{\partial t} = \frac{\partial p}{\partial x} \quad (\text{A-5})$$

Observing that the left-hand side of Eq. (A-5) is a function of r and t and the right-hand side is the function of x and t , to maintain the equality of Eq. (A-5), both sides must be a function of t only.

Consider now a pulsatile sinusoidal flow with the pressure gradient and the axial velocity as

$$\frac{\partial p}{\partial x} = -P e^{i\omega t} \quad (\text{A-6})$$

$$u(r, t) = U(r) e^{i\omega t} \quad (\text{A-7})$$

Where $\omega = 2\pi f$ is angular frequency in radian per second of the oscillatory motion, with f the frequency in Hertz. Meanwhile P is a constant and $U(r)$ is the distribution of axial velocity across the tube of radius R . When flow is fully developed, it is assumed to be identical at each section along the tube. Therefore a traveling wave solution can be neglected. It is clear that when $\omega = 0$ (the steady case), the flow becomes the Poiseuille flow discussed earlier in Chapter 3.

From Eqs. (A-6) and (A-7), it is clear that real part gives the velocity for pressure gradient $P(\cos \omega t)$ and the imaginary part gives the velocity for the pressure gradient $P(\sin \omega t)$. Upon substituting Eqs. (A-6) and (A-7) into Eq. (A-5), and after some arrangements, the following equation can be obtained.

$$\frac{d^2 U}{dr^2} + \frac{1}{r} \frac{dU}{dr} - \frac{i\omega\rho}{\mu} U = -\frac{P}{\mu} \quad (\text{A-8})$$

From Xu (2000), it is known that the general solution of an ordinary differential equation in the form of

$$\frac{d^2 y}{dx^2} + \frac{1}{x} \frac{dy}{dx} + y = 0 \quad (\text{A-9})$$

is

$$y = AJ_0(x) + BY_0(x) \quad (\text{A-10})$$

which involves the first kind and second kind of Bessel functions J_0 and Y_0 respectively of

complex argument. If assuming $x = iKX$, thus, $\frac{dy}{dx} = \frac{1}{iK} \frac{dy}{dX}$, $\frac{d^2 y}{dx^2} = -\frac{1}{K^2} \frac{d^2 y}{dX^2}$, Eq. (A-9)

can be modified as Eq. (A-11).

$$\frac{d^2 y}{dX^2} + \frac{1}{X} \frac{dy}{dX} - K^2 y = 0 \quad (\text{A-11})$$

and the corresponding solution becomes

$$y = AJ_0(iKX) + BY_0(iKX) \quad (\text{A-12})$$

Thus the solution of Eq. (A-8) is

$$U(r) = AJ_0\left(i\sqrt{i\omega\rho/\mu}r\right) + BY_0\left(i\sqrt{i\omega\rho/\mu}r\right) + \frac{P}{\omega\rho i} \quad (\text{A-13})$$

Note that X and K in Eq. (A-11) are equivalent to r and $\sqrt{i\omega\rho/\mu}$ respectively in Eq. (A-8). As U must be finite on the axis (i.e. At $r=0$), and since $Y_0(0)$ is not finite, then B has to be zero. Also because of the no-slip condition $U(r)|_{r=R}=0$, then the following result is obtained

$$AJ_0\left(i^{3/2}\sqrt{\omega\rho/\mu}R\right) + \frac{P}{\omega\rho i} = 0 \quad (\text{A-14})$$

To simplify the expression, a non-dimensional parameter α , known as the Womersley number is introduced.

$$\alpha = R\sqrt{\frac{\omega\rho}{\mu}} \quad \text{or} \quad \alpha = R\sqrt{\frac{\omega}{\nu}} \quad (\text{A-15})$$

Where $\nu=\mu/\rho$ is the kinematic viscosity. From Eq. (A-14)

$$A = -\frac{P}{\omega\rho i} \frac{1}{J_0\left(i^{3/2}\alpha\right)} \quad \text{or} \quad A = \frac{iP}{\omega\rho} \frac{1}{J_0\left(i^{3/2}\alpha\right)} \quad (\text{A-16})$$

and finally, from Eq. (A-13) the axial velocity can be expressed as

$$U(r) = -\frac{iP}{\omega\rho} \left(1 - \frac{J_0\left(i^{3/2}\alpha r / R\right)}{J_0\left(i^{3/2}\alpha\right)} \right) \quad (\text{A-17})$$

In the limit as α approaches zero, i.e. $\omega \rightarrow 0$, the velocity profile becomes parabolic. As α tends to infinity, i.e., viscosity becomes not important ($\mu \rightarrow 0$), it can be shown that

$$\frac{J_0\left(i^{3/2}\alpha r / R\right)}{J_0\left(i^{3/2}\alpha\right)} \rightarrow 0 \quad (\text{A-18})$$

Which implies that

$$U(r) \rightarrow -\frac{iP}{\omega\rho} \quad (\text{A-19})$$

In fact, by introducing the idea that a Stokes boundary layer of thickness δ is proportional to $1/\alpha$, it can be concluded that in this case the boundary layer thickness at the cylindrical tube inner wall disappears.

It is interesting to note that the above expression is independent of viscosity μ , and exactly 90° out of phase with P . Actually this result corresponds to the Euler equation (which only holds for $\mu=0$, i.e., inviscid fluids) namely,

$$\frac{\partial u}{\partial t} = -\frac{1}{\rho} \frac{\partial p}{\partial x} \quad (\text{A-20})$$

Substituting Eqs. (A-6) and (A-7) into Eq. (A-20), it can be easily shown that

$$U = \frac{P}{i\omega\rho} = -\frac{iP}{\omega\rho} \quad (\text{A-21})$$

which is the same as the result in Eq. (A-19).

Hence the final result for the velocity of pulsatile flow in a cylindrical tube of radius R is

$$u(r, t) = -\frac{iP}{\omega\rho} \left(1 - \frac{J_0(i^{3/2}\alpha r / R)}{J_0(i^{3/2}\alpha)} \right) e^{i\omega t} \quad (\text{A-22})$$

To obtain the volume flow rate Q , it is necessary to integrate the velocity across the lumen of the tube. After the integration, Q can be expressed as Eq. (A-23) (Nichols and O'Rourke, 1990).

$$Q = \frac{\pi R^2 P}{i\omega\rho} \left(1 - \frac{2J_1(\alpha i^{3/2})}{\alpha i^{3/2} J_0(\alpha i^{3/2})} \right) e^{i\omega t} \quad (\text{A-23})$$

where J_1 is the first kind Bessel function with order 1.

Dividing Eq. (A-22) by Eq.(A-23), and if the volume flow rate is known, the axial velocity can be expressed as

$$u(r, t) = \frac{Q}{\pi R^2} \left(\frac{1 - \frac{J_0(i^{3/2}\alpha r / R)}{J_0(i^{3/2}\alpha)}}{1 - \frac{2J_1(\alpha i^{3/2})}{\alpha i^{3/2} J_0(\alpha i^{3/2})}} \right) e^{i\omega t} \quad (\text{A-24})$$

Similarly, if pressure gradient and the axial velocity are assumed to be cosinusoidal flow as following:

$$\frac{\partial p}{\partial x} = -Pe^{-i\omega t} \quad (\text{A-25})$$

$$u(r, t) = U(r)e^{-i\omega t} \quad (\text{A-26})$$

The axial velocity can be expressed as

$$u(r, t) = \frac{Q}{\pi R^2} \left(\frac{1 - \frac{J_0\left(i^{5/2}\alpha r / R\right)}{J_0\left(i^{5/2}\alpha\right)}}{1 - \frac{2J_1(\alpha i^{5/2})}{\alpha i^{5/2}J_0(\alpha i^{5/2})}} \right) \quad (\text{A-27})$$

In the case where the flow rate or average velocity is known, Fourier Transform can be used to extract the frequency content of volume flow waveform when the fundamental frequency ω is given. Thus if $Q(t)$ is assumed as the Fourier series,

$$Q(t) \approx \sum_{n=-N}^{n=N} B_n e^{i\omega t} \quad (\text{A-28})$$

the Fourier coefficients, B_n can be determined using the matrix calculation of Matlab. The axial velocity is then given as

$$u(r, t) = \frac{2B_0}{\pi R^2} \left[1 - \left(\frac{r}{R} \right)^2 \right] + \sum_{n=-N}^{-1} \left\{ \frac{B_n}{\pi R^2} \frac{1 - \frac{J_0(i^{5/2} \alpha_n r / R)}{J_0(i^{5/2} \alpha_n)}}{1 - \frac{2J_1(\alpha_n i^{5/2})}{\alpha_n i^{5/2} J_0(\alpha_n i^{5/2})}} \right\} e^{in\omega t} + \sum_{n=1}^N \left\{ \frac{B_n}{\pi R^2} \frac{1 - \frac{J_0(i^{3/2} \alpha_n r / R)}{J_0(i^{3/2} \alpha_n)}}{1 - \frac{2J_1(\alpha_n i^{3/2})}{\alpha_n i^{3/2} J_0(\alpha_n i^{3/2})}} \right\} e^{in\omega t} \quad (\text{A-29})$$

Where R is the radius of cylinder, J_0 and J_1 are first kind Bessel functions of order 0 and 1, respectively, and $\alpha_n = R\sqrt{n\omega/\nu}$.

Eq. (A-30) shows the complex conjugate characters of the following parameters.

$$J_0(i^{5/2} \alpha_n r / R) = \overline{J_0(i^{3/2} \alpha_n r / R)} \quad J_1(i^{5/2} \alpha_n) = \overline{J_1(i^{3/2} \alpha_n)} \quad B_{-n} = \overline{B_n} \quad (\text{A-30})$$

$$J_0(i^{5/2} \alpha_n) = \overline{J_0(i^{3/2} \alpha_n)} \quad i^{5/2} = \overline{i^{3/2}} \quad e^{-in\omega t} = \overline{e^{-in\omega t}}$$

Thus, the axial velocity can be simplified to

$$u(r, t) = \frac{2B_0}{\pi R^2} \left[1 - \left(\frac{r}{R} \right)^2 \right] + 2 * \text{Real} \left\{ \sum_{n=1}^N \left\{ \frac{B_n}{\pi R^2} \frac{1 - \frac{J_0(i^{3/2} \alpha_n r / R)}{J_0(i^{3/2} \alpha_n)}}{1 - \frac{2J_1(\alpha_n i^{3/2})}{\alpha_n i^{3/2} J_0(\alpha_n i^{3/2})}} \right\} e^{in\omega t} \right\} \quad (\text{A-31})$$

Here, $\text{Real}\{\}$ means the real part of a complex value.

APPENDIX B - Simulation Results for 90° and 45° Backward Facing Proximal Anastomosis Models under Steady Flow Condition

Due to the space constraint, the velocity vector and streamlines at the center plane of 90° and 45° backward facing proximal anastomosis models are presented here when changing the graft flow rate as shown in Figures B-1 and B-2 respectively.

(a) 55% valve opening

(b) 75% valve opening

Appendix B

Supplement of Simulation Results (steady flow, proximal anastomosis model)

(c) 85% valve opening

(d) 95% valve opening

Figure B-1 Velocity vector and streamline of 90° graft model of different resistance configurations:(a) 55%, (b) 75%, (c) 85% and (d) 95% of valve opening

Appendix B

Supplement of Simulation Results (steady flow, proximal anastomosis model)

(a) 55% valve opening

(b) 75% valve opening

Appendix B

Supplement of Simulation Results (steady flow, proximal anastomosis model)

(c) 85% valve opening

(d) 95% valve opening

Figure B-2 Velocity vector and streamline of 45° backward facing graft model with different resistance configurations: (a) 55%, (b) 75%, (c) 85% and (d) 95% of valve opening

APPENDIX C - Simulation Results for 90° and 45° Backward Facing Proximal Anastomosis Models under Pulsatile Flow Condition

Due to the space constraint, velocity vectors at the center plane of 90° and 45° backward facing proximal anastomosis models were shown in Figures C-1 and C-2 respectively at seven different time intervals within a complete flow cycle.

(a) Time (t_1) at 1.35s

Appendix C

Supplement of Simulation Results (pulsatile flow, proximal anastomosis model)

(b) Time (t_2) at 1.6s

(c) Time (t_3) at 1.7s

Appendix C

Supplement of Simulation Results (pulsatile flow, proximal anastomosis model)

(d) Time (t_4) at 1.8s

(e) Time (t_5) at 1.85s

Appendix C

Supplement of Simulation Results (pulsatile flow, proximal anastomosis model)

Figure C-1 Velocity vectors at center plane in 90° proximal anastomosis model at different time phases: (a) $t_1=1.35$ s; (b) $t_2=1.6$ s; (c) $t_3=1.7$ s; (d) $t_4=1.8$ s; (e) $t_5=1.85$ s; (f) $t_6=2.1$; (g) $t_7=2.4$ s.

Appendix C

Supplement of Simulation Results (pulsatile flow, proximal anastomosis model)

(a) Time (t_1) at 1.35s

(b) Time (t_2) at 1.6s

Appendix C

Supplement of Simulation Results (pulsatile flow, proximal anastomosis model)

(c) Time (t_3) at 1.7s

(d) Time (t_4) at 1.8s

Appendix C

Supplement of Simulation Results (pulsatile flow, proximal anastomosis model)

(e) Time (t_5) at 1.85s

(f) Time (t_6) at 2.1s

Appendix C

Supplement of Simulation Results (pulsatile flow, proximal anastomosis model)

Figure C-2 Velocity vectors at center plane in 45° backward facing proximal anastomosis model at different time phases: (a) $t_1=1.35s$; (b) $t_2=1.6s$; (c) $t_3=1.7s$; (d) $t_4=1.8s$; (e) $t_5=1.85s$; (f) $t_6=2.1$; (g) $t_7=2.4s$.

APPENDIX D - Experimental Results for 90° and 45° Backward Facing Proximal Anastomosis Models under Steady Flow Condition

The measured velocity vectors of 90° and 45° backward facing proximal anastomosis models with different resistance configurations are shown in Figures D-1 and D-2 respectively.

Figure D-1 Velocity vectors of 90° graft model with different resistance configurations:(a) 55%, (b) 75%, (c) 85% and (d) 95% of valve opening

Appendix D

Supplement of Experimental Results (steady flow, proximal anastomosis model)

(a) 55% valve opening

(b) 75% valve opening

Appendix D

Supplement of Experimental Results (steady flow, proximal anastomosis model)

(c) 85% valve opening

(d) 95% valve opening

Figure D-2 Velocity vectors of 45° backward facing graft model with different resistance configurations: (a) 55%, (b) 75%, (c) 85% and (d) 95% of valve opening

APPENDIX E - Analysis of the Stenosis Influence Length for 75% Stenosis

The profile of a 75% stenosis model as shown in Figure E-1 can be described by Eq. (E-1), where $R(z)$ is the radial position within the constricted tube along x direction and R_0 is the radius of the tube (Siouffi et al., 1998).

Figure E-1 Stenosis Model

$$\frac{R(z)}{R_0} = 1 - 0.5 \exp\left(-\frac{4z^2}{R_0^2}\right) \quad (\text{E-1})$$

Setting down that at a given instant time t , the fluid volume ejected through the stenosis throat, from ωt_0 phase (where flow rate $Q=0$ at initial time, t_0), will reach the axial location $\bar{l} = l / R_0$ in such a way that

$$\int_{t_0}^t Q(t) dt \leq V_{geo} \quad (\text{E-2})$$

where ω and V_{geo} are the angular frequency and volume confined between the stenosis throat and the axial location l respectively.

For the right side of Eq. (E-2), the following Eq. (E-3) can be derived.

$$\begin{aligned} V_{geo} &= \int_0^l \pi R(z)^2 dz = \int_0^l \pi R_0^2 \left(\frac{R(z)}{R_0}\right)^2 dz = \pi R_0^3 \int_0^{\bar{l}} \left[1 - \frac{1}{2} \exp\left(-\frac{4z^2}{R_0^2}\right)\right]^2 d\left(\frac{z}{R_0}\right) \\ &= \pi R_0^3 I(\bar{l}) \end{aligned} \quad (\text{E-3})$$

$$\text{where} \quad I(\bar{l}) = \int_0^{\bar{l}} \left[1 - \frac{1}{2} \exp\left(-\frac{4z^2}{R_0^2}\right)\right]^2 d\left(\frac{z}{R_0}\right)$$

If assuming $x=z/R_0$, then Eq. (E-4) can be obtained.

$$I(\bar{l}) = \int_0^{\bar{l}} \left[1 - \frac{1}{2} \exp(-4x^2)\right]^2 d(x) = \int_0^{\bar{l}} d(x) - \int_0^{\bar{l}} \exp(-4x^2) d(x) + \frac{1}{4} \int_0^{\bar{l}} \exp(-8x^2) d(x) \quad (\text{E-4})$$

Since $\int_0^{\infty} \exp(-bx^2)dx = \frac{1}{2}\sqrt{\frac{\pi}{b}}$, when $b > 0$ (Xu, 2000), then

$$I(\bar{l}) \approx \bar{l} - \frac{1}{2}\sqrt{\frac{\pi}{4}} + \frac{1}{4} \cdot \frac{1}{2}\sqrt{\frac{\pi}{8}} = \bar{l} - 0.36478 \quad (\text{E-5})$$

If $Q(t)$ can be Fourier Transformed as $Q(t) = \sum_{n=-\infty}^{\infty} B_n e^{inwt}$, then the left side of Eq. (E-2)

can be expressed as:

$$\begin{aligned} \int_{t_0}^t Q(t)dt &= \int_{t_0}^t \sum_{n=-\infty}^{\infty} B_n e^{inwt} dt = \int_{t_0}^t \sum_{n=-\infty}^{\infty} B_n (\cos nwt + i \sin nwt) dt + \int_{t_0}^t B_0 dt \\ &= \sum_{\substack{n=-\infty \\ n \neq 0}}^{\infty} B_n \frac{\sin nwt - \sin nwt_0}{nw} + \sum_{\substack{n=-\infty \\ n \neq 0}}^{\infty} B_n i \frac{\cos nwt_0 - \cos nwt}{nw} + \int_{t_0}^t B_0 dt \end{aligned} \quad (\text{E-6})$$

By setting initial time $t_0=0$, Eq. (E-6) become

$$\int_0^t Q(t)dt = \sum_{\substack{n=-\infty \\ n \neq 0}}^{\infty} B_n \frac{\sin nwt + i - i \cos nwt}{nw} + B_0 t \quad (\text{E-7})$$

Assuming $B_n = a_n + b_n i$, and $B_{-n} = a_n - b_n i$, the Eq. (E-7) is transferred as:

$$\int_0^t Q(t)dt = \sum_{n=1}^{\infty} \frac{4}{nw} \sin \frac{nwt}{2} \sqrt{a_n^2 + b_n^2} \left[\frac{a_n}{\sqrt{a_n^2 + b_n^2}} \cos \frac{nwt}{2} - \frac{b_n}{\sqrt{a_n^2 + b_n^2}} \sin \frac{nwt}{2} \right] + a_0 t \quad (\text{E-8})$$

If $\tan \beta_n = \frac{b_n}{a_n}$, the Eq. (E-8) equals to:

$$\begin{aligned} \int_0^t Q(t)dt &= \sum_{n=1}^{\infty} \frac{4}{nw} \sqrt{a_n^2 + b_n^2} \sin \frac{nwt}{2} \cos(\beta_n + \frac{nwt}{2}) + a_0 t \\ &\leq \sum_{n=1}^{\infty} \frac{4}{nw} \sqrt{a_n^2 + b_n^2} + a_0 t = \sum_{n=1}^{\infty} \frac{4}{nw} |B_n| + B_0 t \end{aligned} \quad (\text{E-9})$$

When $wt = \pi$, according to Eqs. (E-3), (E-5) and (E-9), and take the equal sign of Eq.

(E-2), then it can be shown that:

$$V_{geo} = \pi R_0^3 I(\bar{l}) = \pi R_0^3 (\bar{l} - 0.36478) = \int_0^t Q(t)dt \leq \sum_{n=1}^{\infty} \frac{4}{nw} |B_n| + B_0 \frac{\pi}{w} \quad (\text{E-10})$$

So the maximum influence length becomes:

$$\bar{l} = 0.36478 + \frac{1}{\pi R_0^3} \left[\sum_{n=1}^{\infty} \frac{4}{nw} |B_n| + B_0 \frac{\pi}{w} \right] \quad (\text{E-11})$$

For oscillatory flow, flow rate $Q = Q_M \cos wt$, then $B_1 = B_{-1} = \frac{Q_M}{2}$ and $B_0 = 0$,

according to Eq. (E-11), the maximum influence length becomes Eq. (E-12),

$$\bar{l} = 0.36478 + \frac{1}{\pi R_0^3} \left[\frac{4}{w} \frac{Q_M}{2} \right] = 0.36478 + \frac{\nu}{w R_0^2} \frac{2 R_0 Q_M}{\pi R_0^2 \nu} = 0.36478 + \frac{\text{Re}_M}{\mathcal{G}} \quad (\text{E-12})$$

where Re_M represents the peak Reynolds number of oscillatory flow and defined as

$\text{Re}_M = \frac{Q_M}{\pi R_0^2} \frac{2 R_0}{\nu}$ and frequency number is defined as $\mathcal{G} = \omega R_0^2 / \nu$. As Eq. (E-12) is the

same as that derived by Siouffi et al. (1998) for oscillatory flow, Eq. (E-11) can be used

for calculating the maximum influence length of 75% stenosis.

The derived maximum influence length based on right coronary artery waveform as shown in Figure E-2 (Nichols and O'Rourke, 1990) was 59.2mm, when the diameter of coronary artery was assumed to be 2mm.

Figure E-2 Flow waveform of right coronary artery

APPENDIX F - Configurations for the Anastomosis Models used for Experiment and Simulation

Figures F-1 and F-2 show the configurations of the Pyrex glass models used for PIV measurements to mimic the 45° forward (and similarly for 45° backward) and 90° proximal anastomosis respectively. The inner channel was treated as the physical models for numerical simulation. Due to the imperfection of manufacturing, the models used in the experiment were found deviate slightly from the numerical models. Meanwhile Figures F-3 and F-4 illustrate the schematic design of the complete anastomosis model and its side view of distal anastomosis part separately. The connection between coronary artery (downstream part) and graft was depended on a series of ellipse, whose detailed dimensions (in mm) were indicated in Figure F-4. Note that all dimensions shown in figures were in mm and Figures F-3 and F-4 only show the inner part of the model, viz. the fluid channel part, which is essential for numerical simulation.

Figure F-1 Drawing for the Pyrex glass model to mimic 45° forward (similarly for 45° backward) proximal anastomosis

Appendix F

Configurations for the Anastomosis Models used for Experiment and Simulations)

Figure F-2 Drawing for the Pyrex glass model to mimic 90° proximal anastomosis

Figure F-3 Drawing for the complete anastomosis model

Figure F-4 Side view for the distal anastomosis part of complete anastomosis model