Measurements of hemodynamics in coronary artery bypass using particle image velocimetry : an in-vitro study

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**Measurements of Hemodynamics in Coronary
Artery Bypass Using Particle Image Velocimetry:
An In-vitro Study**

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Abstract

Coronary artery bypass grafting, the major treatment for coronary stenosis, has long-term patency problem due to intimal hyperplasia along the graft and at the graft/artery junction (proximal and distal anastomoses). It is well demonstrated that the hemodynamic factors are linked to the development of intimal hyperplasia and have been hypothesized as a cause of bypass graft failure. 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 lacking in the literature and it is important and necessary for a better understanding of CABG. Therefore in this project, flow characteristics and hemodynamic parameters (HPs) distributions of proximal anastomosis and the whole 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. Furthermore, geometrical improvement to the distal anastomosis was proposed to reduce the nonuniformity of hemodynamics and the hemodynamic performance was evaluated and compared with a baseline distal anastomosis model.

At the first stage, the effects of proximal anastomotic angle on local hemodynamics were studied to provide useful information for medical doctors and serve as the basis for the design of a whole anastomosis model, with emphasis on identifying site-specific hemodynamic features that could reasonably be expected in triggering the initiation and further development of anastomotic intimal hyperplasia. PIV measurements revealed that the flow fields in the proximal anastomosis were strongly influenced by the anastomotic angle. A large size of flow separation region was found along the graft inner wall just

after the heel and decreased in size with the increasing of graft angle except the 30° model. The wall shear stress (WSS) distributions also demonstrate significant variations in time and space. Elevated spatial wall shear stress gradients (SWSSG) were found around the anastomotic joints. Along the graft inner wall the size of the elevated SWSSG region and the maximum value of SWSSG were increased with the increasing of anastomotic angle except the 30° model, which had the highest SWSSG and the largest size of elevated SWSSG region at the vicinity of heel. Along the graft outer wall, both the size of the elevated SWSSG region and maximum value of SWSSG were amplified notably with increasing of anastomotic angle. Regions of low-WSS-high-OSI and high-WSS-low-OSI were found around the anastomotic joints, where elevated time-averaged WSSG was also noticed for all models. Among all the models investigated, the 45° proximal anastomotic model is recognized to have higher patency rate as it had the smallest flow separation region along graft inner wall and the smallest region of low-WSS-high-OSI and high-WSS-low-OSI around the anastomotic joint.

The experimental results of the whole anastomosis revealed that disturbed flow (flow separation/reattachment, vortical and secondary flow) was found at proximal and distal anastomoses, especially at the distal anastomosis. Near the heel of distal anastomosis, a large recirculation flow 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. High-OSI-low-WSS and low-OSI-high-WSS regions were found occurred at proximal and distal anastomoses, especially at the toe and heel regions of distal anastomosis. Furthermore, the atherosclerotic lesion were suspected to

have initiated in these regions and were further worsened by modifications in permeability as highlighted with the increase of WSSG.

Geometrical improvement for the distal anastomosis was carried out in order to minimize the hemodynamics nonuniformity of the bypasses. Generally high-OSI-low-WSS regions were found around the heel and stagnation point on the artery floor at both the baseline model and the improved model. Around the toe low-OSI-high-WSS region was also found in the two models. However, at the retrograde flow condition of the improved model the WSS distributed more evenly throughout the anastomotic area; the peak WSS magnitude reduced about 69% at the heel (2.1 Pa vs 6.8 Pa), 42% at the toe (22 Pa vs 37.8 Pa) and 31% at the floor (29 Pa vs 41.9 Pa) when compared with those of the baseline model. In addition, the baseline model exhibited distinctive high SWSSG regions around the heel, toe and the floor of the junction, whereas the SWSSG was reduced tremendously in the improved model, especially around the heel (17.5 Pa/mm vs 24.5 Pa/mm, reduced about 28.5%), toe (13.9 Pa/mm vs 26.4 Pa/mm, reduced about 47.3%) and stagnation point on artery floor (7.9 Pa/mm vs 18.5 Pa/mm, reduced about 57.2%). In summary, with respect to the baseline model, significant flow field improvements leading to measurable reductions in SWSSG magnitude have been achieved in the improved model. At the zero flow condition, the improved model was shown to work well indicated by the reduction in SWSSG magnitude as comparing with that of the baseline model (9.2 Pa/mm vs 13.9 Pa/mm at the heel, reduced about 33.8%; 10.8 Pa/mm vs 23.2 Pa/mm, reduced about 53.4%; 8.02 Pa/mm vs 21.6 Pa/mm, reduced about 62.8%) and would be able to enhance the long-term hemodynamic performance and patency of coronary bypass graft.

Keywords:

Particle Image Velocimetry (PIV); Anastomosis; Hemodynamics

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Nomenclature

a_i	Coefficients of polynomial fitting, $i=1, 2, 3 \dots n$ for degree of polynomial approximation
d	Diameter of the tube (m)
D_G	Diameter of graft (m)
f	Frequency in Hertz
Q or $Q(t)$	Flow rate at time t (m^3/s)
Q_d	Mean flow rate in the distal outlet segment of coronary artery (cc/min)
Q_G	Mean flow rate in the graft during the pulsatile flow cycle (cc/min)
Q_p	Mean flow rate in the proximal outlet segment of coronary artery (cc/min)
r	Radius with respect to the center axis of the tube (m)
R	Radius of the tube (m)
Re	Reynolds number, defined as $Re=\rho u d/\mu$
t	Time (s)
T	Period (s)
u or $\bar{u}$	The average cross sectional velocity (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 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

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
ξ	Local normal distance to the wall (m)
μ	Dynamic viscosity of the working fluid (Pa·s)
ρ	Density of the working fluid (kg/m ³)
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 velocity gradient at the wall
ν	Kinematic viscosity of the working fluid (m ² s ⁻¹)

List of Abbreviations

CABG	Coronary artery bypass grafting
CFD	Computational Fluid Dynamics
DOS	Distal outlet segment
EC	Endothelial cell
FCPP	Femoro-crural patch prosthesis
HP	Hemodynamic parameter
IA	Interrogation area
IH	Intimal hyperplasia
IHT	Intimal hyperplasia thickening
LDA	Laser Doppler anemometry
LDL	Low-density lipoprotein
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
PTFE	Polytetrafluorethylene
SMC	Smooth muscle cell
SNR	Signal-to-noise ratio
SWSSG	Spatial wall shear stress gradient (Pa/mm), defined as $SWSSG = \left \frac{\partial \tau_w}{\partial x} \right $
Time-averaged WSS	Time-averaged wall shear stress (Pa), defined as $TAWSS = \frac{1}{T} \int_0^T \tau_w dt$
Time-averaged WSSG	Time-averaged wall shear stress gradient (Pa/mm), defined as $TAWSSG = \frac{1}{T} \int_0^T \left \frac{\partial \tau_w}{\partial x} \right dt$
WBC	White blood cell
WSR	Wall shear rate (s ⁻¹), defined as $WSR = \partial u / \partial n _{wall}$

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WSS Wall shear stress (Pa), defined as $WSS = \mu(\partial u / \partial n)|_{wall}$, where $\partial u / \partial n|_{wall}$ is the velocity gradient at the wall

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CHAPTER 1

INTRODUCTION

1.1 Background

1.1.1 Cardiovascular Disease and Treatments

Cardiovascular disease, caused mainly by atherosclerosis, continues to be one of the leading causes of death worldwide. In 2001, atherosclerosis contributed to nearly one-third of global deaths. By 2010 cardiovascular disease is predicted to be the leading cause of death in developing countries and by 2020 the WHO estimates nearly 25 million cardiovascular disease deaths worldwide (America Heart Association, 2005). The cost of cardiovascular diseases and stroke in the United States in 2005 is estimated at US\$393.5 billion (America Heart Association, 2005).

Atherosclerosis is a process in which the arterial wall thickens, leading to the growth of a stenosis and the eventual occlusion of blood flow, as shown in Figure 1-1. If an atherosclerotic lesion grows large enough so as to reduce the flow area substantially, blood cannot easily pass through to feed the downstream sites and severe reduction of the arterial blood flow will lead to organ dysfunction. Whatever the reason for reduced blood flow (fatty build up, blood clot, or spasm) the result is the same, not enough blood and oxygen reaching the heart muscle. When the blood supplying to the heart muscle is not sufficient for 15-30 minutes or even stopped, the heart muscle will be impaired, and results in a heart attack or a myocardial infarction. Without enough blood and oxygen, the heart muscle begins to fail and subsequently dies.

Figure 1-1 View of diseased coronary artery

Treatment for the cardiovascular disease varies depending on the severity, number and position of atherosclerotic lesions and the clinical history of the patient. Medications (cholestyramine, colestipol, nicotinic acid etc.) may be recommended to reduce fats and cholesterol in blood, or to trigger the smooth muscles of the arterial walls to relax, thus causing the arteries to dilate to increase blood flow. However, anginal symptoms cannot be effectively alleviated by medical treatment and restenosis may occur frequently (Henderson et al., 2003). Endarterectomy, which involves the surgical removal of the atherosclerotic plaque, is another option but is rarely adopted due to the poor results and the high risk (Alpe, et al., 2004). Balloon angioplasty, a non-surgical procedure is another optional treatment, but it cannot completely solve the problem. Recurrent narrowing has been reported in 28.3% of cases within 6 months (Minar et al., 2000) and 59% at 5 years (Tiia et al., 2002). Another widely used technique is stenting, which involves the deployment of a small metal device inside the artery to keep the artery open. However this procedure also does not eliminate the cause and 37% suffer from recurrences (Kenichi et al., 2004).

For life-threatening coronary disease or intractable angina, coronary artery bypass grafting (CABG) is frequently recommended (Serruys et al., 2001). Coronary bypass surgery involves bypassing the blocked portions of any or all of the three major coronary arteries: the left anterior descending coronary artery (LAD), the right coronary artery (RCA) and the circumflex coronary artery (CIRC) and some of their subsidiary branches with grafts, as shown in Figure 1-2.

Figure 1-2 Schematic View of the Heart with bypass grafts (taken from Hochman, 1982)

The autologous vein is the preferred bypass graft for arterial bypass operations if the size of the recipient artery and vein are compatible and no suitable autologous arterial bypass graft is available (Smith et al., 2001). When the diameter of the recipient artery is at least 6 mm in diameter, the synthetic vascular graft such as Dacron, Teflon and Polytetrafluoroethylene (PTFE) vein are often used particularly for bypassing stenotic

peripheral arteries (Trubel et al., 2004). In the anastomotic operation, one end of the vein graft is sewn to the coronary artery below the area of blockage (known as distal anastomosis), and the other is attached to the aorta, the main artery (known as proximal 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.

Although CABG has many benefits for the patient and provides good initial revascularization, graft failure as a result of restenosis has been the major concern, and remains unresolved. 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 much higher 1-year patency rate of 98% and 10-year patency rate of 90%. Also, 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).

1.1.2 Graft Failure and Intimal Hyperplasia

The early failure (0-6 months) of coronary bypasses is mainly due to the thrombosis caused by surgical trauma or technical error, resulting from long suturing time and high complexity in surgical manipulation (Manchio et al., 2005). The late failure (>1 year) of coronary bypass is related to fibromuscular intimal hyperplasia (IH) and subsequently atherosclerosis (Butany et al., 1998; Vural et al., 2005). Intimal hyperplasia is the rapid

abnormal continued proliferation and overgrowth of smooth muscle cells (SMCs) in response to endothelial injury or dysfunction (Sottiurai et al., 1989; Chervu and Moore, 1990; Virmani et al., 2000; Clowes et al., 2003). Although many theories have been postulated to explain initiation and progression of IH, the exact mechanism is still not fully understood. But many studies have identified that the vascular injury, suture-line stress, compliance mismatch and disturbed local hemodynamics are critical factors involved (Stewart et al., 1992; Ballyk et al., 1998; Newby and Zaltsman 2000; Keynton et al., 2001).

Hemodynamic factors are more critical both in serving as a regulator and modifier of cellular biology and in the development of the disease process (Hofer et al., 1996; Allaire and Clowes, 1997; Greenwald and Berry, 2000). 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; Loth et al., 2002; Ethier, 2002), low and oscillating shear (Bassiouny et al., 1992; He and Ku, 1996; Taylor et al., 1998), high wall shear (Fry, 1969; Friedman, 1992; Wu et al., 1995; Krueger et al., 2000; Stangeby and Ethier., 2002), “safe-bandwidth” of the wall shear stress (WSS) (Nazemi et al., 1989; Kleinstreuer et al., 1991), wall shear stress gradient (WSSG) (Henry et al., 1996; Kleinstreuer et al., 1996; Keynton et al., 2001; Buchanan et al., 2003).

Furthermore, factors such as anastomosis angle (Taylor et al., 1992; Hughes and How

1995, 1996; Henry et al., 1996; Loth et al., 1997; Shipkowitz et al., 1998; Song et al., 2000; Jackson et al., 2001), wall curvature (Lei et al., 1995; Rowe et al., 1999; How et al., 2000), flow rate ratio (Fei et al., 1994; Hughes and How, 1995 and 1996; Henry et al., 1996; Khunatorn et al., 2002), wave form (White et al., 1993; Kleinstreuer 1996; Ethier et al., 1998; Ku et al., 2002) were considered as the parameters to affect the flow fields and would be able 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 electrochemical method (Yamaguchi and Kohtoh, 1994), flow visualization using dye-injection (Crawshaw et al., 1980), laser illumination of particles suspended in the fluid (White et al., 1993; Hughes and How., 1995) and the hydrogen bubble technique (Keynton et al., 1991). Velocity profile and wall shear stress have also been determined using the photochromic tracer techniques (Ojha, 1993; Ojha et al., 1993; Guo et al., 2001) and Laser Doppler Anemometry (LDA) (Keynton et al., 1991; Loth et al., 1997; Li and Rittgers, 2001). Particle Image Velocimetry (PIV) (Bates et al., 2001; Heise et al., 2004) has also been implemented to investigate the hemodynamics.

1.1.3 Motivations

Most of the studies were carried out on subsections of the bypass flow domain, especially the distal anastomosis. Rare efforts have been put on proximal anastomosis except Ojha et al., (1993), Hughes and How (1995) and Zhang (2005) and the entire bypass domain. However, the distal anastomosis is not isolated but systematic linked with aorta through proximal anastomosis with curved graft and it is not surprising that the flow patterns at the distal anastomosis will be significantly affected and complicated by the upstream flow, e.g. flow characteristics at the proximal anastomosis and curved graft tube. 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). Especially for the vein graft, apparent intimal hyperplasia plaques were usually found at the proximal anastomosis, where eddy blood flows formed, and progressed toward the distal anastomosis (Liu and Fung, 1998). For the reverse vein graft, most common graft lesions developed adjacent to the proximal anastomosis, which is the narrowest part of a reversed vein graft (Berkowitz et al., 1992).

In addition, a coronary artery bypass flow model must be anatomically accurate so as to capture the essential hemodynamics of the true geometry (Moore et al., 1999). For considering the influence of hemodynamic factors on graft patency, it is important to replicate the in-vivo geometry of the entire bypass conduit. The complex anatomy of coronary vessel has made the investigation of coronary flow and hemodynamics one of the most difficult and challenging studies until now.

Therefore in order to obtain the physical insight of the flow characteristics of the bypass graft domain, experimental work was done to explore the flow structure in the proximal anastomosis at the first stage of study. In end-to-side/side-to-end anastomoses, the geometry of the anastomosis in particular the anastomotic angle may be a more important factor in the flow characteristics, rather than the mismatch in elastic properties between the graft and host aorta/artery (Chandran and Kim, 1994). Hence investigation on proximal anastomosis models with different anastomotic angle was carried out and the hemodynamic performances of the models were evaluated to propose the optimal proximal anastomotic angle. Subsequently investigation on the whole anastomosis model, which was designed based on the real-life situation, was carried out to enhance the understanding of stenosis pathophysiological process in CABG.

Bypass configurations, especially the bypass geometry, are recognized as the primary factors that strongly alter anastomotic hemodynamics and thus long-term bypass graft patency (Jackson et al., 2001). As a consequence, restenosis and thrombosis may be greatly mitigated if specific junction geometries could be determined such that nonuniformity of hemodynamics are avoided or reduced. Studies have been performed to optimize the distal anastomotic configuration for better hemodynamic performance including the using of Miller cuff (Cole et al., 2002a and 2002c; Leuprecht et al., 2002; Perktold et al., 2002), Taylor patch (Taylor et al., 1992; Cole et al., 2002b) and optimal femoral bypass geometry (Lei et al., 1997). However, most of the studies are focused on the peripheral bypasses, such as below-keen popliteal bypasses and femoral bypasses, and little has been done for coronary artery regions. Based on the experimental investigation on the whole anastomosis and numerical study of Zhang (2005), it is noted that disturbed flow patterns occurred most seriously at the distal anastomosis and elevated WSSG was found near the toe and the arterial floor of the distal anastomosis where the intimal hyperplasia was shown to be more susceptible to occur. In order to maintain the long-term bypass patency, it is necessary to reduce the nonuniformity of hemodynamics at the distal anastomosis by improving its geometrical configuration. Therefore in present study the improvement on the geometry of the distal anastomosis was carried out and its hemodynamic performances was evaluated under typical physiological flow conditions.

Particle Image Velocimetry method was recently implemented for hemodynamics investigation (Bates et al., 2001; Stanislas et al., 2003; Heise et al., 2004). Compared to PIV technique, LDA, the traditional point-wise velocity measurement technique, is not able to reveal information on the instantaneous spatial structure of the flow. In addition, the shortcoming of flow visualization method is that the quantitative information about

the flow field is difficult to be extracted for further analysis. However, since PIV is a spatial measurement technique, instantaneous coherent flow structures can be visualized and related flow quantities can be extracted and computed. Therefore, the PIV was selected as the research tool in the study.

1.2 Objectives and Scope

The PIV measurements were carried out in order to accomplish the following objectives:

1. To investigate the 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 for the proximal anastomosis models.
2. To evaluate the hemodynamic performance of different proximal anastomosis models according to the flow characteristics and HPs distributions.
3. To investigate the hemodynamics of the whole anastomosis model under both steady and pulsatile flow conditions for better understanding of the path physiological process of stenosis.
4. To propose a geometry improvement for the distal anastomosis of coronary artery bypass and to evaluate its hemodynamic performance by comparing with that of baseline model.
5. To investigate the effect of proximal coronary artery flow (retrograde and zero proximal flow conditions) on local hemodynamics of the distal anastomosis.

Distributions of both flow field and HPs are presented, as they are the important factors contributing to the growth of intimal hyperplasia, and/or atherosclerosis. The investigation of steady flow is to provide some physical insight into the causes of specific flow features that may also exist in pulsatile flow. Physical flow condition would allow

these features to be specifically identified as geometric phenomena rather than unsteady phenomena.

In this study, two experimental test rigs were designed and constructed to conduct the PIV measurements for (1) proximal & whole anastomosis models and (2) distal anastomosis models. Computer controlled piston pump and gear pump systems were used as the pulsatile flow generators. The test models were fabricated as rigid tubes for both Pyrex glass model and silicon rubber model, with the assumption that synthetic graft and diseased arteries are expected to be relatively stiff. The physiological data for the sizes of the graft and the coronary artery was provided by Singapore National Heart Centre, and is based on local Asian patients who have suffered from the disease. Since saphenous vein graft is most commonly used and has much lower patency rate than arterial grafts, the physiological data of saphenous vein graft are adopted in the experiment. The anastomotic test models are designed in true scale and the fluid is specially mixed to match the mechanical properties of the blood (viscosity, density, etc.), in order to provide more realistic scenarios and results.

1.3 Outline of the Report

Chapter 2 reviews the previous investigation on the hemodynamics of bypass anastomosis and the graft failure, which includes the in-vivo and numerical simulation, as well as the in-vitro experiments. Chapter 3 describes the experimental arrangements used in the investigation. Detailed information about the flow circuit, test models, working fluids and pulsatile flow waveform generators are presented. Chapter 4 gives an introduction to Particle Image Velocimetry and its application in the experiment. Chapter 5 presents and discusses experimental results in proximal models with different anastomosis angle.

Chapter 6 presents and discusses the results of the whole anastomosis model. The hemodynamic performances of the baseline and improved models are evaluated and compared in Chapter 7. 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 pathogenesis and theory of IH formation is firstly reviewed. Then studies of hemodynamics upon the coronary artery bypass anastomosis are reported.

2.1 Pathogenesis and Theory of IH Formation

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 2-1 illustrates the intimal thickening process of rat carotid artery after injury obtained by Clowes (2003). 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 (Allaire and Clowes, 1997). 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.

Figure 2-1 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).

Although the pathogenic mechanisms responsible for the development of IH remain elusive, it is generally believed that these pathological changes are remodeling process wherein a change in the mechanical environment which stimulates cellular responses and subsequently results in the remodeling (Vorp, 1997).

2.1.1 Biological Factors

The endothelial cells (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.

Monocytes and cholesterol (oxidized low-density lipoproteins (LDL)), also aided by endothelial cytokines and adhesion molecules, accumulate in the intima creating foam cells. 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 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). In human aortocoronary artery vein grafts, significant cellular hyperplasia occurs mainly at the suture line in the early stages (6 weeks or less post-operatively) with IH becoming greatest on the hood of the graft and at the suture line at later stages (1.5-15 years post-operatively) (Butany et al., 1998). 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). These findings, together with the observation that IH forms around the injury site after balloon angioplasty, suggest the involvement of a wound healing process in IH formation. However, unlike a generally wound healing process which becomes quiescent in a short period of time, some IH continues to develop for years.

2.1.3 Compliance Mismatch

Compliance is a measure of blood vessel dispensability and may be defined as the fractional increase in diameter per unit change in pressure. 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 pseudo-aneurysms. 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. Study by Bassiouny (1992) has shown that a higher degree of compliance mismatch (graft stiffer than artery) results in a greater amount of IH formation. This proposal was again verified by numerical studies and in-vitro studies carried out by Stewart et al. (1992) and Moore et al. (1999). Even if grafts have the same compliance as the host artery upon implantation, the grafts often do not retain their original compliance after extended use (Uchida et al. 1989). The graft reacts with the host environment having its compliance changed. Moreover, the suture line, whatever the technique used, is the point of greatest compliance mismatch. Helal et al. (1994) stated that there were no significant differences in the flow delivery between the compliant graft and stiff graft. 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).

2.1.4 Hemodynamic Factors

The process of atherogenesis is complicated and involves a lot of physiological and pathological events. Many researchers think atherosclerosis begins because the innermost layer of the artery, the endothelium, becomes damaged (Stary et al., 1992; Libby et al., 2002). The wall of an artery is composed of several layers. The lining or inner layer (endothelium) is usually smooth and unbroken. Atherosclerosis begins when the lining is injured or diseased. Then certain white blood cells called monocytes are activated and

move out of the bloodstream, and penetrate through the lining into the artery's wall. Inside the lining, they are transformed into foam cells, which are cells that collect fatty materials, mainly cholesterol. In time, smooth muscle cells move from the middle layer into the lining and multiply there. Platelets also play a role in the atherosclerosis process by releasing a substance called "platelet growth factor" which can stimulate the growth of smooth muscle cells (Jawien et al., 1992). Connective and elastic tissue materials also accumulate there as cell debris, cholesterol crystals, and calcium. Excess low-density-lipoproteins (LDL) in the blood are trapped with the artery wall and oxidized. These "modified" lipoproteins are rapidly taken up by smooth muscle cells, which in turn lead to the formation of foam cells that result in the deposition of connective tissue cells and element (Virmani et al., 2000). This accumulation of fat-laden cells, smooth muscle cells and other materials forms a patchy deposit called an atheroma or atherosclerotic plaque. As they grow, atheromas thicken the artery's wall and bulge into the channel of the artery.

Local hemodynamic forces control the development, structure, and function of blood vessels (Resnick et al., 2003); therefore, it is not surprising that these forces have been implicated in the pathogenesis of atherosclerosis. The luminal surface of the blood vessel and its endothelial surface are constantly exposed to hemodynamic shear stress. Earlier studies identified that high wall shear stress (WSS) 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 (Fry, 1968). Endothelial adaptations to high stress also include the redistribution of F-actin microfilaments from the cell junctional regions to the central stress fibers, where the F-actin is important in regulating cell permeability (Schnittler, 1998). Therefore, the permeability control may be compromised by high shear stress. In contrast, the low and oscillating wall shear stress exhibits greater smooth muscle

cell proliferation and the higher levels of the platelet-derived growth factor-A protein and mRNA (Mattsson et al., 1997). Also, low and oscillating wall shear stress affects the elongation and orientation of the endothelial cells in the direction of shear stress and results in an aggressive and proliferative phenotype (Davies, 1995) and responses to early atherosclerotic lesion (Buchanan et al., 1999 and 2003). In addition, spatial wall shear stress gradient (SWSSG) induces morphological and functional changes in the endothelium, which contribute to the elevation of the wall permeabilities and hence possible atherosclerotic lesions (Depaola et al., 1999).

In summary, high WSS will cause the endothelial injury and increase transmural filtration and elevate the LDL influx. Furthermore, high WSS could enhance the activity of the vessel wall and the vasoactive substance released from these regions might exert their action in the low WSS environment where a better interaction with the vessel wall is possible due to the longer residence time. On the other hand, low and oscillating WSS is related to high LDL concentration as well as reducing the oxygen flux into the wall (Ethier, 2002). SWSSG also contributes to the elevated wall permeability and possible atherosclerotic lesions. Taken all these factors into consideration, it can be concluded that the disease process may be influenced by the combination of several hemodynamic parameters. Therefore, in this study, the hypotheses that regions of low-WSS-high-OSI and high-WSS-low-OSI are corresponded to the early atherosclerotic lesion development (Buchanan et al., 1999 and 2003) and elevated time-averaged WSSG region is susceptible to atherosclerotic lesions (Lei et al., 1995 and 1996) were adopted as indicators of susceptible sites.

2.2 Studies of Hemodynamics upon Anastomosis

It is well accepted that hemodynamics plays an important role in the formation of intimal thickening in vascular graft anastomosis, which in turn is a major cause of graft failure. It is not unexpected that numerous research works had thus been carried out intensively to investigate the hemodynamic related factors, such as geometry of anastomosis, compliance mismatch between graft and host artery, wall shear stress and strain and flow characteristics in the vessels. The main purpose is to establish the correlation of fluid dynamic variables with biological factors, such as mitogenic factors, platelet activation and etc. The most commonly used methods include in-vivo studies, computational simulations and in-vitro model experiments.

2.2.1 In-Vivo Study

In-vivo study is an important research method to get the first-hand feedback information in bioengineering area. Since 1970s, many researchers have put a lot of effort on in-vivo studies about the relationship between the hemodynamic factors and the number of occurrence and locations of intimal hyperplasia, using both animal experiments and human implantations.

2.2.1.1 Geometry of Anastomosis

The angle of anastomosis of the graft was believed to be the major determinant factor of local hemodynamics. Many researchers had put a lot of effort on these studies, trying to find the optimal anastomosis angle to improve graft patency rate. As far as 1976, Bond et al. constructed autologous arteriovenous bypass grafts, at 55, 90 or 120-degree angles relative to the proximal anastomosis, between external iliac arteries in 20 mongrel dogs to determine the development of intimal fibromuscular hyperplasia. Grafts placed at 55-

degree angle relative to the proximal anastomosis were found developing a consistently thicker fibromuscular layer in the tunica intima when compared to the other groups.

In 1995, Staalsen et al. did similar work to study the effect of anastomosis angle on the flow fields at the end-to-side anastomosis, by implanting polyurethane grafts of 8mm in diameter into 10 pigs with different anastomotic angles (15, 45 and 90 degrees). Figure 2-2 shows the interpretation and summary of the flow fields in different anastomosis. The figures indicate that the characteristics of the flow field determined from the color-flow Doppler data and show the location of the highest, the lowest, and the reverse velocities by arrows at each anatomic position at different phases of the flow cycle. The results suggested that the smallest anastomotic angle (15 degrees) is associated with the least flow disturbances at the toe and one diameter downstream. This study confirms the in-vivo existence of regions of low and reverse velocities at the preferential sites in vascular end-to-side anastomoses where neointimal hyperplasia tends to form.

Figure 2-2 Summary and interpretation of flow visualization (Taken from Staalsen et al., 1995)

The studies about the effect of anastomotic angle on the local hemodynamics and pathologic response were carried out by Jackson et al. (2001). 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.

Beside anastomosis angle, some other geometry parameters were investigated in the in-vivo studies. Mark et al. (1990) explored graft geometry and hemodynamics in a reproducible canine arteriovenous loop graft model of intimal-medial hyperplasia. Ten untapered 6 mm diameter polytetrafluoroethylene grafts ($n = 10$) were paired with 4 to 7 mm taper ($n = 5$) or 7 to 4 mm taper ($n = 5$) grafts for a 12-week period. The result showed that graft geometry could have a significant impact on hemodynamic factors and venous intimal-medial hyperplasia in arteriovenous loop grafts.

Jones et al. (1997) recorded the in-vivo velocity profiles with a 20 MHz, 80-channel pulsed Doppler ultrasound velocimeter in canine end-to-side ilio-femoral anastomotic grafts. Three cases including a “standard” geometry, a stenosed geometry and a case with below average flow rate were reported as shown in Figure 2-3. The left side of the figure shows the graft geometries and probe positions for the three anastomoses, the standard geometry, the stenosed geometry and the low-flow case, and arrows indicate the locations and orientations of the ultrasound probe. The other side of the figure shows the velocity directions of corresponding anastomosis model at different flow phase. Observed flow

features include 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 appear to have a strong effect on the flow fields. In addition, compliance affects the instantaneous flow rates within the proximal and distal branches. As a conclusion, variations in graft geometry may be an important determinant of the spatial distribution of the intimal hyperplasia.

Figure 2-3 Summary of Flow pattern in three different cases (taken from Jones et al., 1997)

2.2.1.2 Wall Shear Stress

Since Endothelial Cells (ECs) have been shown to be shear sensitive (Davies, 1991), theories about vascular response involving high, low and oscillatory shear stresses, and high shear stress gradients have received extensive attention (Fry et al. 1968; Ojha et al. 1993; Lei et al. 1996). The high shear stress theory was first proposed by Fry et al. (1968) who demonstrated endothelial damage at high levels of shear stress by directing a jet of fluid onto the surface of excised arteries. Thereafter many efforts have been put on the investigation on wall shear stress and graft failure.

In 1985, Morinaga et al. investigated the effect of wall shear stress on the intimal thickening of arterially transplanted autogenous veins in dogs. Two models of canine femoral arteries were developed to determine whether changes in wall shear stress play a determinant role in the induction of hyperplasia of intimal tissue of arterially transplanted vein grafts. In group I, grafts were implanted under flow conditions of $79.7 \pm 3.2 \text{ ml/min}$ of the normally high flow rate with $33.1 \pm 1.9 \text{ dynes/cm}^2$ of low wall shear stress. In-group II, model grafts were implanted under conditions of $2.9 \pm 1.8 \text{ ml/min}$ of the normally low flow rate with $178.8 \pm 11.0 \text{ dynes/cm}^2$ of high wall shear stress. The intimal thickness after implantation of group I was statistically significant comparing with group II. The study revealed that change in wall shear stress and not the rate of blood flow is the essential hemodynamic factor related to intimal hyperplasia.

Later on, in 1989 Binns et al. continued to investigate the effect of wall shear stress on vascular healing and tried to determine the optimal graft diameter. Forty polytetrafluoroethylene grafts with internal diameters of 3, 6 and 8 mm were inserted end-to-end in the femoral and carotid arteries of 10 mongrel dogs. Total flow and diameter

were measured, and 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 result showed that the percentage of graft surface covered with neointima did not differ among the grafts of differing diameter either proximally or distally. Lower shear stresses produced greater amounts of pseudointimal thickening within polytetrafluoroethylene grafts and neointimal thickening at their anastomoses. Conversely, the high shear stress from small-diameter grafts was associated with poor graft patency. The result also suggested that an optimal graft diameter might help to prevent neointimal hyperplasia and graft thrombosis.

The low shear stress theory was first proposed by Caro et al. (1969) who established that atherosclerosis usually developed in regions of the artery exposed to a low level of average shear stress. They postulated that at low shear rates, the ECs did not receive a sufficient amount of nutrients, and, simultaneously, waste products tended to accumulate on the cell surface that led to the necrosis of cells.

Further research on role of the low shear stress in the vein graft failure and neointimal thickening (NIT) was carried out by Meyerson et al. (2001) using a new experimental model, which maintained patency at low shear stress ($<2 \text{ dyne/cm}^2$) to delineate possible deviations from linearity in the low shear stress $\rightarrow$ NIT hypothesis. In their study, thirty-two New Zealand White rabbits (3-3.5kg) underwent creation of a common carotid vein patch with a segment of ipsilateral external jugular vein. A 1.5-cm longitudinal arteriotomy was made in the common carotid artery proximal to the cranial thyroid branch. Patches were created such that the final reconstruction diameter ranged 1.5-3.0 times of the native artery. As shown in Figure 2-4, normal flow and shear were created in

11 patches, and low shear stress was created in 13 patches by ligation of the ipsilateral common carotid artery just distal to the cranial thyroid branch. Finally, high shear was created in 8 patches by ligation of the contralateral common carotid artery, which resulted in increasing ipsilateral carotid artery flow. All patches harvested after 2 weeks were patent. Mean flow at implantation ranged from 0.4 to 1.8 ml/min in the low flow group and 20 to 52 ml/min in the normal flow group. This corresponded to a mean shear stress less than 1 dyne/cm^2 in all low flow patches and more than 10 dyne/cm^2 in all normal flow patches. In the high shear stress construction, only the vein patch exhibited NIT and the artery appeared histologically normal. In contrast, low shear stress generated significant and reproducible NIT, which affected not only the vein patch but also the arterial half of the construct and produced significant luminal reduction (28%-33%). The study revealed that the relationship between shear stress and NIT in vein graft is nonlinear and that extremely low shear stress ($<2 \text{ dyne}/\text{cm}^2$) stimulates high rates of smooth muscle cell activation, proliferation, and hyperplasia.

Figure 2-4 Experimental model of vein patch angioplasty in Common Carotid Artery. (Taken from Meyerson et al. 2001)

Similar conclusion was obtained by Passerini et al. (2003) in the investigation of the relationship between wall shear stress and the development of intimal hyperplasia from a new aspect: simultaneously monitor the transcriptional levels of 12 endothelial growth factor genes. The response of ECs to biomechanical stimuli is of importance in both normal vascular physiology and numerous pathologies. Growth factors expressed by ECs in response to luminal wall shear stress may contribute to the pathology of intimal hyperplasia, a major cause of bypass graft failure. In the study, human umbilical vein endothelial cells were preconditioned in-vitro under steady flow (15 dyne/cm^2) for 24 hours before being subjected to wall shear stress at 25, 15, 5, 2.5, and 0 dyne/cm^2 or low magnitude wall shear stress reversal (-2.5 dyne/cm^2) for 6 hours. A focused complementary DNA array was used to simultaneously measure the endothelial growth factor genes. Marked changes were seen in the group exposed to a step increase in wall shear stress or to wall shear stress reversal and low magnitude retrograde wall shear stress evoked significant transcriptional changes in multiple genes, which leading to intimal hyperplasia at regions of low magnitude reversing wall shear stress.

2.2.1.3 Wall Shear Stress Gradient

Studies of wall shear stress gradients (WSSG) have demonstrated that a spatial wall shear stress gradient ($\text{SWSSG} = d\tau/dz$) leads to changes in the ECs which cause them to reduce the gradient microscopically, this playing a key role in the morphological remodeling of the vascular endothelium (Depaola et al. 1992). A higher spatial wall shear stress gradient also causes higher EC loss and proliferation (Tardy et al. 1997). While fluid shear stress regulates EC-released mitogens and growth factors in a very complex way by decentralized signal transduction, the effects of strain applied to the EC are believed to be no less important (Ziegler et al. 1998). For example, application of an external support

can reduce IH formation in a venous bypass graft, suggesting the importance of circumferential wall stress in the uniform thickening of the vein graft implanted into the arterial system (Liu et al. 2000).

In 1999, Keynton et al. used 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, plays 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 showed that wall shear rate (WSR) varies widely within end-to-side distal graft anastomoses, particularly along the artery floor, and may play a role in the development of intimal hyperplasia through local alteration of mass transport and mechano-signal transduction within the endothelium.

Keynton et al. (2001) further investigated the relationship between intimal hyperplasia development and WSSG and WSR in arterial bypass graft. Tapered (4–7 mm I.D.) e-PTFE synthetic grafts 6cm long were placed as bilateral carotid artery bypasses in six adult mongrel dogs weighing between 25 and 30kg 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 in the plane of the anastomosis at radial increments of 0.35mm, 0.70mm, and 1.05mm using a specially designed 20MHz triple crystal ultrasonic wall shear rate transducer. Mean, peak, and pulse amplitude WSR, their absolute values, the spatial and temporal wall shear stress gradients, and the oscillatory shear index (OSI) were computed from

these velocity measurements. All grafts were harvested after 12 weeks implantation and measurements of the degree of intimal hyperplasia (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, although 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. Although these correlation coefficients were not high, they were found to be statistically significant as evidenced by the large F-statistic obtained. Finally, it was observed that over 75 percent of the IH occurred at or below a mean WSR value of 100 s^{-1} while approximately 92 percent of the IH occurred at or below a mean WSR, which equals to one-half of the native artery's WSR. Therefore, while not being the only factor involved, wall shear stress (and in particular, oscillatory wall shear stress) appears to provide a stimulus for the development of anastomotic intimal hyperplasia.

However, an 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. A major assumption of the study was that the synthetic and venous Miller's cuffs constructed with the same geometry should result in a similar hemodynamic environment in both anastomoses. They, therefore, stated 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.

2.2.1.4 Compliance Mismatch

In arterial bypasses, compliance mismatch between the artery and the graft is regarded as another mechanical factor that may lead to IH formation. As far as 1985, Hasson et al. studied the relationship between compliance mismatch and the graft failure using a simplified model based on isocompliant arterial grafts and pulsed ultrasound, which was used to generate detailed longitudinal profiles of diameter and compliance near the anastomoses. These longitudinal profiles revealed that although arterial diameter decreases monotonically to a minimal level at an anastomosis, arterial compliance first increases by approximately 50% before decreasing to 60% of the control value. This para-anastomotic hypercompliant zone (PHZ) is centered 3.6 mm from the anastomosis. PHZ also occurs in the artery adjacent to compliant or stiff grafts and is probably caused by transmitted effects of the suture line on the arterial wall. PHZ adds to any mismatch in compliance that already exists between artery and graft and can produce a compliance mismatch even between an artery and a nominally isocompliant prosthetic graft. It was hypothesized that PHZ, a region of increased cyclic stretch, promotes subintimal hyperplasia near anastomoses and may thus be a link between the mechanical properties of arteries and the failure of bypass grafts.

Bassiouny et al. (1992) investigated the localization of experimental anastomotic intimal thickening in relation to known biomechanical and hemodynamic factors. Bilateral iliofemoral saphenous vein and polytetrafluoroethylene grafts were implanted in 13 mongrel dogs. The distal end-to-side anastomotic geometry was standardized, and the flow parameters were measured. Model flow visualization studies revealed a flow

stagnation point along the arterial floor resulting in a region of low and oscillating shear where the second type of intimal thickening developed. High shear and short particle residence time were observed along the hood of the graft, an area devoid of intimal thickening. Regions of relatively low shear and long particle residence time formed along the lateral walls and heel of the anastomoses were not specifically related to intimal thickening at the suture line. They concluded that at least two different types of anastomotic intimal thickening exist, as shown in Figure 2-5. Suture line intimal thickening represents vascular healing; greater prominence with prosthetic grafts may be related to compliance mismatch. Arterial floor intimal thickening is unrelated to graft type and develops in regions of flow oscillation and relatively low shear. Trubel et al. (1994) also obtained similar results in their research on compliance and formation of intimal hyperplasia of arterial bypass graft. The results showed that a higher degree of compliance mismatch (graft stiffer than artery) results in a greater amount of IH formation.

Figure 2-5 Distribution of intimal hyperplasia in recipient artery following end-to-side anastomosis (taken from Bassiouny et al, 1992)

However, research conducted by Okuhn et al. (1989) indicated that compliance mismatch alone is an insufficient stimulus for the development of neointimal hyperplasia in the canine model. In the study, one 3 cm segment of common iliac artery was externally banded in seven dogs, thereby fixing the arterial diameter at end diastole and end-diastole

diameter and its change with pulse pressure were measured by induction angiometry. Okuhn et al (1989) showed that no matter what the primary mechanical stimulator is, it seems that compliance mismatch alone, without trauma, only caused limited amounts of IH formation. Likewise, investigation carried out by Wu et al. (1993) did not show the similar trend in host arterial IH formation..

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 Computational Simulations

The development of computational fluid dynamic (CFD) techniques provides a powerful tool for determining complex biofluid phenomena, such as particle streamlines in various grafting configurations, which are difficult to study accurately in-vivo or in-vitro experiments with less expense. Numerous studies had been carried out about the role of mechanical factors in the development of IH and bypass graft failure.

2.2.2.1 Geometry of Anastomosis

It is well known that the hemodynamic environment depends heavily on the anastomotic geometry. The primary geometric feature that influence the hemodynamic environment in the conventional end-to-side anastomosis includes the graft angle (Fei et al. 1994) and graft-to-host artery area ratio (Moore et al. 1999), while other features, such as out-of-plane curvature and surface roughness have much less influence (Sherwin et al. 2000). However, other researchers found that the out-of-plane curvature alters the distribution of wall shear stress at the bed of anastomosis and reduces the peak wall shear stress value (Sherwin et al. 2000, Papaharilaou et al. 2002).

In 1990, a numerical investigation of the influence of bypass geometrical parameters, such as degree of coronary stenosis, the bypass diameter and the anastomotic angle, on the fluid dynamics around the distal anastomosis, using a two-dimensional finite element model, was conducted by Pietrabissa. The result 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.

Fei et al. (1994) investigated the effect of angle and flow rate upon hemodynamics in distal vascular graft anastomoses using numerical simulation. The purpose of the study is to examine flow patterns and wall shear rate under various conditions of anastomotic angle configurations and flow rates. In the study, steady flow in distal end-to-side anastomoses of iliofemoral artery bypass graft using various three-dimensional numerical models of varying angles from 20 to 70 degrees were simulated. Separated flow regions were seen along the inner arterial wall (toe region) while a stagnation point existed along the outer arterial wall (floor region) and the stagnation point moved downstream relative

to the toe of the anastomosis with decreasing angles. Normalized shear rates (NSR) along the arterial wall varied widely throughout the anastomotic region with negative values seen in the separation zones and upstream of the stagnation points which increase in magnitude with angle. The NSR increased with distance downstream of the stagnation point and with magnitudes which increased with the angle. The results of in-vivo studies appear to support the hypothesis of greater intimal hyperplasia occurring in regions of low fluid shear.

Ballyk et al. (1995) conducted the investigation on stress distribution at an end-to-side anastomosis. In this study, the mechanics of a 45-degree end-to-side graft-artery anastomosis were simulated numerically in order to determine what impact the geometry itself has on stress distribution, and the resulting stress distribution was then compared with the known distribution of intimal hyperplasia at the end-to-side anastomosis. The result predicted that the hyperplasia in the heel might be influenced by either the large stress concentration or large stress gradients that occur at this location. Significant stress concentration and gradients may also contribute to hyperplasia around the suture line.

In 1999, Moore et al. attempted to determine how much an anatomically realistic geometry can be simplified without the loss of significant hemodynamic information, by using the numerical simulation of the blood flow patterns in an anatomically realistic and simplified end-to-side anastomoses. A human femoral-popliteal bypass graft was used to reconstruct an anatomically faithful finite element model of an end-to-side anastomosis. Nonideal geometric features of the model were removed in sequential steps to produce a series of successively simplified models. Blood flow patterns were numerically computed for each geometry, and the flow and wall shear stress fields were analyzed to determine

the significance of each level of geometric simplification. The results showed that the removal of small local surface features and out-of-plane curvature did not significantly change the flow and wall shear stress distributions in the end-to-side anastomosis. Local changes in arterial caliber played a more significant role, depending upon the location and extent of the change. The graft-to-host artery diameter ratio was found to be a strong determinant of wall shear stress patterns in regions that are typically associated with disease processes. Hence they concluded that for the specific case of an end-to-side anastomosis, simplified models provide sufficient information for comparing hemodynamics with qualitative or averaged disease locations, provided the "primary" geometric features are well replicated. The ratio of the graft-to-host artery diameter was shown to be the most important geometric feature. "Secondary" geometric features such as diameter changes, out-of-plane curvature, and small-scale surface topology are less important determinants of the wall shear stress patterns. However, if patient-specific disease information is available for the same arterial geometry, accurate replication of both primary and secondary geometric features is likely required.

The influence of out-of-plane geometry, the so-called "Secondary" geometric feature, was further investigated by Sherwin et al. (2000). They conducted a computational and experimental investigation of flow in a model geometry of a fully occluded 45-degree distal end-to-side anastomosis, where the centerlines of the bypass and host vessel lie within a plan, whereby producing a plane of symmetry within the flow. Subsequently they extended the investigation by deforming the bypass vessel out of the plane of symmetry, thereby breaking the symmetry of the flow and producing a nonplanar geometry, as shown in Figure 2-6. Experimental data were obtained using magnetic resonance imaging of flow within perspex models and computational data were obtained from simulations

using a high-order spectra/hp element method, by assuming that the model is noncompliant, the flow is unsteady, and the fluid is Newtonian. It was found that the nonplanar three-dimensional flow notably alters the distribution of wall shear stress at the bed of anastomosis, reducing the peak wall shear stress by approximately 10% 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% was observed in the nonplanar geometry when compared with the planar geometry.

The further study on the influence of out-of-plane geometry was conducted by Papaharilaou et al. (2002) by introducing flow pulsatility and using the same model geometries, which were used in Sherwin et al. (2000). The result indicated that a significant change in the spatial distribution of wall shear stress and a reduction of the time-averaged peak wall shear stress magnitude by 10% in the non-planar model as compared to the planar configuration. In the planar geometry the stagnation point follows a straight-line path along the host artery bed with a path length of 0.8 diameters of artery. By contrast in the non-planar case the stagnation point oscillates about a center that is located off the symmetry plane intersection with the host artery bed wall, and follows 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 non-planar geometry was reduced by 22% as compared to the planar configuration. They conclude that these changes in the dynamic behavior of the stagnation point and the oscillatory shear stress distribution introduced by out-of-plane graft curvature may influence the localization of vessel wall sites exposed to physiologically unfavorable flow conditions.

Figure 2-6 Model geometries of distal of the 45-degree end-to-side anastomosis (a) planar, (b) nonplanar. (Taken from Sherwin et al. 2000)

Lee et al. (2001) carried out a numerical simulation of steady flow fields in a complete bypass tube, including both the bypass and the host tubes. The changes of the hemodynamics were investigated with the inlet flow Reynolds number, anastomotic angle and the position of the occlusion in the host tube. The result revealed that the higher flow rate tends to expand the size of recirculation zones in the host tube and in the bypass as well. The smaller angle has weakened the secondary flow and smoothened overall flow, however it takes longer suture line, which is not the usual practice and may induce other problems.

Since the local arterial geometry is an important determinant of local hemodynamics, it has been proposed that an individual's "geometric risk factor" may strongly influence the risk for arterial disease (Friedman et al. 1989). For bypass graft, intimal hyperplasia was found most prominently in the distal end-to-side anastomosis whose geometry differs considerably from that of a natural arterial bifurcation (LoGerfo et al. 1983, Butany et al.

1998). Therefore, efforts have been made to optimize the anastomotic design by eliminating or reducing the hemodynamic factors that are suspected of stimulating IH formation.

Kleinstreuer et al. (1996) employed the wall shear stress gradients (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 wall shear stress gradient, thus enhance the patency of graft. The performance of these near-optimal graft-artery connectors were then evaluated by analyzing the effects of various flow input waveforms on the temporal and spatial WSSG distributions. They also believed that high gradients of wall shear stress would contribute to the development of intimal hyperplasia. Lei et al. (1997) also carried out numerical simulation on the geometric design improvement.

The modification of the distal anastomosis of polytetrafluoroethylene (PTFE) bypass grafts with vein interposition cuffs (VCs) has been reported to increase graft patency. Kissin et al. (2000) investigate the mechanisms that are responsible for this improved patency. Twenty-three female domestic Yorkshire pigs underwent 42 femoral PTFE bypass grafting procedures and the PTFE grafts were separated into three groups according to distal anastomotic configuration: end-to-end anastomoses (ES), VCs, and cuffs constructed with PTFE (PCs). The result showed that PTFE bypass grafts with VCs had less IH develop than did grafts with ES and PC anastomoses. Furthermore, VCs caused a redistribution of hyperplasia to the vein-PTFE interface, delaying IH-induced outflow obstruction in the recipient artery. The marked increase in IH with PCs, despite a

similar geometric configuration to VCs, suggested that the biologic properties of autogenous tissue dissipate IH development. In these studies, however, only the physiologically loaded geometries were considered in the optimization, making the specifications of initial geometry difficult to define in the construction process.

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 2-7 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 2-8 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 2-8 Symmetry plane of the Taylor bypass model (S1 indicates sites at which results are plotted) (taken from Cole et al., 2002b)

2.2.2.2 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.

Ballyk et al. (1998) studied the effect of compliance mismatch on the development of intimal hyperplasia by altering suture line stresses. A large strain finite element analysis of vascular wall mechanics was performed to compare the influence of compliance mismatch on intramural stresses in end-to-end versus end-to-side anastomoses by using a novel modeling approach which identified suture-induced stress concentrations. Greater influence of compliance mismatch can be found in the end-to-side anastomosis other than the end-to-end model, which always led to less hyperplasia than end-to-side model. Therefore they concluded that compliance mismatch might promote graft-artery intimal hyperplasia by altering suture-line stresses.

Further study was also done by Leuprecht et al. (2002), who suggested that increased compliance mismatch leads to increased intramural stresses, and thus have a proliferative influence on suture line hyperplasia, as it was observed in the in-vivo study.

2.2.2.3 Property of Blood and Vessel Wall

In order to verify the assumption of Newtonian blood properties, Xu et al. (1992) investigated the three-dimensional flow through canine femoral bifurcation models under physiological flow conditions by numerically solving the time-dependent three-dimensional Navier-Stokes equations. In the calculations, two models (a) a Newtonian fluid and (b) a non-Newtonian fluid obeying the power law were assumed for the blood respectively. The non-Newtonian effects on the bifurcation flow field were also investigated and no great differences in velocity profiles were observed. The result indicated that the non-Newtonian characteristics of the blood might not be an important factor in determining the general flow patterns and neglecting of Newtonian effects still enables representation of major features of blood flow adequately.

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.

For the rigid wall assumption, several studies have been done to investigate the effects of elastic property of the wall on flow characteristics. In 1994, Steinman and Eicher explored the effect of vessel wall distensibility on flow patterns in 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 that the presence of elevated temporal variations and low average magnitudes of wall shear stress at sites known to be susceptible to the development of intimal hyperplasia. At these same sites, large spatial gradients of wall shear stress were also noted. Comparison between distensible-walled and corresponding rigid-walled simulations showed moderate changes in wall shear stress at isolated locations, primarily the bed, toe and heel. However, other than these locations, only minor changes in overall wall shear stress patterns were observed. Therefore they concluded that the effects of wall distensibility were less pronounced than those brought about by changes in arterial geometry and flow conditions.

Perktold and Rappitsch (1995) further investigated the effect of the distensible artery wall on the local flow field in the human carotid artery bifurcation by using a numerical model. Geometrically non-linear shell theory where incrementally linearly elastic wall behavior was assumed and was applied to the wall displacement and stress analysis. Note that the time-dependent, three-dimensional, incompressible Navier-Stokes equations were used in the flow analysis for non-Newtonian inelastic fluids. The comparison of the 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 wall shear stress magnitude decreased by 25% in the distensible model.

In 1996, two distensible models with different graft elasticity and one rigid model were used by Hofer et al. to investigate the effect of wall mechanics and fluid dynamics in 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 acts 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 intimal hyperplasia at the suture line was dependent on the wall mechanical factors such as intramural stress and strain.

Ethier et al. (1998) 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 to compare the waveform effects. The results showed that peripheral flow waveform (iliac and femoral) produced large temporal and spatial wall shear stress gradients on the host artery bed than the coronary flow waveform, even though the average bed wall shear stress magnitude were similar. If the anastomotic intimal hyperplasia was promoted by large spatial and /or temporal gradients of wall shear stress, intimal hyperplasia was predicted less on the host artery bed of coronary bypass grafts than the peripheral bypass grafts.

Another work was done by Moayeri and Zendehbudi (2003) to study the effects of elastic property of the wall on flow characteristics by numerically investigating the hemodynamic characteristics of blood flow through arterial stenosis. The blood was assumed as a Newtonian fluid and the pulsatile nature of flow was modeled by using measured values of the flow rate and pressure for the canine femoral artery. An isotropic elastic and incompressible material was assumed for the wall at each axial section, but a nonuniform distribution of the shear modulus in axial direction was used to model the high stiffness of the wall at the stenosis location. The results indicated that deformability of the wall causes an increase in the time average of pressure drop, but a decrease in the maximum wall shear stress.

2.2.2.4 Hemodynamics Parameters

A pseudo-elastic stress-strain relationship is generally used in representing the mechanical properties of biological tissues. Strain-energy functions are utilized to simplify the analysis with polynomials and exponentials as commonly used functions, which depend on their fits with experimental data. Under normal physiological conditions, the strain of an artery is about 60% (Fung 1993).

In the computational stress analysis, however, small strain (large deformation) approximations are commonly used (Hofer et al. 1996). Very few studies have used a large strain and non-linear approximation, such as Ballyk et al. (1998) developed a large strain model and applied the mean physiological pressure, but the material constants in the study were determined by a single value of compliance despite the fact that the stiffness of a vascular vessel varied with the strain (Fung 1993). In most anastomotic stress analyses, the geometry was constructed at the mean physiological loading condition

and a linear stress-strain relationship with a single Young's modulus was used to simulate each material, an approach that fails to show the whole loading history.

In 1993, Kim et al. carried out a numerical simulation of steady flow across an end-to-end vascular bypass graft anastomosis. In the study finite analytic numerical solution technique and the in-vitro experimentally determined geometries were used to simulate steady flow through the end-to-end anastomosis. The result demonstrated a region of flow separation 2mm distal to the anastomosis at higher transmural pressures. Moreover, wall shear stresses increased proximal to the anastomosis in flow from the artery to the graft and low shear stresses were observed distal to the anastomosis at higher transmural pressures with uniform inlet velocity condition.

In order to understand the possible role that hemodynamic factors may play in the pathogenesis of distal anastomotic intimal hyperplasia, Steinman et al. (1993) carried out numerical simulations of flow field within a two-dimensional 45-degree rigid-walled end-to-side distal anastomosis. The numerical code was tested and compared with experimental studies (using photochromic dye tracer) when using steady and near-sinusoidal waveforms, and agreement was generally very good. Using a normal human superficial femoral artery waveform, numerical simulations indicated elevated instantaneous wall shear stress magnitudes at the toe and heel of the graft-host junction and along the host artery bed. These sites also experienced highly varying wall shear stress behavior over the cardiac cycle, as well as elevated spatial gradients of wall shear stress. These observations provide additional evidence that intimal hyperplasia may be induced by the wall shear stresses over the cardiac cycle, high wall shear stress gradients or a combination of the two.

The relationship between high wall shear stress gradient and intimal hyperplasia was further proved by the numerical result obtained by Henry et al. (1996). They showed that relatively high values of spatial gradients of shear stress were predicted to occur in areas where know to be prone to intimal hyperplasia, and suggested that high gradients of wall shear stress might create the necessary conditions for intimal hyperplasia for steady flows in proximal and distal end-to-side anastomosis model. Based on the fact that the level of shear and pressure variation were predicted to be lower in the 30 degrees anastomoses, they suggested that there could be some benefits to constructing anastomoses with small angels. However, Ojha (1995) suggested relatively slow recirculating flow, increased residence time and the oscillation of the stagnation point together with the low shear stress promote the development intimal hyperplasia.

Kute and Vorp (1999) studied the effect of proximal artery flow on the hemodynamics at the distal anastomosis of a vascular bypass graft. Their findings supported the hypothesis that the local flow patterns and the spatial distribution of wall shear stress and wall shear stress gradient are dependent on the proximal artery inlet condition. The flow condition in the proximal artery significantly affected the resulting hemodynamics at the distal anastomosis and could potentially be manipulated in order to optimize the clinical success of vascular bypass grafts.

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 maxima 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.

2.2.3 In-Vitro Model Experiments

In-vitro mechanical analysis of the end-to-side anastomosis has been primarily focused on hemodynamics. The methods employed include qualitative flow visualization and quantitative laser Doppler anemometry (LDA). The anastomotic geometries used in these studies include simple, rigid straight tubes intersecting each other as well as more realistic, compliance anastomotic configurations. The inlet waveforms used include simple steady flow and purely sinusoidal waveforms as well as more physiological waveforms.

2.2.3.1 Laser Doppler Anemometry Measurements

Keynton et al. (1991) investigated the effect of angle and flow rate upon hemodynamics in distal vascular graft anastomoses using an in-vitro model under steady flow condition. Three anastomotic models with 30, 45 and 60 degrees junction angles were fabricated using Plexiglas tubing of 25.4 mm in diameter. Both flow visualization and laser Doppler anemometry (LDA) measurements were performed and 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 2-9. From the figure it could be found that axial velocities and shear rates along the outer wall were higher than those along the inner wall and occurred in the order of 45, 60 and 30 degrees junction angles. This study clearly identified changes in wall shear stress, which varied with the anastomotic angle and flow rate.

Figure 2-9 Flow pattern and velocity profile for $Re = 205$ at various anastomotic angles (taken from Keynton et al., 1991)

In order to investigate the role of compliance, Friedman et al. (1992) carried out the study on the effects of arterial compliance and non-Newtonian rheology on correlations between intimal thickness and wall shear stress. In the study, a minimally diseased human aortic bifurcation was replicated in rigid and compliant flow through casts, and both casts were perfused with physiological flow waves having the same Reynolds number. Wall shear rate histories was estimated from near-wall velocities obtained by laser Doppler velocimetry at identical sites in both casts. 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 is, the intimal was thicker at sites exposed to higher shear rates, consistent with earlier results for relatively healthy vessels. The result also revealed that there was no significant effect of either model compliance or

fluid rheology on the slopes of the correlations of intimal thickness against any normalized shear rate measured.

Another study on compliance was carried out by Anayiotos et al. (1994) by constructing two models of the carotid bifurcation which were used in the in-vitro investigations. The inner geometry were identical for both models, although one was made of compliant material while the other one was rigid. Each model was placed in a pulsatile flow system that produced a physiological flow waveform, and velocity was measured with a single component laser system and wall shear rate was estimated from near wall data. A wall motion transducer was used to measure wall motion in the compliant model and the maximum diameter varied between 4-7 percent in the model with the greatest change at the axis intersection. 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 variation in peak shear stress was greater and occasionally 100 percent higher than the compliant model which consistently has smaller positive and negative peaks. Furthermore the separation point was seen to move further upstream in the compliant cast. The result indicated the prominent influence of compliance.

In 1997, Loth et al. carried out LDA measurements of velocity and wall shear stress inside a PTFE vascular graft model under steady flow conditions. The wall shear stress distribution, computed from near-wall velocity gradients, revealed a relatively low wall shear stress region on the wall opposite to the graft near the stagnation point occupied 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 wall shear stress region created by the stagnation flow.

Vortex shedding at vascular anastomoses was investigated by Gaupp et al. (1999) in-vitro using a 20 MHz pulsed-wave Doppler velocimeter. Centerline velocity measurements were made at various axial distances in simplified polyurethane models of proximal and distal end-to-side anastomoses of angles 15, 30, 45, 60 and 80 degrees, using pulsatile flow waveforms similar to those in femoropopliteal bypass grafts. The results showed that higher vortex amplitude were found in the proximal anastomoses under resting flow conditions. 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. The vortex structures were investigated using spectrograms, which had shown prominent features at 40-50 Hz indicative of the short-duration oscillatory signals during the deceleration phase of systole expected from the passage of vortices.

In 2001, Li and Rittgers. examined the effects of different flow ratios between the proximal outlet segment (POS) and the distal outlet segment (DOS) have on the flow patterns and the distributions of hemodynamic factors in the anastomosis, using a pulsatile flow in- vitro model of the distal end-to-side anastomosis of an arterial bypass graft. The flow circuit is shown in Figure 2-10. Flow visualization method was used to determine the overall flow patterns and velocity measurements were made with LDA. The statistical results showed that there were 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. However, significant difference of

mean OSI can be found in all places. Comparing these mechanical factors with histological findings of intimal hyperplasia formation obtained by previous canine studies, they suggested that the regions exposed to a combination of low mean WSS and high oscillatory shear index (OSI) may be most prone to the formation of intimal hyperplasia.

Figure 2-10 Mock pulsatile flow system showing distal anastomosis model, proximal (POS) and distal (DOS) outflow segments, and LDA measurement device. (Taken from Li and Rittgers. 2001)

Loth et al. (2002) carried out the study that was designed to examine the relative contribution of wall shear stress and injury to the induction of intimal hyperplasia thickening (IHT) at defined regions of experimental end-to-side prosthetic anastomoses. An upscaled transparent model was constructed using the in-vivo anastomotic geometry, and wall shear stress was determined at 24 axial locations from laser Doppler anemometry measurements of the near wall velocity under conditions of pulsatile flow similar to that present in-vivo. The distribution of intimal hyperplasia thickening (IHT) was determined from seven canine iliofemoral PTFE grafts after 12 weeks of implantation using computer-assisted morphometry. A greater amount of IHT was found on the graft hood (PTFE) and ranged from $0.09 \pm 0.06\text{mm}$ to $0.24 \pm 0.06\text{mm}$. Nonlinear multivariable logistic analysis was used to model IHT as a function of the reciprocal of

wall shear stress, distance from the suture line, and vascular conduit type (i.e. PTFE versus host artery). An inverse correlation between wall shear stress and IHT was found only for those regions located on the juxta-anastomotic PTFE graft. The data were consistent with a model of intimal thickening in which the intimal hyperplastic pannus migrating from the suture line was enhanced by reducing levels of wall shear stress at the PTFE graft/host artery interface.

2.2.3.2 Flow Visualization Measurements

As early as 1989, Shu et al. carried out the studies on hemodynamic models in vascular crafting. They fabricated an elastic, transparent Silastic flow model to represent the detailed geometry of anastomoses, and constructed an experimental flow loop system. Dye injection technique was used to study the flow patterns, detailed flow measurements were carried out using laser Doppler anemometry and the wall shear stress was calculated from the velocity profile gradients near the wall, as shown in Figure 2-11. The results showed that more variations of wall shear stress were limited around the joint of anastomosis, where it is prone to the intimal hyperplasia.

Figure 2-11 Wall shear stress distributions at two phasic angles for two planes are shown at the left and right sides respectively (taken from Shu et al. 1989)

In 1993, White et al. investigated the effects of pulsatility, flow division, Reynolds number and hood length on the hemodynamic patterns in two models of end-to-side vascular graft anastomoses under steady and pulsatile flow conditions respectively. In-vivo flow waveforms and anastomotic geometry were obtained from acute experiments in five dogs in which iliofemoral bypass with end-to-side anastomoses were constructed and then the data were used to fabricate the in-vitro experiment model. Flows in the scaled-up, transparent models were visualized with white, neutrally buoyant particles, which were photographed under laser illumination and also recorded on videotape. Strong three-dimensional helical patterns, which formed in 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. The result combined with observations reported in animal model supported the concept that hemodynamic conditions, particularly low wall shear stress, plays a role in the localization of intimal hyperplasia in the region of end-to-side vascular graft anastomosis.

In order to provide a detailed description of spatial and temporal variations of wall shear stress within the end-to-side arterial anastomosis, Ojha (1993) had used a photochromic tracer technique to provide an overall view of the velocity field and to determine the instantaneous value of the wall shear stress in a 45-degree anastomosis model. The wall shear stress characterization was done under pulsatile flow conditions of a 2.9 Hz sinusoidal waveform and the Womersley number is 7.9. Figure 2-12 highlights the variations of the wall shear stress 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. In addition, the sudden motion of the stagnation point around peak flow produced sharp temporal gradient of the wall shear stress. When compared to the sites where intimal hyperplasia tends to occur, a strong correlation is seen with low wall shear stress at the heel and toe, and with the sharp temporal variations of the magnitude and spatial gradient of the wall shear stress on the bed at the junction.

Figure 2-12 Variations of the wall shear stress over the flow cycle at six different locations (taken from Ojha, 1993)

Later on, Ojha et al. (1993) further investigated 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 photochromic tracer technique was used to determine the instantaneous WSS and to visualize the overall flow field under pulsatile flow conditions. The results showed that positive wall shear stresses were very high at the toe and heel junctions, together with substantial nonperiodic fluctuations as shown in Figure 2-13. The peak wall shear stress 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% of 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 to 320, the variations in the wall shear stress magnitude 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 intimal hyperplasia at the distal end-to-side anastomosis might be promoted by low wall shear stress 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 2-13 Wall shear stress 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)

Ojha et al. (1994) studied the influence of angle on wall shear stress distribution for an end-to-side anastomosis under pulsatile flow conditions. The photochromic tracer technique was used to visualize the flow field and to determine the instantaneous wall shear stress at multiple locations simultaneously and models with angles of 20, 30, 45,

and 60 degrees were examined. For all angles, low shear stress was presented at the heel and on the bed opposite to the heel of the anastomosis apparently as a result of the complete occlusion of the proximal end of the host vessel as shown in Figure 2-14. In the figure it can be observed that near the toe, increased flow separation was found with increasing angle. On the bed across from the toe, increasing the graft angle led to increased shear stress. Furthermore, in this region the anastomotic angle significantly altered some properties of the shear stress field such as the mean and peak-to-peak magnitude and the cycle-to-cycle fluctuations.

Figure 2-14 Wall shear stress waveforms at indicated sites of the anastomoses. Points represent averaged of five measurements, and connecting lines are spline-fitted profiles through data points (taken from Ojha et al., 1994).

Ojha (1994) continued another study on the relationship between the wall shear stress temporal gradient and anastomotic intimal hyperplasia. The in-vitro study using the photochromic tracer technique, the shear stress variation on the bed of a 30 degrees anastomosis was examined before and after the development of hyperplasia. With the

disease-free model, a rapid downstream shift in the stagnation point was seen on the bend during the systolic phase of the flow cycle, which led to sharp temporal changes in the shear stress shiftily from positive to negative values, i.e., rapid changes in the direction of the shearing force, and this sharp temporal changes may lead to endothelial deformation or injury and eventually to intimal thickening. With the diseased model, the simulated tissue overgrowth on the bed appeared to act as a flow divider that restricted the motion of the stagnation point, and this drastically reduced the rapid changes in the directions of the shearing forces. Ojha (1994) suggested that the development of bed anastomotic intimal hyperplasia might be a response designed to reduce shear-induced endothelial deformation or injury.

In 1995 and 1996, Hughes and How investigated the effects of geometry and flow division on the flow structure in models of the proximal and distal end-to-side anastomoses. Flow structures under steady and pulsatile flow conditions were visualized in models with anastomosis angles of 15, 30 or 45 degree by using planar illumination of suspended tracer particles. At the proximal anastomosis, the flow patterns were highly three-dimensional and were characterized by a series of vortices in the fully occluded distal artery and two helical vortices aligned with the axis of the graft. The presence of a patent distal artery 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 anastomosis, 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. In pulsatile flow, the secondary flow components in the distal artery became more pronounced during flow deceleration. The results had agreed that intimal hyperplasia occurred in regions of flow separation at the toe and the heel, and flow stagnation on the floor of the anastomosis.

Rhee and Lee. (1994 and 1998) investigate the effect of radial wall motion on the wall shear rate distribution in the end-to-end anastomosis model. Rigid and elastic models were constructed and the wall shear rate 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 wall shear rates in the elastic models, it shall be paid attention when studying the arterial hemodynamics for the effect of radial wall motion is different for different geometry.

2.2.3.3 Particle Image Velocimetry Measurements

Bates et al. (2001) firstly applied the PIV measurement into the graft anastomosis to study the flow instabilities. Based upon water as the working fluid, the flow structure inside a 30-degree Y-junction with different fillet radii at the intersection between the graft and the host artery at various Reynolds numbers and distal outlet segment (DOS) to proximal outlet segment (POS) flow ratio was investigated. Three idealized scaled models of an arterial bypass distal anastomosis were manufactured from 50mm internal diameter QVF transparent glass. From the investigation it was found that the essential flow features in the junction, such as the stagnation point on the junction floor and the vortex under the heel, were identified from the measurements by means of the velocity data. Fluctuation of

the wall shear stress on the junction was found during the flow cycle. The two-dimensional instantaneous velocity fields confirm the existence of a very complex flow, especially in the toe and heel regions for the different models 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 2-15 (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 2-15 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)

2.2.3.4 Comparison with Cuffed Anastomoses

All these in-vitro models experiments have identified complex vortices occurring in the anastomosis, which produce low shear stress and/or high oscillatory shear indices (OSI) in some locations. Noori et al. (1999) compared the flow patterns in the distal end-to-side anastomosis constructed by the conventional surgical method with those resulting from various patch/cuff techniques and found that a continuous washout vortex occurred in the anastomosis which may constitute an advantage for the venous Miller's cuff. Wijesinghe et al. (1999) also compared conventional and cuffed end-to-side anastomosis by flow visualization and speculated that the improved patency rates of cuffed end-to-side anastomosis may not be due to decreased IH formation, but rather to an increased ability

of the cuff to accommodate IH because of a larger anastomotic area and a shifted zone of flow separation toward the center of the artery floor.

Similar study was conducted by Rowe et al. (1999) that the flow pattern of two different types of precuffed grafts and comparison with the flow patterns in the Miller cuff and the conventional end-to-side anastomoses using flow visualization were investigated. The wall shear rate was calculated from the near-wall velocity measured by 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.

This was confirmed in a quantitative study by How et al (2000) which showed that low mean wall shear stress was found only on the artery floor in the cuffed anastomosis and this was generally less extensive than in the conventional end-to-side anastomosis. Detailed flow velocity measurements were made in life-size models of conventional end-to-side (ETS) and IVC anastomoses using a two-component laser Doppler anemometer under pulsatile flow conditions. Velocity vectors were determined in the plane of symmetry of the anastomosis, and the variation of WSS was estimated from near-wall velocity measurements on the floor and upper wall of the artery. The results showed that in the IVC anastomosis, a coherent vortex that occupied most of the cuff volume was present from the systolic deceleration phase to end diastole. Stagnation point on the anastomosis floor was found to oscillate by about 4mm. Furthermore, in IVC anastomosis the low mean WSS was found only on the floor, and it was generally less extensive than in the ETS anastomosis. The vein cuff anastomosis altered the mean WSS distribution within the recipient artery and removed the area of low WSS at the heel, and contributed

to the redistribution of intimal hyperplasia as shown in Figure 2-16, which would be able to improve the graft patency rate.

Figure 2-16 Mean WSS distribution in the IVC anastomosis for a flow split of 50:50 of (a) ETS anastomosis and (b) IVC anastomosis. The horizontal dashed lines at ± 0.5 N/m² represent the range of low mean WSS that has been associated with a high increase in myointimal hyperplasia (MIH) (taken from How et al., 2000)

2.4 Summary

Based on the above literature findings, various means have been exploited by researchers to understand in depth the effect of fluid hemodynamics on the development of intimal hyperplasia. Generally, intimal hyperplasia can be seen developing at regions on the bed and around the suture line, the toe and heel, as shown in Figure 2-17. 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). In particular, IH is more prevalent at the distal anastomosis of an end-to-side graft, where the flow is more

disturbed, than at proximal anastomosis, where the flow is more uniform (Logerfo et al. 1983). Therefore the hemodynamic environment at the anastomosis appears to be a crucial element in the formation of IH.

Figure 2-17 Distribution of intimal hyperplasia (black regions) in recipient artery following end-to-side anastomosis

Both experimental and computational studies have been performed to investigate the hemodynamic related to the distal anastomotic IH. Some studies have shown a correlation between wall shear stress and IH development (Bassiouny et al. 1992; Ojha et al. 1990 and 1993; Keynton et al., 2001; Loth et al., 2002; Ethier, 2002), while others have suggested that high wall shear stress or wall shear stress outside a prescribed “safe range” initiates IH formation (Steinman et al. 1993). In addition to these studies, a number of in-vitro and in-vivo experimental studies have shown that both high and low wall shear stresses cause a pathophysiological response in endothelial cells that may lead to IH formation (Fry et al. 1968; Nazemi et al. 1989; Davies, 1994; Malek and Izumo 1995; Resnick and Gimbrone 1995; Stangeby and Ethier., 2002). Furthermore, the correlation between spatial wall shear stress gradient and IH formation was suggested by some

researchers (Steinman et al. 1993; Kleinstreuer et al. 1996; Lei et al. 1997; Kleinstreuer et al. 2001; Buchanan et al., 2003).

Hemodynamics is believed to be critical in serving as a regulator and modifier of cellular biology and in the development of the disease process (Hofer et al., 1996; Greenwald and Berry, 2000). Non-uniform hemodynamics may trigger a cascade of abnormal biological processes leading to the intimal thickening, and in turn the nonuniformity of hemodynamics can be employed to determine the susceptible site for the onset of vessel disease (Kleinstreuer et al., 2001). Therefore, great efforts have been put on the study of coronary artery bypass grafting in order to explore the hemodynamic factors with the aim in improving the graft patency rate. Many factors such as anastomosis angle (Taylor et al., 1992; Hughes and How 1995, 1996; Henry et al., 1996; Loth et al., 1997; Shipkowitz et al., 1998; Song et al., 2000; Jackson et al., 2001), wall curvature (Lei et al., 1995; Rowe et al., 1999; How et al., 2000), flow rate ratio (Fei et al., 1994; Hughes and How, 1995 and 1996; Henry et al., 1996; Khunatorn et al., 2002), wave form (White et al., 1993; Kleinstreuer et al., 1996; Ethier et al., 1998; Ku et al., 2002) were considered as the parameters affecting the flow fields and would be able to influence the development of stenosis.

The complex anatomy of coronary vessel has made the investigation of coronary flow and hemodynamics, one of the most difficult and challenging studies until now. One short fall of current literature is that most of the studies were carried out on the distal anastomosis except Ojha (1993), Hughes and How (1995) and Zhang (2005). However, the distal anastomosis is not isolated but is linked systematically to the aorta through the proximal anastomosis and curved graft. 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). Especially for the vein graft, apparent intimal hyperplasia plaques were usually found at the proximal anastomosis, where eddy blood flows formed and progressed towards the distal anastomosis (Liu and Fung, 1998). Another shortcoming of the current literature is that although Lee et al. (2001) and Cole et al. (2002) investigated the flow fields of complete bypass models, these models failed to replicate the entire coronary artery bypass grafting with sufficient anatomical geometry. In addition, little has been done on the optimization of the anastomotic configuration for coronary artery grafting but focused on the peripheral arteries such as below-keen popliteal bypasses and femoral bypasses.

Therefore, in this study, the investigation on the proximal anastomosis models with different anastomotic angles was carried out and the hemodynamic performances of the models were evaluated to propose the optimal proximal anastomotic angle. Subsequently, the whole anastomosis model, which was designed with essential in-vivo geometrical features based on the clinical data from the Singapore National Heart Centre, was investigated in order to enhance the understanding of stenosis pathophysiological process in CABG. From the distributions of the hemodynamic parameters found in the complete CABG model, efforts were put on the geometrical improvement of the distal anastomosis in order to reduce the nonuniformity of the hemodynamics and increase the potential patency rate of the bypass graft.

CHAPTER 3

EXPERIMENTAL ARRANGEMENTS

3.1 General Description of Test Rig

Figures 3-1 and 3-2 show the experimental test rig constructed for the PIV measurements of the proximal & whole anastomosis models and the distal anastomosis models respectively.

Figure 3-1 Experimental test rig for proximal and complete anastomosis models

Figure 3-2 Experimental test rig for distal anastomosis models

The schematic drawings of the test rig for proximal & whole anastomosis models and the distal anastomosis models are shown in Figures 3-3 and 3-4 respectively. The test rig for the measurement of the proximal and whole models consists of piston pump system (including a gear pump and a piston pump), calming chamber, two flow meters, two resistance adaptors (needle valves connected to the outlets of model and backpressure tank) and reservoir, as shown in Figure 3-3. The piston pump system, which consists of a gear pump, a piston pump and two piston pump interfaces, is used to generate the pulsatile waveform. The calming chamber is used to eliminate disturbance due to the mixing of output from piston pump and gear pump, and to ensure the flow is fully developed before entering the flow meter 1 and the test model. Flow meter 1 (Endress+Hauser Promag 33F) is used to monitor the pulsatile waveform (generated by the piston pump system) by sending the flow rate signals to an oscilloscope (Tektronix TDS 210) as well as providing feedback signal to the piston pump interface unit, whereas flow meter 2 (Endress+Hauser Promag 53) is used to measure the graft outlet flow rate. Besides the backpressure tanks the needle valves located after the exits of the test model are used to provide extra resistance modification through adjusting not only the flow rate ratio between the two outlets but also the waveforms. In addition, the amplitude of the waveform is also modified using the compliance chamber by adjusting the height of fluid in it.

Generally the test rig for distal anastomosis is smaller than that for proximal and complete anastomosis models in not only the tubing sizes but also the maximum instantaneous flow rate as shown in Figure 3-4. The gear pump system, which consists of a DC pump (HG0024-G050, Mocropump, U.S.A.) and an AC pump (HG0024-N23 PF1SGB1, Micropump, U.S.A.), is used to generate the pulsatile waveform for the distal anastomosis

model. The calming chamber, compliance chamber and resistance adaptor (needle valves connected to the outlets of model and backpressure tanks) have the same function although smaller in size. Flow meter 1 (Endress+Hauser Promag 53) located before the test section provides the monitoring of the waveform with connection to the oscilloscope (Tektronix TDS 210) as well as feedback signals to the gear pump interface, whereas flow meter 2 (Endress+Hauser Promag 53) is used to monitor the flow rate ratio between the two outlets of test model.

Figure 3-3 Schematic drawing of the experimental test rig for proximal and complete anastomosis models

Figure 3-4 Schematic drawing of the experimental test rig for distal anastomosis models

3.1.1 Piston Pump System Pulsatile Flow Generator

The piston pump system is custom designed for use in experimental in-vitro hemodynamic modeling. The system consists of the following parts:

1. Piston Pump
2. Gear Pump (DC Pump)
3. Piston Pump Interface 1 for DC Pump control
4. Piston Pump Interface 2 for Piston Pump control
5. Data Acquisition Board PCI-DAS1200
6. HP VEE Program PistonPumpControl.vee

The computer-controlled servomotor (Maxon Motor EC60 with DES 70/10 Servo Amplifier, Maxon Motor Control, U.K.), which is capable of producing the time-displacement function of any given waveform, drives a 7 cm diameter piston periodically. Note that a displacement of the piston of only 2cm will generate a stroke volume of 75ml and the maximum piston travel is about 9cm. As shown in Figure 3-5, the piston pump system produces pulsatile flow by superimposing an oscillatory flow (AC) component produced by the piston pump to a steady flow component produced by the DC gear pump (GC M35PSF, Micropump, U.S.A.). The AC waveform generated by the HP VEE program, which was used to control the servomotor, has a zero mean value so that the piston reciprocates about a mean position.

Figure 3-5 Working principle of the piston pump system pulsatile flow generator

3.1.2 Gear Pump System Pulsatile Flow Generator

The gear pump system consists of the following parts:

1. Gear Pump 1 (AC Pump): Mocropump HG0024-N23 PF1SGB1
2. Gear Pump 2 (DC Pump): Mocropump HG0024-G050.
3. Gear Pump Interface Unit
4. Data Acquisition Board PCI-DAS1602/12
5. HP VEE Program GearPumpControl.vee

The gear pumps operate only in the forward direction and the output of the gear pump is determined by the speed of the drive. The AC gear pump speed is modulated by mean of an AC voltage signal in the range 0-5V and the pump will generate a flow waveform, whereas the DC pump is operated at a constant speed and is controlled by means of a precision 10-turn potentiometer on the Gear Pump Interface unit. The output of the DC pump must be subtracted from the AC pump to produce bi-directional flow, as shown in Figure 3-6. If only unidirectional flow is required, the DC pump should be unplugged from the gear pump interface unit and the gate valve on the DC pump should also be shut down.

Figure 3-6 Working principle of the gear pump system pulsatile flow generator

3.2 Working Fluid

3.2.1 Physical Properties of Human Blood

The human blood composition can be divided into about 55% plasma and 45% blood cells including red blood cells, white blood cells and platelets. The basic properties are shown in the Table 3-1.

Table 3-1 Physical properties of human blood

Whole Blood		
	PH	7.35-7.40
	Viscosity (37 °C)	4.0 cP (at high shear rates)
	Specific Gravity (25/4 °C)	1.056/1.0621
	Venous Hematocrits-Male	0.47
	-Female	0.42
Plasma		
	Colloid Osmotic Pressure	~330 mm H ₂ O
	PH	7.3-7.5
	Viscosity (37 °C)	1.2 cP
	Specific Gravity (25/4 °C)	1.0239/1.0310

Blood plasma alone behaves as Newtonian fluid with a viscosity of about $1.2 \times 10^{-3} \text{ Pa} \cdot \text{s}$ at 37 °C. The whole blood exhibits a yield stress and a decrease in viscosity with the increasing shear rate. Brooks et al. (1970) examined the effect of hematocrits on the flow properties of human blood at shear rates up to 700 sec^{-1} . An illustration of their finding is shown in Figure 3-7. Up to hematocrits of approximately 14% (H_n equals to 12.6%), the whole blood was found to be Newtonian at all shear rates. As the hematocrits increase, 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 hematocrits. As a consequence, the viscosity of blood is associated with the shear rate and the haematocrit.

Figure 3-7 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).

Minlor (1982) studied the shear rates in the human circulation, which are calculated from radius and average blood velocity, with the assumption of parabolic flow, as shown in Table 3-2. The result showed that the shear rates of blood flow at the aorta and arterial are higher than 50 sec^{-1} . Moreover, hematocrit for an adult is typically 40-45% and the old people always have lower hematocrits than the younger ones. As it is known, bypass surgery is usually done on the older people and associated only with aorta, graft and coronary artery.

Table 3-2 Representative of shear rates at vessel walls in the human circulation (Taken from Minlor, 1980)

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

Applying the high shear rate and low hematocrits to Figure 3-7, the viscosity can be found almost constant with an asymptotic value ($3.5 - 4.0 \times 10^{-3} \text{ Pa} \cdot \text{s}$), which suggests that human blood can be considered as a Newtonian fluid in this study.

3.2.2 Blood Analogue

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, two kind of blood analogue were used for Pyrex glass model and silicon rubber respectively. During the measurement of proximal anastomosis models (Pyrex glass models), working fluid involved mixing 30% of glycerin with 70% of aqueous ammonium thiocyanate (NH_4SCN) solution by volume was used as the blood analogue. 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 $4.08 \times 10^{-3} \text{ Pa} \cdot \text{s}$ at 22°C respectively. For the silicon rubber models (complete and distal anastomosis models), working fluid of mixing 30% of glycerin with 70% of sodium chloride (NaCl) solution by volume was used in the measurement. The NaCl solution was made up of NaCl and water by 1:3 of weight. The working fluid was measured to have the refractive index of 1.4089, which is close to that of silicon rubber (1.41), and a dynamic viscosity of $4 \times 10^{-3} \text{ Pa} \cdot \text{s}$ at room temperature.

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 increase 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, 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. In addition, measurements of viscosity and refractive index were made for the working fluid with seeding particles. No significant discrepancy was found between properties of working fluid with and without seeding particles.

3.3 Test Models

3.3.1 Proximal Anastomosis Models

The design of the test models will require some fundamental medical knowledge especially on the actual anastomotic joint in the bypass operation. The surgical operation procedures (Doty, 1997) at the proximal anastomosis were illustrated in Figure 3-8. 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 to the aorta. 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.

Figure 3-8 Suturing at the proximal anastomosis.(a) stitches around the heel and (b) the completed anastomosis (taken from Doty, 1997)

The Pyrex glass test models design is to represent the proximal anastomotic joint in a bypass operation. All models are designed and fabricated to its true scale based on medical data provided by a cardiac surgeon from Singapore National Heart Center. In the design of the proximal anastomosis model as shown in Figure 3-9, a hole of 5mm is punctured at the central plane of a 20mm internal diameter glass tube. A glass tube of inner diameter (ID) of 6mm and a length of 70mm is then fused onto the 5mm hole. The angle of the joint varies from 30 to 90 degrees with an interval of 15 degrees. As stated in vascularhealing at the anastomotic joints, the internal joint surfaces of the glass tubes must be smooth so as to allow smooth flow and to reduce turbulence (Lei et al., 1997) and this can be achieved through a reheating process.

Figure 3-9 Typical designed and fabricated proximal anastomosis model (45° model)

3.3.2 Distal and Whole Anastomosis Models

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 3-5 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 contour 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 3-10 provides a better view on the operation procedures.

Figure 3-10 Suturing operations at the distal anastomosis. (a) & (b) stitches around the anastomosis and (c) the completed anastomosis (taken from Doty, 1997)

The right coronary artery (RCA) bypass graft had higher potential for restenosis and the typical location and course of RCA bypass graft surgery shown in Figure 3-11 (Galjee et al., 1996) can be assumed approximately in the same plane, therefore, planar whole anastomosis model was designed to represent the bypass system from the aorta to right coronary artery. Computer aided method was applied in the design and fabrication of the distal and whole anastomosis models, which will be described in detail in Section 3.3.3.

Figure 3-11 Schematic view of CABG (taken from Galjee et al., 1996)

3.3.3 Computer Aided Design and Manufacture of Test Models

With the advance in computer aided design/computer aided manufacture (CAD/CAM), the design and fabrication of complex vascular models can be more easily and reliably accomplished. Friedman (1995) described the fabrication of a scaled model of an aortic bifurcation from magnetic resonance imaging (MRI) scans. Chong et al., (1999) described two methods, the computer numerical control (CNC) method and the stereolithography (STL) method to design and fabricate the vascular models, as shown in Figure 3-12. In the present study the CNC method was used in the design and fabrication of the bypass models. However, a low melting point alloy rather than the wax was used in casting the solid model because the alloy is easy to handle and surface defects can be more easily repaired.

Figure 3-12 Schematic diagrams of vascular models production using CAD/CAM techniques (Taken from Chong et al., 1999).

At the first stage, computer aided design (CAD) method was used to define the complex surface geometry of the vascular anastomosis model. Two-piece of perspex modules was manufactured based on the detailed geometry information from CAD data. The modules were used to produce a solid low-melting-point alloy (Mining and Chemical Products Limited, U. K.) cast. Figures 3-13 (a) and (b) show the Perspex modules and solid alloy cast of a complete bypass model.

(a)

(b)

Figure 3-13 Fabrication of complete anastomosis model (a) Perspex modules (b) solid alloy cast

After polished and repaired the surface defects of the solid cast, the cast was spray painted and dried. An acrylic container with holes on the sidewalls was fabricated to place the painted cast and special designed connectors were placed in the holes to sustain the cast. Then the container was injected with the silicon rubber (Sylgard 184, Dow Corning, U.S.A.) and placed in the vacuum oven at $60 \pm 5^\circ\text{C}$ overnight to degas and cure. Thereafter the oven temperature was increased to 90°C to melt the alloy. After cooling, the adherent paint is removed by gentle brushing with detergent solution followed by flushing with acetone. The fabrication of silicon rubber model was accomplished after removing the container from the model gently, as shown in Figure 3-14.

Figure 3-14 Accomplished silicon rubber of whole anastomosis model

In real situation, the vessel has an uneven surface characterized by small-scale surface features and the cross section is far from circular and constant. Also along the main coronary artery are rich small branches. Moore et al. (1999) compared blood flow patterns in anatomically realistic and simplified end-to-side anastomoses in order to determine how much a realistic geometry can be simplified without the loss of significant hemodynamic information. They concluded that surface features and small changes in arterial caliber could be classified as trifling geometrical features. It is thus not required to be accurately replicated. Therefore in this study, the cross sections of the aorta, graft and coronary artery were assumed to be circular and of constant area except the anastomosis region. The vessel surface was smooth and coronary artery was free of small tributaries.

CHAPTER 4

EXPERIMENTAL METHODOLOGY

4.1 Introduction to Particle Image Velocimetry

Particle Image Velocimetry (PIV), a measurement technique that yields an instantaneous realization of velocities within a planar cross section of the flow, 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 (Grant, 1994). 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, since PIV is a spatial measurement technique, instantaneous coherent flow structures can be visualized and related flow quantities such as vorticity, strain and divergence can be computed using this technique.

Figure 4-1 showed a schematic viewing for demonstrating the principles of PIV measurement techniques. The 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 was used as the illumination source and a CCD camera was used to capture two consecutive images of the scatter passing through the test section. Then the two images were transferred to the processor to calculate the flow field using some arithmetic such as cross-correlation method.

Figure 4-1 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 measurement 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 4-2.

Figure 4-2 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 by the FlowMap processor.

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 4.3.1.

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 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 System Hub in which the correlator units, input buffers and synchronization unit were integrated, and a PC with FlowManager software installed, as shown in Figure 4-3.

Figure 4-3 Architecture of the FlowMap PIV instrumentation (Taken from FlowMap PIV Installation & User's Guide, Dantec, 2002)

4.2.1 Illumination System

The Gemini PIV 200-15 (New Wave Research, USA), a double cavity pulsed Nd: YAG laser system that has a repetition rate of 15 Hz and 200 mJ emitting ability, was used as the illumination source in the FlowMap system. Two pulsed Nd:YAG infrared laser heads are mounted on a single baseplate. The 1064 nm beams are polarization combined and then enter a second harmonic generator to produce visible (532 nm) light. Dichroic mirrors separate the visible light from the residual infrared light and direct the beam to the experiment. The delay between the two pulses may be varied using an external trigger source.

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 in emitting the energy 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. The synchronization unit will instruct the laser cavity when to fire their flash lamps and when to allow their Q-switches to emit laser radiation, as shown in Figure 4-4.

Figure 4-4 Communication signals between the synchronization units in the processor and a double cavity laser system (Taken from FlowMap PIV Installation & User's Guide, Dantec, 2002)

4.2.2 CCD Camera

The CCD camera used in the FlowMap PIV system is HiSense MkII camera. It consists of a high resolution Hamamatsu C8484-05 digital CCD chip and Nikon AF Micro-Nikkor lens 60/2.8. It is a cross-correlation camera and contains a high-performance progressive scan interline CCD chip with no mechanical shutter, 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, Hamamatsu C8484-05
Active pixels	1344 by 1024 pixels
Camera bit resolution	12-bit
Pixel pitch	6.45×6.45μm
Dynamic range	1800:1
Readout noise	10 electrons r.m.s
Pixel clock rate	14.7MHz
Max. single-frame rate*	12.2
Pulse interval range*	0.3 μs and up
Double-frame rate*	Up to 5.6Hz

Note: * means restrictions may apply in actual operation mode

A so-called Asynchronous reset mode was used to drive the camera when the camera is used with the FlowMap system. 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 4-5.

Figure 4-5 Timing sequence for recording of a series of three PIV images (Taken from FlowMap PIV Installation & User's Guide, Dantec, 2002)

4.2.3 FlowMap System Hub

FlowMap System Hub 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.

4.2.4 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.

4.3 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 magnificent 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)	5.6-11
Particle diameter	20 μm , 10 μm
Interrogation size	32 $\times$ 32 pixels
Overlap	50 %
Pixel size	6.45 $\times$ 6.45 μm

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

4.3.1 Seeding Particle

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 and optimum with 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 proximal models is around $24 \times 18 \text{ mm}^2$ and the active area of camera is $8.7 \times 6.6 \text{ mm}^2$:

$$M = \frac{6.6}{18} = 0.36 \quad (4-1)$$

- Particle geometric diameter (d_{geo})

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

$$d_{\text{geo}} = M \times d_{\text{particle}} \quad (4-2)$$

- Point Response Function (PRF) of the lens

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

$$d_s = 2.44(M+1)F\lambda \quad (4-3)$$

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})

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

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 on proximal anastomosis models is polyamid-seeding particles (PSP-20, Dantec Measurement Technology) with mean diameter of $20\mu\text{m}$. Similarly for the measurements of distal anastomosis models the specific area is around

$15 \times 11 \text{ mm}^2$, it has a magnification coefficient $M=0.6$. To achieve the optimum particle image diameter (2 pixels= $12.9 \mu\text{m}$) a particle diameter of $9.3 \mu\text{m}$ is needed ($F=5.6$, $\lambda=532\text{nm}$, $M=0.6$ and $d_s=11.6 \mu\text{m}$). Therefore the hollow glass sphere particle (HGS-10, Dantec Measurement Technology) with a mean diameter of $10 \mu\text{m}$ was used in the investigation on distal anastomosis models.

4.3.2 Parameters of Acquisition Control

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.

$$t_{\text{pulseduration}} < \frac{d_{\text{image}}}{2 \times V_{\text{particle}} \times M} \quad (4-5)$$

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 the requirement 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.

$$t_{separation} > \frac{3.5 \times d_{image}}{V_{particle} \times M} \quad (4-6)$$

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

$$t_{separation} < \frac{l_{interrogation}}{4 \times M \times V_{particle}} = \frac{N_{int} d_{pitch}}{4 \times M \times V_{particle}} \quad (4-7)$$

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

$$V_{measured}(t) = \frac{1}{t_{separation}} \int_t^{t+t_{separation}} V_{particle}(t) dt \quad (4-8)$$

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.

4.4 Pre-validation of the PIV measurement and Input Flow

Before measuring, it is necessary to quantify the accuracy of the velocity obtained from the PIV measurement. In this application, one straight glass tube, which has the same

inner diameter as the aorta, 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 would be paid much more attention.

4.4.1 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 across a diameter. PIV measurements were carried out on a straight glass tube of inner diameter 20 mm and of length of 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 flowmeter was 0.06 m³/hr. In order to calculate the average flow rate value from the velocity profile, the equation as following was applied,

$$\bar{Q} = \int_0^r u(r) 2\pi r dr \quad (4-9)$$

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 thickness of the cross sectional ring along the radius of the tube. Based on the velocity values obtained from the vector plots at the two planes, the average flow rate is computed numerically using the Simpson's rule and the calculated average flow rate at plane 1 ($x/D = 1$) and plane 2 ($x/D = 2$) was 0.0580 m³/hr and 0.0577 m³/hr respectively. Note that x represents the distance from the inlet and D is the inner diameter of the tube, the values attained by the two methods were within 4%. The reason of this small discrepancy could be due to the disturbance of background noise, wall

reflection and the accuracy of positioning the measuring plane in the PIV technique as well as the accuracy of the flow meter.

In the PIV experiment, extra assistant techniques, such as the prolonged tube circuit and the calming chamber before the test section etc., were used to ensure that the flow into the test section was fully developed. Hence, the verification of the accuracy of the velocity plots could be done by comparing the normalized velocity profile obtained from the velocity plots with the theoretical Hagen-Poiseuille solution for the circular pipe flow. The normalized velocities were calculated at the two planes and the comparison between them and the normalized velocity profile of the theoretical solution was shown in Figure 4-6. From the figure, it is found that the two curves resembled very closely to the Hagen-Poiseuille solution, that is the accuracy of the velocity plots obtained from PIV measurements is acceptable.

Figure 4-6 Comparison of normalized velocity profiles

4.4.2 Pulsatile Flow

As described in Chapter 3, program-controlled pumps produce the pulsatile flow input applied in the experiment. As the pulsatile flow is relatively more complex than the steady flow, the verification of the pulsatile 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 piston pump system 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, as shown in Figure 4-7.

Figure 4-7 Pulsatile flow rate waveform obtained from oscilloscope

Figure 4-8 compares the pulsatile velocity waveform generated by the piston pump with the input physiological waveform obtained from Nichols and O'Rourke (1990). It is observed that the experimental pulsed waveform agrees well with that from literature. The pulsed waveform achieved the highest peak Re of 5430 at the 0.3s and experienced the maximum reverse flow with $Re = 865$ at 0.7s. Note the Re is determined based on the 20mm diameter of aorta. The average mean velocity of the pulsed waveform is estimated as 26.5 cm/s and the corresponding flow rate of 5L/min. The period of each pulsed cycle was set at 1.0 second and the Womersley number calculated is 13.4.

Figure 4-8 Comparison of the present experimental flow rate waveform with those of Nichols and O'Rourke (1990)

4.5 Experimental Procedure

Preparation Work:

First the test model is installed in the test section and the whole test rig is assembled. The working fluid, which has the same refractive index of the test model, was prepared and degassed in order to eliminate bubbles. A small quantity of working fluid was mixed sufficiently with seeding particles and placed in a container for 24 hours. Since the

density of the seedings could not be uniform, lighter seedings would stay at the surface whereas heavier seedings deposited. At the middle part the seeding particles would have uniform density with the working fluid, therefore this part of working fluid with seedings was degassed for PIV measurement.

It is important to ensure that all the PIV components, including the monitoring computer, laser, CCD camera and FlowMap System Hub, and components of pump system are correctly connected. The laser's position is adjusted by observing the thickness and position of the laser sheet on the burn paper.

Initiation and Carrying out the Measurement:

When all the preparations were done, put the fluid without seeding particles into reservoir of the flow loop. Activate the DC pump at low speed to let the fluid fill the whole loop and eliminate air bubbles in the tubes. Then add the working fluid with seeding to the flow circuit bit by bit under steady flow condition and trial run the PIV system to check the particle density and other parameters until best particle image and flow field are achieved. For steady flow measurements, adjust the speed of DC pump and resistance behind the model to get expected flow rate ratio. Then try different acquisition parameters discussed in Section 4.3.2 and proceed the analysis method to obtain best velocity field. For each condition ten measurements were carried out and averaged to avoid accident error.

For the pulsatile flow measurement, DC pump was firstly activated to get the mean flow rate of the pulsatile input flow. After that AC pump was activated to generate the pulsatile waveform. Monitored the waveform measured by the flow meter and improved it until

the expected flow waveform by adjusting the resistance, compliance and amplitude of AC component etc. During this period the laser should be adjusted to run in asynchronous pulse mode and was triggered by the external trigger signal provided by the pulsatile flow generator system. The time interval between the trigger signals was set as 0.02s and ten measurements were averaged for each time step. Since the flow rate varied drastically within the flow cycle, acquisition parameters of the PIV should be adjusted accordingly for each time step.

Post-Processing

The velocity vectors were visualized using an arrow with the tail of the arrow situated at the same particle location and with a length proportional to the local fluid velocity. Regarding the fluid shear measurement of within the bypass, most studies employ a more versatile, although less direct, approach based on the detection of flow velocities in the vicinity of the vessel wall, while some researchers have used techniques capable of direct shear measurement. 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). Therefore in this study, the velocity field obtained by PIV was used to calculate the wall shear stress and other hemodynamic parameters. A program developed in-house based on the finite element shape function was used to detect the near wall velocities within the viscous boundary layer. These data were then curve fitted to obtain the near wall velocity profile and the slope of the curve at the wall was determined as a measurement of velocity gradient or shear rate.

The primary sources of error in WSR estimation are velocity measurement error and curve fitting approximation error. Walsh et al. (2003) found that the estimated WSS distributions were highly depended on the curve-fitting method used to calculate the WSR. 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.

$$\frac{du(\xi)}{d\xi} = a_1 + 2a_2\xi + 3a_3\xi^2 + \dots + na_n\xi^{n-1} \quad (4-10)$$

$$\left. \frac{du(\xi)}{d\xi} \right|_{\xi=0} = a_1 \quad (4-11)$$

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.

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. 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 at plane 1 ($x/D=1$) 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.

Table 4-3 Comparison of estimation of WSR using different number of near wall velocities (n) and degree of the polynomial approximation (N)

Location	N	2	3		4			5			
A ($x/D=1$)	n	1	1	2	1	2	3	1	2	3	4
	a_1	32.5	19.75	46.25	18	28.25	59.58	17.25	20.82	42.32	72.08
Location	N	2	3		4			5			
B ($x/D=2$)	n	1	1	2	1	2	3	1	2	3	4
	a_1	32	20	47	18.5	25.5	57.33	18	20.86	41.61	74.58

In order to validate the curve-fitting method under pulsatile flow condition, comparison of the estimated of WSS using different number of near wall velocities and degree of polynomial approximation was carried out in this study and validated with numerical simulation results obtained by Zhang (2005). From the numerical simulation (Zhang, 2005) and flow field measurements in this study, the flow field of the anastomosis was found to be more complicated at the acceleration flow, especially at the peak flow phase.

Therefore the assessment of influence of different WSS estimation methods and validation with numerical results were carried out at the peak flow phase of the 45° proximal anastomosis model. Figures 4-9 (a) and (b) show the experimental and numerical WSS distributions along the graft inner wall and outer wall respectively. As shown in Figure 4-9, the WSS distributions along the graft inner wall obtained from linear approximation with 3 near wall velocity points and 2nd order polynomial with 5 near wall velocity points match the numerical simulation results better than others. Similarly, for the WSS along the graft outer wall, linear approximation with 3 points and 2nd order approximation with 5 points were found to provide better agreement with numerical simulation than other methods.

There is an assumption set behind this curve-fitting technique that all near-wall velocity measurements are within the fluid boundary layer so that the calculated wall shear rates are accurately estimated the actual wall shear rates (Walsh et al., 2003). As stated earlier in the thesis, the boundary layer thickness under steady flow for a straight tube is found to be 1.24 mm, and the boundary layer for the test model under pulsatile flow would be thinner due to the bifurcation and complexity of flow patterns (Fatemi and Rittgers, 1994). Therefore the linear approximation with 3 near wall velocity points was applied in the WSS estimation in this study, since the fifth point was outside the viscous boundary layer under pulsatile flow condition. Loth et al. (1994) also found that errors of less than 10 percent occur in estimating the WSS obtained from linear curve-fits.

Discrepancy between the experimental and numerical results was found at the location of stagnation point and peak value of WSS. The difference between locations of stagnation point found is because the coordinate system defined in the experiment may not exactly

coincide with that of numerical simulation. In addition, errors occurred during the test model manufacturing procedure and the experimental model could not be reproduced exactly the same as the numerical model. The minor difference in the detailed geometry feature between the experimental and numerical models would contribute to the discrepancy in peak WSS magnitude. Furthermore, under unsteady flow condition, particularly at bifurcations and bends, errors are introduced in the curve-fitting estimation, resulting in underestimated shear rate (Zheng et al., 1993).

Figure 4-9 Experimental and numerical wall shear stress distributions
(a) along the graft inner wall (b) along the graft outer wall

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. 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). As a result the first PIV measurement point in this study is around 0.1mm from the wall and the increment between the subsequent points is 0.25mm.

Hemodynamic Parameters including spatial wall shear stress gradient (SWSSG), time-averaged WSS (TAWSS), time-averaged SWSSG (TASWSSG) and oscillating shear index (OSI), were obtained through further processing the WSS found. Spatial wall shear stress gradient was calculated using the first order central difference approximation,

$$SWSSG = \left| \frac{\partial \tau_w}{\partial x} \right| \quad (4-12)$$

The TAWSS and TASWSSG were defined as

$$TAWSS = \frac{1}{T} \int_0^T |\tau_w| dt \quad (4-13)$$

$$TASWSSG = \frac{1}{T} \int_0^T \left| \frac{\partial \tau_w}{\partial x} \right| dt \quad (4-14)$$

where T is the period of a complete cardiac cycle and t is the instantaneous time.

Note that the time-averaged SWSSG represents the spatial fluctuation and variation of WSS and the SWSSG may not reflect the WSS variation curve closely. This is because WSS is calculated based on the velocity profile near the wall. Furthermore, it can be resulted in either positive or negative due to the definition of the coordinate system. Whereas the WSSG is calculated based on the absolute value of $\partial\tau_w/\partial x$, which takes only positive value, and the time average of the variation of $|\partial\tau_w/\partial x|$ at a particular location throughout the whole physiological flow cycle would result in presenting only the mean trend of the WSSG and thus could not following the variation of WSS closely.

The OSI was calculated as following:

$$OSI = \frac{1}{2} \left(1 - \frac{\left| \int_0^T \tau_w dt \right|}{\int_0^T |\tau_w| dt} \right) \quad (4-15)$$

Note that the OSI ranges between 0, where a unidirectional flow occurred, and 0.5, where the flow changes its direction throughout the period.

4.6 Measurement Uncertainty

The spatial resolution of the PIV measurement is restricted by the effective diameter of particle image when projected back into the flow field. The uncertainties caused by the PIV measurement system are affected by several essential factors such as the magnification factor, seeding particle, and wavelength of the laser sheet etc. In the present study, the uncertainties of PIV measurements were evaluated by the sum-square of the precision index and the bias limit by the elemental error based on the method described in the ASME Performance Test Codes (1985).

According to the principle of PIV measurement, the velocity, u (in m/s), is expressed by the following equation:

$$u = \frac{\Delta s L_O}{\Delta t L_I} \quad (4-16)$$

Where Δt is the time interval between laser pulses, Δs is the number of pixels corresponding to the displacement of particle in the images. L_O is the width of the camera view in the object plane and L_I is the width of the digital image. The total error, ε , in a measured quantity is a sum-square of the bias component, B , and a component, P . the bias error of the measured velocity is related to the elementary bias errors based on the sensitivity coefficient, i.e.

$$B_u^2 = \eta_{\Delta s}^2 B_{\Delta s}^2 + \eta_{\Delta t}^2 B_{\Delta t}^2 + \eta_{L_O}^2 B_{L_O}^2 + \eta_{L_I}^2 B_{L_I}^2 \quad (4-17)$$

Where the sensitivity coefficient is defined as $\eta_x = \partial u / \partial x$, $x = (\Delta s, \Delta t, L_O, L_I)$. The elementary bias limits of Δs and Δt are determined by the specifications of the PIV measurement system. The width of the camera view in the objective plane, L_O depends on the distances and configurations related to the experimental arrangements and the width of the digital image, L_I , is determined by the number of pixels corresponding to these dimensions.

In the present study, L_O are 24mm and 15mm for the proximal and distal anastomoses respectively, whereas L_I is 1344 pixels for all measurements. From the equations (4-16) and (4-17) it is clear that the total bias error for the velocity is proportional to the bias error caused by the Δs , whereas reverse proportional to the bias error caused by the Δt . In the present study, the PIV image pairs are cross-correlated with a 32×32 pixel interrogation window and 50% overlap. The time between pulses was chosen to ensure

the maximum displacement does not exceed a quarter of the size of the interrogation area. At the peak flow phase, the maximum velocity magnitudes of 0.913m/s and 1.980m/s were obtained in the measurements of proximal and distal anastomoses respectively, meanwhile the time interval between pulses Δt were correspondingly selected as 150 μs and 50 μs . Therefore, these yield displacement values Δs of 5.90 and 6.82 pixels respectively, and the bias errors of measurements at the proximal and distal anastomoses were calculated and listed in Tables 4-4 and 4-5 respectively.

Table 4-4 Bias error (Proximal anastomosis measurements)

Variable	Magnitude	B_x	η_x	$B_x\eta_x$	$(B_x\eta_x)^2$
L_O (m)	2.4E-02	0.0001	3.804E+1	3.804E-03	1.447E-05
L_I (pixel)	1344	0.5	-8.83E-04	-4.415E-04	1.949E-07
Δt (s)	1.50E-04	1E-07	-6.086E+03	-6.086E-04	3.704E-07
Δs (Pixel)	5.90	0.0295	0.1547	4.56E-03	2.079E-05
U (m/s)	0.913	Bias error $B_u=0.00598$; %Bias error=0.66%			

Table 4-5 Bias error (Distal anastomosis measurements)

Variable	Magnitude	B_x	η_x	$B_x\eta_x$	$(B_x\eta_x)^2$
LO (m)	1.8E-02	0.0001	1.015E+02	1.015E-02	1.030E-04
LI (pixel)	1344	0.5	-1.359E-03	-6.795E-04	4.617E-07
Δt (s)	5.0E-05	1E-07	-3.654E+04	-3.654E-03	1.335E-07
Δs (Pixel)	6.82	0.0341	0.2679	9.133E-03	8.341E-05
U (m/s)	1.980	Bias error $B_u=0.0136$; %Bias error=0.69%			

The precision error (P) of an average value, $\bar{X}$ measured from N samples is given by

$$P = \frac{K\sigma}{\sqrt{N}} \quad (4-18)$$

Where K is the confidence coefficient and K equals to 2 for a 95% confidence level when $N \geq 10$ (Coleman and Steele, 1995). σ is the standard deviation for N sample images and is defined as follows,

$$\sigma = \sqrt{\frac{1}{N-1} \sum_{k=1}^N (X_k - \bar{X})^2} \quad (4-19)$$

The averaged quantity is defined by the following equation

$$\bar{X} = \frac{1}{N} \sum_{k=1}^N X_k \quad (4-20)$$

Typical standard deviation at the proximal anastomosis is 3.8% and is 5.6% at the mainstream and near-wall region respectively, whereas for the distal anastomosis the standard deviation is 4.3% and is 6.2% at the mainstream and near wall-region respectively. These values give precision limits of 2.41% and 3.54% for velocity in the mainstream and near-wall region at the proximal anastomosis respectively, meanwhile precision limits of 2.72% and 3.92% for the velocity of the mainstream and near-wall region at the distal anastomosis respectively. Consequently the total uncertainty resulting from this measurement was calculated by the following equation at different locations,

$$E_u = \sqrt{B_u^2 + P_u^2} \quad (4-21)$$

The total uncertainty of the velocity u was estimated to be 2.49% and 3.60% respectively at the mainstream and near-wall region of the proximal anastomosis, and correspondingly 2.81% and 3.98% for the distal anastomosis. Therefore, in the present study, the maximum uncertainty of the velocity measurement using the PIV system was estimated to be less than 4%.

CHAPTER 5

MEASUREMENTS OF

PROXIMAL ANASTOMOSIS MODELS

5.1 Introduction

CABG remains the standard surgical practice at many medical centers for the treatment of occlusive coronary disease and the reoperation of occluded bypass grafts, despite the development of less invasive technique, e.g. endovascular stenting (Hoffmann et al., 1999; Serruys et al., 2001). The saphenous vein graft is used most commonly because it is relatively plentiful, readily accessed, and easily harvested. Although it provides adequate flow to the recipient artery, its tendency to occlude is an important drawback (Nwasokwa, 1995). Based on literature review, SV graft failure is the primary reason for coronary artery bypass reoperation and the major cause of failure is the occurrence of intimal hyperplasia together with the progression of atherosclerosis, which has been attributed to mechanical injury and the disruption of flow at the anastomosis (Bassiouny et al., 1992; Newby and Zaltsman, 2000; Eckstein et al., 2002).

The distal anastomosis has been the subject of intensive investigations and most of the studies have been performed to investigate the hemodynamics related to the distal anastomotic IH (Bassiouny et al., 1992; Ojha et al., 1990, 1993; Steinman et al., 1993; Kleinstreuer et al., 1996; Lei et al., 1997; Kleinstreuer et al., 2001). Rare efforts have been put on proximal anastomosis except Ojha et al. (1993), Hughes and How (1995) and Zhang (2005). However, the distal anastomosis is not isolated but systematic linked with

aorta through proximal anastomosis and it is not surprising that the flow patterns at the distal anastomosis will be significantly affected by the upstream flow, e.g. flow characteristics at the proximal anastomosis. 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 et al., 1995). Especially for the vein graft, apparent intimal hyperplasia plaques were usually found at the proximal anastomosis, where eddy blood flows formed, and progressed toward the distal anastomosis (Liu and Fung, 1998). For the reverse vein graft, most common graft lesions developed adjacent to the proximal anastomosis, which is the narrowest part of a reversed vein graft (Berkowitz et al., 1992).

Therefore it is necessary to fully explore the flow characteristics of the proximal anastomosis and build up the upstream flow condition before studying the whole CABG anastomoses. In this study what we are interested in is the bypass graft for right coronary artery, for which the typical location and course of bypass graft surgery can be assumed approximately in the same plane (Galjee et al., 1996), therefore symmetric models were designed and fabricated to represent the proximal anastomosis. In end-to-side/side-to-end anastomoses, the geometry of the anastomosis in particular the anastomotic angle may be a more important factor in the flow characteristics, than the mismatch in elastic properties between the graft and host aorta/artery (Chandran and Kim, 1994). Hence in this chapter, discussions on the experimental results obtained for the proximal models with different anastomotic angle are presented. Based on the hypothesis that regions of low-WSS-high-OSI and high-WSS-low-OSI are corresponded to the early atherosclerotic lesion development (Buchanan et al., 1999 and 2003) and elevated time-averaged WSSG region is susceptible to atherosclerotic lesions (Lei et al., 1995 and 1996), the hemodynamic

performances of the models will be evaluated and the optimal proximal anastomotic angle which would provide best graft patency will be proposed.

5.1.1 Test Models

The physical models used in the PIV experiments 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 view of models with anastomotic angle of 45° was shown in Figures 5-1. Note that in the study, five models with anastomotic angles varying from 30° to 90° in 15° interval were constructed to investigate the effect of anastomotic angle on local hemodynamics and provide useful information in whole anastomosis study.

Figure 5-1 Schematic design of the 45° proximal anastomotic model

5.1.2 Flow Conditions

The investigation on steady flow condition is to provide fundamental knowledge and understanding on some phenomenon that may occur under pulsatile flow conditions. The 45° model, which was selected as the representative model, was studied under steady flow condition. The inlet flow rate of aorta was 5l/min and the outlet flow of graft was

60ml/min according to the typical mean flow rate in the saphenous aortocoronary vein graft (Galjee et al., 1996; Eckstein et al., 2002). For physiological flow condition, the computer controlled piston pump system was used to generate the pulsatile flow waveform and flow meters were used to monitor the real time waveform and provide feedback signal to the piston pump interface, as described in Chapter 3. A typical physiological aortic flow waveform reported by Nichols and O'Rourke (1990) was used as the piston pump input. Figure 5-2 shows the comparison of experimental velocity profile obtained at the aorta inlet and input waveform. The characteristics of the pulsatile waveform were listed in Table 1.

Figure 5-2 Comparison the aorta inlet velocity waveform with in vivo aorta inlet waveform from Nichols and O'Rourke (1990).

After the bypass surgery, the flow waveform in the graft and host artery would be much different with native coronary artery flow, especially for the RCA graft due to the weaker contraction of the right myocardium which has been already noticed by Berne and Levy as early as 1967. Some researchers investigated the flow in graft after CABG surgery and the flow waveforms published were quite different (Moran et al., 1971; Kajiya et al., 1987;

Galjee et al., 1996; Lu et al., 2001). However most of the reported flow rate values of graft were quite similar. Moran et al. (1971) reported flow was greater in left-side graft, $73\pm 23\text{ml/min}$, than those in 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. Recently Lu et al. (2001) have even observed that a patent bypass graft had a flow waveform morphologically similar to that of the aorta by means of electron beam tomography (EBT) investigation for 589 CABGs undergone after 3 month to more than 5 years old. Therefore in this study the graft was assumed to have the flow rate of 60ml/min and the outlets of graft and aorta were assumed to be fully developed with mean flow rate ratios of $Q_3/Q_1=1.2\%$ and $Q_2/Q_1=98.8\%$ within the cycle respectively. Note that Q_1 is the inlet flow rate of aorta, and Q_2 and Q_3 are the outlet flow rates of the aorta and the graft respectively, as indicated in Figure 5-1.

Table 5-1 Characteristics of the pulsatile waveform

Description	Characteristics
1 st Peak (at t_2)	$Re = 5430$
2 nd Peak (at t_5)	$Re = 667$
Reverse Flow (at t_4)	$Re = 865$
Mean Velocity	16.8 cm/s
Frequency	1.0 Hz
Womersley Number	13.6

5.2 Hemodynamics in Proximal Anastomosis Models for Steady Flow

5.2.1 Flow Characteristics

Figure 5-3 shows the flow field of the 45° model under steady flow condition. The main flow from the aorta maintains its flow path upon reaching the joint at the heel, and only part of the fluid is diverting into the graft. The flow reattaches at the further downstream of the graft inner wall, which results in the formation of a low velocity region close to the heel. Along the graft outer wall, the deviated main flow approaches the curved surface, and then bifurcates into two streams, with the formation of a stagnation point at the toe. The velocity distribution in the graft is skewed towards the graft outer wall at the entrance, and at further downstream of the graft, the flow is observed to have shifted slightly towards the inner wall.

Figure 5-3 Velocity vectors in the center plane of 45° proximal anastomosis model under steady flow condition.

5.2.2 WSS Distributions

As low WSS (Rittgers et al., 1978; Binns et al., 1989; Keynton et al., 2001; Loth et al., 2002), high or unidirectional WSS (Fry, 1969; Friedman et al., 1992) and WSSG (Ojha, 1993; Lei et al., 1996; Buchanan et al., 2003) were proposed to correlate with the development of IH at the suture joint, WSS of 45° proximal anastomosis model under steady flow was calculated and presented in this section.

Figures 5-4 (a) and (b) show the WSS distributions of the proximal anastomosis along the graft inner and outer walls respectively. Note that for the ease of presentation, two arbitrary coordinates are used to present the results. The origin of x_1 is the point selected approximately at the end of the straight aortic wall and is going along the direction of the graft inner wall, while the annotation x_2 is used to indicate the spatial location along the graft outer wall, as shown schematically at the upper right corner of the figures. From Figure 5-4 (a) it was observed that when approaching the heel the WSS increased steadily and reached the peak value of 2.8 Pa at $x_1 = 0\text{mm}$. After that the WSS decreased drastically and stayed about the same level to form a low WSS region, which was due to the low velocity region occurred there. After the low velocity region the WSS increased slightly and reached the second peak of 1.7 Pa at $x_1 = 13.4\text{mm}$ where the flow skewed toward the graft inner wall. Then the WSS decreased and maintained at low level with minor variation at further downstream of graft where the disturbance caused by the suddenly change of flow direction disappeared.

Along the graft outer wall, as demonstrated in Figure 5-4 (b), the WSS remained as negative value at the downstream of aorta which was due to the definition of the

x_2 coordinate and the flow direction. At the toe region a stagnation point (at $x_2 = 3.5\text{mm}$) with zero WSS was found. After the stagnation point the WSS was found to increase along the graft outer wall and decrease at further graft downstream due to the skewed velocity vector shifted slowly back to the graft centerline. Generally along the graft outer wall the WSS was slightly higher than those along the graft inner wall, the WSS overall are low at proximal anastomosis under steady flow condition.

Figure 5-4 WSS distributions of the 45° proximal anastomotic model (a) along the graft inner wall (b) along the graft outer wall

5.3 Hemodynamics of Proximal Anastomosis Models with Different Anastomotic Angle for Pulsatile Flow

In present study five proximal models with anastomotic angles varying from 30° to 90° in 15° interval were investigated under the same pulsatile flow condition. In this section the 30° model was selected as the baseline model to present the flow fields in detail throughout the flow cycle, whereas results of other models were presented and discussed subsequently to demonstrate the effect of the anastomotic angle on the hemodynamics. Figure 5-5 shows the flow rate waveform measured at the aorta inlet during the PIV

measurement. Note that the period of each cycle was maintained at 1.0s and nine representative time intervals were selected to present the flow fields.

Figure 5-5 Aortic inlet flow rate waveform and location of time intervals selected for presenting the experimental results

5.3.1 Flow Characteristics of 30° Model

At $t_1=0.1s$, as observed in Figure 5-6 (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 on the outer wall. The velocity magnitude was generally small as the inlet flow just began to accelerate. With the evolution of acceleration, at $t_2=0.2s$, a flow separation indicated by the streamlines diverged from a point was found near the heel due to the drastic change in flow direction of the fluid entering the graft, as shown in Figure 5-6 (b). The flow separation induced a low and recirculation flow region near the heel and a reattachment point on the graft inner wall.

As shown in Figure 5-6 (c), at the peak flow phase ($t_3=0.3s$), the size of the low and circulating flow region increased to occupy almost half of the anastomosis and another flow separation point was found on the graft inner wall. When the inlet flow entering the deceleration phase ($t_4=0.35s$), the low and circulation flow region caused by the two separation flows developed continuously and occupied almost all the anastomosis region and the graft cross section at the vicinity of graft inner wall, as shown in Figure 5-6 (d). At this time interval the flow separation that caused the vortex still existed whereas another flow separation was indicated by streamlines converged into a point located further downstream near the graft inner wall.

With the evolution of the deceleration, at $t_5=0.45s$, the vortex caused by the first flow separation moved slightly toward the aorta and the second flow separation which was found earlier disappeared at this time interval. The low and recirculating flow region was observed to reduce in size, as shown in Figure 5-6 (e). At $t_6=0.55s$, with further deceleration of the aorta inlet flow, backflow from the graft into the aorta was found due to the pressure gradient caused by the flow deceleration whereas forward inlet flow dominated in the aorta, as shown in Figure 5-6 (f). Most part of the backflow from the graft merged with the aortic forward flow at the anastomosis and formed a large recirculation region near the toe, whereas a small part of the backflow near the heel flowed in reversed direction along the aortic ceiling. At $t_7=0.6s$ the inlet flow decreased continuously and more fluid from the graft near the heel flowed back along the aortic ceiling, as shown in Figure 5-6 (g). Buchanan et al. (1999) also reported that 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 $t_8=0.70s$, the net flow rate was in the reverse direction dominated by the backflow in both the aorta and the graft, as shown in Figure 5-6 (h). It was found that the velocity profile of the backflow in the aorta skewed toward the graft when accessing the anastomosis. A nodal point indicated by the streamlines converged into a point was found near the graft outer wall where the backflow from the aorta met that from the graft. The nodal point, which can be viewed as sink in the streamlines inside the anastomosis, was the attachment point of three dimensional flow separation (Filippone, 2004). Near the heel two backflow streams merged and flowed toward the upstream of aorta. At $t_9=0.85s$, the flow was accelerating again with a low positive flow rate. From Figure 5-6 (i) it was found that along the aorta upper wall backflow still dominated at this time interval. Although the flow velocity magnitude was quite small, the flow pattern was found to be more complicated than that of $t_8=0.70s$ especially at the toe region that a nodal point existed.

(a) $t_1=0.1\text{ s}$

(b) $t_2=0.2\text{ s}$

(c) $t_3=0.3\text{ s}$

(d) $t_4=0.35\text{s}$

(e) $t_5=0.45\text{s}$

(f) $t_6=0.55\text{s}$

Figure 5-6 Flow fields of the 30° proximal model at different time intervals

5.3.2 Hemodynamic Parameters of 30° Model

Figures 5-7 (a) and (b) show the contour maps of the WSS distribution of the 30° proximal model along the graft inner wall and outer wall respectively. Note that the x -axis represents the distance along the graft and the y -axis represents the time interval of the flow cycle. It can be observed that along the graft inner wall the WSS was relatively small at the beginning of the flow cycle. The WSS increased in magnitude with the time and reached the peak value at about 0.26s near the heel. During the time of acceleration phase and the late deceleration phase ($t=0.2s$ to $t=0.55s$), low and negative WSS region, which was highlighted in the contour map, was found after the heel. From $t=0.55s$ onward when the backflow fully occupied the graft and aortic ceiling, due to the flow separation formed in the flow fields as demonstrated in Figure 5-6, the WSS were low and negative in the whole region. Note that the sign of the WSS is determined by the flow direction and the definition of the coordinate. The WSS was found to maintain negative at the reverse flow phase until the inlet flow reached the diastolic acceleration phase.

The WSS distributions along the graft outer wall were found to be higher in magnitude than those along the graft inner wall in general, as indicated in Figure 5-7 (b), which is due to the flow skewed toward the graft outer wall especially during the acceleration phase. Note that the presentation of x_2 coordinate is opposite to the usual convention, that is x_2 is increased from right to left for the flow from aorta to graft outer wall. The WSS along the graft outer wall was relatively small at the beginning of the flow cycle and increased in magnitude with the time and reached the peak value at 0.3s. Note that the negative WSS is due to the flow direction and definition of x_2 coordinate. Stagnation point was found on the graft outer wall from the beginning of the flow cycle until the reversed flow phase ($t=0.6s$). From Figure 5-7 (b) it can be observed that the stagnation

point (indicated by line in Figure 5-7 (b)) moved toward toe slightly before entering the acceleration phase, which is due to the gentle increment of flow rate at the beginning of the cardiac cycle. After that the stagnation point moved toward graft downstream during the acceleration phase and shifted backward to the toe during the deceleration phase. At the late deceleration and reversed flow phases, flow separation point (indicated by dark line) emerged at the downstream of the graft outer wall and moved toward the toe, it then shifted slightly back until the end of the reverse flow phase. At the diastolic flow phase, the separation point disappeared and the stagnation point re-emerged on the graft outer wall. The WSS was found to be relatively low in magnitude during the reverse flow and diastolic flow phase which is due to the low inlet flow rate during these time intervals.

Figure 5-7 Contour maps of the WSS distribution of the 30° proximal model (a) along the graft inner wall (b) along the graft outer wall (Line on the figure (a) indicated the low and negative WSS region; line on figure (b) indicated locations of the stagnation/reattachment/separation point on the graft outer wall)

Figures 5-8 (a) and (b) show the contour maps of the spatial wall shear stress gradient (SWSSG) of the 30° proximal anastomosis model along the graft inner and outer walls respectively. As shown in Figure 5-8 (a), the SWSSG distribution was relatively smooth beside the heel region (ranging from $x_1 = -0.2\text{mm}$ to $x_1 = 2\text{mm}$) where SWSSG was found to have more variation and larger in magnitude during the acceleration and deceleration phase ($t=0.1\text{s}$ to $t=0.6\text{s}$). This is due to the drastically changed in velocity at this region shown earlier in Figure 5-6. On the other hand, smaller SWSSG was found on the graft outer wall although the WSS was generally larger than those along the graft inner wall, as shown in Figure 5-8 (b). Relatively high SWSSG region on the graft outer wall occupied much larger area (ranging from $x_2 = 11\text{mm}$ to $x_2 = -2\text{mm}$) during the acceleration and deceleration phase, which is due to the stagnation point movement during these time intervals.

Figure 5-8 Contour maps of the SWSSG distribution of the 30° proximal anastomosis model (a) along the graft inner wall (b) along the graft outer wall.

In order to quantitatively investigate the distributions of hemodynamic parameters, the time-averaged WSS, OSI and time-averaged WSSG along the graft inner and outer walls were calculated and presented in Figures 5-9 (a) and (b) respectively. Along the graft inner wall the time-averaged WSS increased steadily when accessing the heel and reached the peak value of 4.5 Pa at $x_1 = 0\text{mm}$, as shown in Figure 5-9 (a). After that the time-averaged WSS decreased drastically into a low WSS region from $x_1 = 2\text{mm}$ onwards, which is consistent with the low and recirculation region along the graft inner wall as observed earlier. The low time-averaged WSS region was area of flow separation/reattachment throughout the flow cycle as indicated by the elevated OSI value at the same region with a peak at $x_1 = 1.75\text{mm}$. The time-averaged SWSSG was small at the aortic ceiling and varying drastically with distinct peaks when entering the anastomosis region; after that the time-averaged WSSG decreased and maintained at low level with minor variations. Note that elevated time-averaged WSSG was also found to be associated with the low-WSS-high-OSI region at the vicinity of heel especially at $x_1 = 1.75\text{mm}$.

Along the graft outer wall the time-averaged WSS was generally higher than those along the graft inner wall, as shown in Figure 5-9 (b). The WSS were kept around 1.5 Pa level with minor variation at graft downstream and increased sharply to the peak value of 4.5 Pa at the toe and decreased when entering the aortic ceiling. The time-averaged WSSG was relatively high (with maximum value of 2 Pa/mm) at the hood region proximal to the toe, however maintained a small magnitude of 0.5 Pa/mm in the graft outer wall. High OSI region was found on the hood slightly shifted to graft downstream and away from the peak WSSG region, where the time-averaged WSS was low.

High-WSS-low-OSI regions were both found at the heel and toe. As reported by Buchanan et al. (1999 and 2003) regions of low-WSS-high-OSI and high-WSS-low-OSI combination were corresponded to the early atherosclerotic lesion development. In addition, the elevated WSSG also contributed to the modification of the endothelium cell permeability, and resulted in the continued growth of the lesions. Therefore regions of heel, toe and region along the graft inner wall after the heel would be more prone to disease and more attention should be paid in the performance evaluation of the proximal anastomosis.

Figure 5-9 Time-averaged WSS, WSSG and OSI distributions of the 30° proximal anastomosis model (a) along the graft inner wall (b) along the graft outer wall.

5.3.3 Effect of the Anastomotic Angle on the Local Hemodynamics

As demonstrated in the flow fields of the 30° proximal anastomosis model, the flow patterns during the peak acceleration and deceleration flow phases were more complicated than those in other time phases. Therefore four time intervals during the peak flow ($t=0.3s$), deceleration phase ($t=0.35$, $t=0.45$) and the reverse flow phase ($t=0.7s$) were selected to present the effect of the anastomotic angle on the flow characteristics of the proximal anastomosis models and results at other time intervals were shown in the Appendix-A. As shown in Figure 5-10 (a) at 45° model a flow separation indicated by streamlines diverged from a point was found within the anastomosis region near the heel, which caused minor low velocity backflow along the graft inner wall at the peak flow phase ($t=0.3s$). However the size of the low velocity region was smaller in both length and width when compared with other models. Furthermore the flow separation was not happened on the blood vessel surface of 45° model, but was occurred on the wall at other models (as shown in Figures 5-6 (c), 5-10 (b), (c) and (d)). When entering the deceleration phase ($t=0.35s$), the low velocity regions of all models were found in Figure 5-11 to reduce in size except the 30° model as shown earlier in Figures 5-6 (d). At this time interval more uniform velocity profile was found at the 45° and 60° models at further downstream of the graft.

As shown in Figure 5-12, with the evolution of deceleration, the vortex within the anastomosis regions increased in size of all models except the 90° model where flow separations on the graft inner wall and the center of the graft were found. It can be observed that the disturbed flow patterns became more serious with the increase of the anastomotic angle at this time interval. At the reverse flow phase, as demonstrated in Figure 5-13, flow patterns of all models were similar and backflows were found from

both the aorta and graft. The 45° model has more uniform flow pattern (Figure 5-13 (a)) whereas recirculating flows along the graft inner wall were found in 60° and 75° models (Figures 5-13 (b) and (c)) and flow separation were found on the graft wall at the 90° model (Figure 5-13 (d)). Furthermore, a recirculation flow with an extent over 10mm was found at the 90° model along the graft outer wall.

Figure 5-10 Flow patterns during the peak flow phase ($t=0.3s$) of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

Figure 5-11 Flow patterns during the deceleration flow phase ($t=0.35s$) of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

Figure 5-12 Flow patterns during the deceleration flow phase ($t=0.45s$) of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

Figure 5-13 Flow patterns during the reverse flow phase ($t=0.7s$) of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

Figures 5-14 and 5-15 show the contour maps of the WSS distributions for the model investigated along the graft inner and outer walls respectively. For all models, the general trend of the WSS distributions is similar. Along the graft inner wall, as shown in Figure 5-14, the WSS increased in magnitude with the time and reached the peak value at about 0.3s. From the acceleration phase ($t=0.2s$) to the late deceleration phase ($t=0.55s$), low and negative WSS region was found after the heel, as outlined in Figure 5-14. The WSS remained negative at the reverse flow phase until the inlet flow reached the diastolic acceleration phase. As shown in Figure 5-15, elevated WSS was found along the graft outer wall, especially during the acceleration phase. Stagnation points were found on the graft outer wall from the beginning of the flow cycle until the reverse flow phase. It was observed that the stagnation point moved toward the toe from the beginning of flow cycle till the end of the deceleration phase except a small time interval at the acceleration phase it was being shifted toward the graft outer wall.

It is clear that the anastomotic angle affects the WSS distribution. At the vicinity of heel, high WSS region was found at all models. This region was small in size in the 45° model, but became prominent in the other three models not only in size but also in time span. Along the graft inner wall an extensive region with extremely low WSS appeared in the 90° model, however, this region was greatly reduced with the decrease of anastomotic angle. For WSS at the vicinity of toe no significant difference was observed among the models, whereas elevated WSS region along the graft outer wall was found to increase in both size and maximum magnitude in larger anastomotic angle models. In addition, the movement trace of the stagnation point was similar at 45° , 60° and 75° models and was kept shifting toward the toe, whereas almost fixed stagnation point at the vicinity of toe was found in the 90° model during the acceleration and deceleration phases.

Figure 5-14 Contour maps of WSS distribution along the graft inner wall of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

Figure 5-15 Contour maps of WSS distribution along the graft outer wall of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

Figures 5-16 and 5-17 show the contour maps of the SWSSG distributions along the graft inner wall and outer wall respectively. In general the SWSSG was found to have more variation from the systolic acceleration ($t=0.2s$) to the late deceleration phases ($t=0.55s$) along both the graft inner wall and outer wall, whereas the SWSSG distributed relatively smoothly and maintained in low level during other flow phases. For SWSSG along the graft inner wall, as shown in Figure 5-16, elevated SWSSG regions were found at the vicinity of heel for all models during the systolic acceleration and deceleration phases. Comparing the SWSSG distributions for all models it was found that the elevated SWSSG region around the heel increased to the maximum (5.77 Pa/mm in 45° model, 7.63 Pa/mm in 60° model, 8.40 Pa/mm in 75° model and 12.2 Pa/mm in 90° model). In addition, at the downstream of graft inner wall more variations were found in 90° model as shown in Figure 5-16 (d).

Generally the SWSSG on the graft outer wall was higher than those on the graft inner wall, especially in the vicinity of the stagnation point, resulting from the impinging and splitting of the high-momentum flow about the point. Elevated SWSSG regions were also found around the toe, as demonstrated in the contour maps of SWSSG along the graft outer wall in Figure 5-17. Both the size of the high SWSSG region and the maximum value of SWSSG were increased with the increase of the anastomotic angle (6.35 Pa/mm in 45° model, 8.54 Pa/mm in 60° model, 13.7 Pa/mm in 75° model and 16.3 Pa/mm in 90° model). For the 90° model several minor elevated SWSSG regions were found at the downstream of graft.

Figure 5-16 Contour maps of SWSSG distribution along the graft inner wall of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

Figure 5-17 Contour maps of SWSSG distribution along the graft outer wall of proximal models with different anastomotic angle (a) 45° (b) 60° (c) 75° (d) 90°

5.3.4 Evaluate the Hemodynamic Performance of Proximal Models

Intimal hyperplasia in graft conduit, the main cause of the poor long-term patency of bypass system, is associated with multiple factors including disturbed flow patterns, extremities (high and low) in WSS and high level of OSI. On the basis of the preponderance of clinical evidence that “disturbed flow” patterns, including flow separation and reattachment, low oscillatory wall shear, vortical flows, high shear stress, play a key role in the onset and progression of atherosclerosis and intimal hyperplasia. Disturbed flow indicators, regions of low-WSS-high-OSI, high-WSS-low-OSI and elevated SWSSG, were postulated to represent favorable conditions for the onset and/or progression of the graft disease (Ku et al., 1985; Berceli et al., 1990; Friedman et al., 1992; Hughes and How, 1996; Kleinstreuer et al. 2001)

The PIV instantaneous flow fields of the proximal models revealed severe flow skewing from the mainstream impinges on the graft outer wall, vacating a large area in the vicinity of the graft inner wall which is experiencing low and reverse flows. The low velocity region, which was shown to have low WSS, was found along the graft inner wall from the early acceleration phase ($t=0.1s$) until the reverse flow phase ($t=0.6s$) in all models studied. The size of this region was observed to decrease slightly with the increase of anastomotic angle from 30° model to 45° model, however, increased from 45° model to 90° model where the low and reverse flow region occupied almost the whole investigated graft inner wall area, as described earlier in the velocity plots (Figures 5-6, 5-10, 5-11 and 5-13) and WSS distributions (Figures 5-7 and 5-14). Within the low velocity region, the disturbed flows could prolong the residence time for circulating pro-inflammatory cells to adhere to the endothelial monolayer cells of the vessel, and thus increased the chances in forming mitogens and activating platelets. Once the mitogens formed and the platelet

activated, they might be carried down to the distal site on the physiological cycle and fastened the formation of the intimal hyperplasia (Clowes et al., 1993; Hughes and How, 1995).

In a uniform flow region, the magnitude of WSSG would be zero, so any magnitude of WSSG would show a nonuniform hemodynamic environment. Elevated WSSG was believed to contribute to the high LDL permeability (Buchanan et al., 1999) and intimal hyperplasia (Lei et al., 1995). Unfortunately the WSSG in the bypass graft cannot be totally eliminated but can only be minimized due to the bifurcation, diameter mismatch and so on. For all models elevated WSSG regions were found at the vicinity of heel and toe as well as the stagnation point (Figures 5-8, 5-16 and 5-17). At the vicinity of heel the elevated WSSG region increased in both size and peak magnitude from 45° model to 90° model, however, the 30° model has worst performance because highest WSSG occurred in this model. For WSSG along the graft outer wall the maximum value of WSSG increased with the increase of anastomotic angle. The 90° model was found to have the worst performance at the graft outer wall because the much more elevated magnitude and extend of the high WSSG region. In addition, the elevated WSSG region shifted slightly toward the toe with the increase of anastomotic angle, which would worsen the situation due to extra damage to the injured endothelium of the vein graft and coronary artery caused by the overlap of stagnation point and the suture line where high stress and strain were concentrated.

In order to show a quantitative comparison among the five models, the time-averaged WSS, time-averaged WSSG and OSI along the graft inner and outer walls were shown in Figures 5-18 and 5-19 respectively. It can be observed that in Figures 5-18 and 5-19,

hemodynamic parameters of all models were distributed in a similar trend. Relatively low time-averaged WSS region was observed along the graft inner wall where flow separation/reattachment occurred with elevated OSI due to rapid change of flow direction within the cycle. The low-WSS-high-OSI location was also found to be associated with elevated time-averaged WSSG along the graft inner wall, especially for 90° model at $x_1 = 1.8\text{mm}$ as shown in Figure 5-18 (d). Along the graft outer wall as demonstrated in Figure 5-19, high OSI occurred at the location where the low WSS was formed. In general, at the vicinity of heel and toe, regions of elevated time-averaged WSS and WSSG associated with low OSI value were observed. High WSS could increase transmural filtration and elevate LDL influx whereas low WSS is related to high LDL concentration as well as reduced oxygen flux into the arterial wall (Perktold et al., 2002; Stangeby and Ethier, 2002; Wada and Karino, 2002). Therefore regions of low-WSS-high-OSI and high-WSS-low-OSI were corresponded to the early atherosclerotic lesion development (Buchanan et al., 1999 and 2003).

Although different anastomotic models have similar hemodynamic parameters distribution, their hemodynamic performances varied significantly. Firstly, the size of the region of low-WSS-high-OSI along the graft inner wall varied significantly at different anastomotic model. The 45° model has the smallest area for such region whereas the 90° model has the largest one. In addition, the time-averaged WSSG increased significantly with the increase of anastomotic angle except the 30° model, which has the highest WSSG and largest region of elevated WSSG. Along the graft outer wall, both the size of the elevated WSSG region and maximum value of WSSG were amplified notably with the increase of anastomotic angle, as demonstrated in Figure 5-19. It was believed that the elevated time-averaged WSSG, which aggravates impact of changes in surface

and causes cell dysfunction, excessive release of growth factors, smooth muscle cell proliferation, platelet aggregation etc, are associated with regions susceptible to atherosclerotic lesions (Lei et al., 1995 and 1996). Considered all models together, hemodynamic performances at both graft inner and outer walls deteriorated with increasing anastomotic angle except the 30° model, which has good performance along graft outer wall but worst performance along the graft inner wall.

Figure 5-18 Time-averaged WSS, WSSG and OSI distributions along the graft inner wall of (a) 45° (b) 60° (c) 75° (d) 90° anastomotic model

Figure 5-19 Time-averaged WSS, WSSG and OSI distributions along the graft outer wall of (a) 45° (b) 60° (c) 75° (d) 90° anastomotic model.

5.4 Comparisons with Other Published Works

Zhang (2005) studied numerically the flow characteristics of the 45° forward, 45° backward and 90° proximal anastomosis models under steady and pulsatile flow conditions. Similar flow pattern can be found from the results of the PIV experiment and numerical simulation, i.e. for both studies, flow separation region was found near the heel region at the peak flow phase; the flow separation region evolved into a big vortex gradually within the flow deceleration phase; backflow from the aorta to the graft was found at the reverse flow phase. In order to quantitatively validate the numerical simulation and indirectly verified the present experimental work, comparison of the wall shear stress along the graft inner wall and graft outer wall between the results of the PIV measurements and the numerical simulation by Zhang (2005) were carried out. Figures 5-20 (a) and (b) show the comparison of the wall shear stress distributions along the graft inner wall and outer wall of proximal anastomosis at the peak flow phase respectively. Generally, the wall shear stress distributions along the graft inner wall share a similar pattern for both experimental and numerical studies, as shown in Figure 5-20 (a). It is noted that along the aorta floor (where $x_1 < 0\text{mm}$) and the downstream of graft (where $x_1 > 10\text{mm}$) the experimental data agree with the numerical results well, whereas relatively large discrepancy was detected around the anastomosis region and the experimental wall shear stress was generally smaller than the corresponding numerical simulations. Similarly, the wall shear stress distributions along the graft outer wall also showed the same pattern as those along the inner wall, as indicated in Figure 5-20 (b). That is relatively high difference was found around the anastomosis region ($0\text{mm} < x_2 < 10\text{mm}$), while the experimental and numerical results match quite well at

other locations. Furthermore the experimental results were found to be generally a little smaller than those obtained numerically.

Figure 5-20 Comparison of wall shear stress of PIV measurements and numerical simulation by Zhang 2005 (a) along the graft inner wall (b) along the graft outer wall

The reason for the relatively smaller magnitude in experimental results is that, according to the principle of PIV measurement, the velocity, u (in m/s), is expressed by the following equation:

$$u = M \frac{\Delta s}{\Delta t} \tag{5-1}$$

Where Δt is the time interval between laser pulses, Δs is the number of pixels corresponding to the displacement of particle in the images, M is the transition coefficient.

The determination of the mean displacement using the cross-correlation function to which

that all particle pairs have the same contributions is assumed. But, several bias errors result from the fact that some particles contribute more to the correlation function than others. One of the most important bias errors is due to the loss of particles between the first and second images. For instance, a fast moving particle has a chance of moving out of the interrogation window and therefore not contributing to the correlation function. The particles present in only one of the two images will be ignored and do not contribute to the correlation function since the mean particle displacement is measured by fitting a curve to the discrete correlation function and locating the peak value of this curve. Since slower particles are more likely to be captured in both images, they have higher possibility in contributing to the correlation function than the fast moving particles. This effect tends to skew the correlation function towards the lower displacements, especially when the interrogation window is in a region of the flow with high velocity gradient. Therefore more discrepancy would be expected in the WSS estimation around the anastomosis region when comparing the experimental result with the simulation result.

Another possible reason is that velocity in the anastomosis region changes tremendously both in direction and magnitude due to the high curvature variations and the 0.25mm spatial resolution of the PIV may not be fine enough to capture the detailed variations of velocity distribution, which is important in the estimation of WSS. Whereas the numerical simulation does not have such spatial resolution limitations, since more meshes can be allocated near the wall to overcome this problem. Therefore large discrepancy was found between the WSS estimations around the anastomosis region. In addition, it can be observed that the PIV measurements are in better agreement with the simulation results at the aorta and graft regions, where the geometries are cylindrical in shape, therefore the detailed geometrical variations between the experimental and numerical models

especially at the anastomosis regions would be another important reason for the discrepancy in the WSS estimation.

Further comparison of time-averaged wall shear stress along the graft inner wall and graft outer wall of proximal anastomosis were carried out and shown in Figures 5-21 (a) and (b) respectively. Just as the wall shear stress distribution, similar pattern can be observed in the time-averaged wall shear stress distributions with relatively smaller magnitude in experimental data. However, larger discrepancy was found around the anastomosis region along the graft inner wall, as shown in Figure 5-21 (a). The reason for the larger discrepancy is that the frequency of the flow waveforms applied in the experiment is 1 Hz while 0.8 Hz is used in the numerical simulation. Discrepancies at the different flow phase accumulated for a whole flow cycle and resulted in the higher discrepancy at the time-averaged wall shear stress distributions, as shown in Figures 5-21 (a) and (b). Especially for the region along the graft inner wall, the flow field was much more complicated (flow separation regions occurred) than that along the graft outer wall. Therefore, the difference in the weight factor of the flow waveform frequency would be much larger along the graft inner wall than that along the graft outer wall. That is the reason why the experimental time-averaged wall shear stress match the numerical results along the graft outer wall better than along the graft inner wall, as demonstrated in Figures 5-21 (a) and (b)

Figure 5-21 Comparison of the time-averaged WSS of PIV measurements and numerical simulation by Zhang 2005 (a) along the graft inner wall (b) along the graft outer wall

To further verify the experimental results, some comparisons between the present experimental results and other published works were carried out. Figure 5-22 shows the WSS variations within a complete pulsatile cycle at the heel ($x_1 = 0 mm$) and the toe ($x_2 = 0 mm$) of 45° model. 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 17.8 degree, and the magnitude of WSS at the toe was higher than those at the heel in most of the time phases as demonstrated in Figure 5-22. All these results followed the similar trend of the photochromic tracer study obtained by Ojha et al. (1993), although it was

difficult to compare quantitatively due to the different flow ratio, graft diameter and flow waveform used.

Figure 5-22 Wall shear stress variations on the heel and toe

Since there were little published works available on the proximal anastomosis, the studies of the bifurcated artery flows were used to give some clue about the WSS distribution along the wall to compare with the present results. Buchanan et al. (1999) carried out the numerical investigations on the hemodynamics of the bifurcating blood vessel by using rabbit aorto-celiac junction as the representative atherosclerotic model. At the peak flow phase in their study, flow divider generated vortices along the inner wall of the celiac branch and along the aorta and the reversed flow along the entire dorsal wall of the aorta was found at the deceleration phase. Backflow dominated along the dorsal wall; however, the core of the flow was still positive in the aorta when the inlet flow decelerated into the reverse flow phase. Comparing with the flow fields of the 90° proximal model (as shown in Figures 5-10 to 5-13) quite similar flow patterns can be found, although with some minor discrepancy in the detailed variations of the flow fields. Figure 5-23 shows the wall shear stress distribution at the peak flow phase in their study. Comparing Figure 5-23

with the experimental results shown in Figures 5-14 (d) and 5-15 (d) of the report, a good agreement can be found at the center plane of the test model, including the elevated wall shear stress magnitude at the heel and toe, low wall shear stress regions along the graft inner wall and around the stagnation point on the graft outer wall.

Figure 5-23 Transient wall shear stress at the peak flow phase
(obtained from Buchanan et al., 1999)

To further verified the experimental work, Figure 5-24 shows the surface contour of the time-averaged wall shear stress, OSI and time-averaged wall shear stress gradient obtained by Buchanan et al. (1999). Comparing Figures 5-18 (d) and 5-19 (d) with hemodynamic parameter distributions at the model center plane in Figure 5-24, a good agreement can be found except that along the graft outer wall, several minor peaks of wall shear stress gradient were found in the present study. Possible reason for the discrepancy is that the difference in the test model and flow conditions. Large diameter ratio (3.33) between the aorta and graft was applied 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. In addition, different anastomosis configuration would also induce some discrepancy in both the flow fields and hemodynamics.

Figure 5-24 Hemodynamic parameters distributions: WSS_{nd} (a-b); $WSSG_{nd}$ (c-d) and OSI (e-f) (obtained from Buchanan et al., 1999)

Generally the present experimental study is comparable to other studies and is able to demonstrate the flow characteristics and hemodynamics with acceptable accuracy. Especially in the numerical study of Zhang (2005) suggested that the 45° backward facing model would provide the best graft patency rate among the three models investigated. This conclusion is consistent with present PIV measurements.

In present study, PIV measurements were carried out on the center plane of the test models and only show the 2-D flow pattern. Although the actual graft bypass is 3-D, all the test models were idealized to be in-plane in this study, which is because for the right coronary artery, the bypass grafting can be assumed approximately in the same plane (Galjee et al., 1996). It is noted that the secondary flow would not dominate the flow fields in this study, which has been shown in the flow fields obtained by Zhang (2005). In addition, from the principle of 3-D PIV, the measurement accuracy is highly depended on the calibration procedure and a calibration target with traverse system is required during the calibration. Unfortunately, due to the limitations of experimental facilities and the complicated geometry of the test models in the current study, the normal calibration target cannot be used in the measurement. Especially for the measurement on the distal anastomosis, the inner diameter of coronary artery is only 2mm. Concerning the facility limitations and other factors, the 2-D PIV system was applied only in the present study.

As the preliminary study for the design of sutureless Sleeve connector device for the coronary artery bypass grafting, although only two components of velocity vector were investigated at the center plane, the present experiment would be useful and the results for both the proximal and whole anastomosis models were found to have a fair match with the numerical simulation results by Zhang (2005). Furthermore, the experimental results were also comparable to the published results by Ojha (1993) and Buchanan et al. (1999). Therefore the present experimental work would be able to enhance the understanding of the stenosis pathophysiological process in the coronary artery bypass grafting, and also validating the numerical simulation by Zhang (2005). Finally, the present work would be useful in the further study of the hemodynamics of graft/artery anastomosis and provide useful information to the surgeon and the Sleeve connector design.

5.5 A Summary for the Chapter

This study was designed to examine the effects of anastomotic angle on the flow and wall shear stress distribution patterns of the proximal anastomoses, with emphasis on identifying site-specific hemodynamic features that could reasonably be expected to trigger the initiation and further development of anastomotic intimal hyperplasia. PIV measurement revealed that the flow field in the proximal anastomosis was strongly influenced by the anastomotic angle. Under pulsatile flow condition, large size of low recirculation flow, resulting in low WSS, was found along the graft inner wall just after the heel and decreased in size with decreasing of graft angle except the 30° model. Notable movement of the location of stagnation point at the graft outer wall was found at all models except the 90° model. The existence of flow separation, vortex and the small shifting of stagnating locations may accelerate the formation of IH.

The wall shear stress distributions in the pulsatile flow also demonstrate significant variations in time and space along the walls of the anastomotic joint. Elevated spatial wall shear stress gradients, which were believed to correspond to the elevated LDL permeability, were found around the anastomotic joints. Along the graft inner wall the size of the elevated SWSSG region and the maximum value of SWSSG were increased with the increase of anastomotic angle except the 30° model, which had the highest SWSSG and biggest elevated SWSSG region at the vicinity of heel. However, along the graft outer wall the SWSSG increased with angle for all models. Regions of low-WSS-high-OSI and high-WSS-low-OSI were found around the anastomotic joints, where elevated time-averaged WSSG was also noticed for all models. The size of the low-WSS-high-OSI region along the graft inner wall varied significantly at different anastomotic model. The 45° model has the smallest size of such region whereas the

90° model has the largest one. Furthermore, the time-averaged WSSG increased significantly with the increase of anastomotic angle except the 30° model, which has the highest WSSG and largest region of elevated WSSG. Along the graft outer wall, both the size of the elevated WSSG region and maximum value of WSSG were amplified notably with the increase of anastomotic angle.

To conclude, the 45° anastomosis model would provide the best graft patency rates among the five models investigated. All these findings would be useful in the design and optimization of complete bypass model, which included the flow from aorta through the graft to the coronary artery and would be reported in Chapter 6.

CHAPTER 6

MEASUREMENTS OF A WHOLE ANASTOMOSIS MODEL

6.1 Introduction

In spite of CABG being an effective surgical technique to revascularize the myocardium, 20-50% of bypass grafts fail due to the formation of intimal hyperplasia (Clowes, 1995). Studies suggested that suture line hyperplasia is initiated by surgical injury and promoted by compliance mismatch, but the bed hyperplasia has a hemodynamic origin (Bassiouny et al., 1992; Hofer et al., 1996). Therefore a thorough understanding of the flow fields is critical in treating the problems hemodynamically. Many researcher have analyzed the complex flow patterns in the distal coronary anastomotic region, using various simulated model in an attempt to explain the site of preferential intimal hyperplasia based on the flow disturbances and differential wall shear stress distributions. Most of the studies were carried out on subsections of the bypass flow domain, especially only on the distal anastomosis and usually idealized geometry of the anastomosis was assumed.

However, it is obvious that the flow fields in a simple end-to-side anastomosis tube are seriously affected and complicated by the upstream flow condition and the curvature of the graft tube. 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 addition, the complex anatomy of coronary vessel has made the investigation of coronary flow and hemodynamics, one of the most difficult and challenging studies to date. For considering the influence of hemodynamic factors on graft patency, it is important to replicate the in-

vivo geometry of the entire bypass conduit. In other words, a coronary artery bypass flow model must be anatomically accurate so as to capture the essential hemodynamics of the true geometry (Moore et al., 1999). Therefore in this study these drawbacks were addressed by studying the flow characteristics in the complete bypass model involving the entire flow domain from the aorta to the perfused artery under representative physiological conditions and the flow patterns and resulted hemodynamic parameters were highlighted and analyzed which are deemed to play a major role in the formation of intimal hyperplasia. It would be an important step towards realistic flow investigation and enhance the understanding of the stenosis path physiological process in CABG.

6.1.1 Test Model and Flow Conditions

The experimental model used in this study was designed to mimic the complete anastomosis based on the real-life situations according to the medical data provided by the National Heart Centre of Singapore. The diameters of aorta, graft and coronary artery were 25mm, 4mm and 2mm respectively. As the typical location and course of saphenous vein for RCA bypass graft surgery can be assumed approximately in the same plane (Galjee et al., 1996), therefore the representative planar model was designed and fabricated using silicon rubber as described earlier in Section 3.3.3.

The anastomotic angles at the proximal and distal anastomoses have been identified as a primary geometric feature that will profoundly affect the hemodynamic patterns of the bypass graft. Based on the findings in Chapter 5, the 45° proximal anastomosis model would provide better hemodynamic environments than other models, therefore in designing the whole anastomosis model the proximal anastomotic angle was set as 45°. For the distal anastomosis, smaller anastomotic angle (10-15°) was favored by a number

of studies in order to minimize the WSSG (Lei et al., 1996) and reduce the energy loss (Song et al., 2000), whereas the large anastomotic angle ($45 - 90^\circ$) contributed to greater velocity profile skewing in the host artery which increased the tendency to flow separation at the toe (Moore et al., 1999). Additionally, the high shear stress and high spatial shear gradients related to wall atrophy with both cell loss and matrix degradation which would cause maximal aneurismal dilation in the host vessel (Jackson et al., 2001). However, for the very acute anastomotic angle low mean shear stresses were delivered to the bed region opposite to the graft orifice, where intimal hyperplasia was identified (Fei et al., 1994), and large temporal gradients in shear stresses with pulsatile flow were accentuated by the movement of the stagnation point which would induce intimal proliferation (Jackson et al., 2001). Therefore both too large and too small angles are unfavorable and in this study an intermediate distal anastomotic angle of 30° was chosen in designing the whole anastomosis model.

Figure 6-1 showed the schematic view of complete design model and the regions of measurement were outlined in three rectangular boxes. The blood flow into the aorta (Q_1), and then some of them flow through the graft to enrich the coronary artery. The test rig was fine-tuned to achieve the same flow conditions for both steady and pulsatile flow as described in Section 5.1.2. This is because the proximal coronary artery was assumed fully occluded ($Q_4=0$) since it usually was occluded within a month after surgery and the compliance effect of the blood vessel was not taken into consideration in present study.

Figure 6-1 The Schematic view of the designed whole anastomosis model.

6.2 Hemodynamics of the Whole Anastomosis Model under Steady Flow Condition

Since abnormal hemodynamic events often labeled as “disturbed flow” play an important role in the regulation of vascular biology and the localization of atherosclerosis, PIV measurements were carried out to determine hemodynamic factors which encapsulated the “disturbed flow” and identify local sites in the CABG system which were susceptible to the onset of atherosclerotic lesions. 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 more vulnerable to the formation of plaques. Therefore in this study the flow characteristics in the proximal and distal anastomoses were investigated with more attention. In addition, the flow characteristics in the middle section of the graft were also investigated to reveal the evolution of the flow within the CABG system.

6.2.1 Flow Characteristics

Figures 6-2 (a) and (b) showed the flow fields of the proximal anastomosis and graft respectively. The velocity profile was parabola in shape at the upstream of aorta. When approaching the anastomosis, some parts of the fluid diverted into the graft, causing a low

velocity region along the graft inner wall and stagnation point at the toe. It was also noticed that the velocity profile skewed toward the graft outer wall slightly at the beginning part of the graft, as shown in Figure 6-2 (a). The velocity vectors basically parallel to the graft axis with the maximum velocity shifted closer to the outer wall due to the curvature of the graft, as shown in Figure 6-2 (b).

Figure 6-2 Flow fields of (a) proximal anastomosis and (b) graft

The flow field became much more complicated at the distal anastomosis, as shown in Figure 6-3 (a). The velocity profile showed that the fluid at the entrance of coronary artery skewed toward the toe and demonstrated a strong downwash toward the bed of the coronary artery, which was also observed by Lee et al. (2001). An obvious phenomena was observed in the experiment that the fluid near the occluded part of the anastomosis was almost stationary, although a weak recirculation region was found, as indicated in Figure 6-3 (a) and demonstrated as an enlarged view in Figure 6-3 (b). In addition, a stagnation point can be found on the bed of coronary artery. Since low velocity regions, vortex and stagnation point were supposed to correlate with IH (Hughes and How, 1996; Jones et al., 1997), the complex flow characteristics of distal anastomosis were more crucial than those at the section of proximal anastomosis and graft in terms of graft patency rate.

Figure 6-3 (a) Flow field of distal anastomosis (b) Enlarged view of the weak recirculation region.

6.2.2 WSS Distribution

As low WSS (Rittgers et al., 1978; Binns et al., 1989; Keynton et al., 2001; Loth et al., 2002), high or unidirectional WSS (Fry, 1969; Friedman et al., 1992) and WSSG (Ojha, 1993; Lei et al., 1996; Buchanan et al. 2003) were proposed to correlate with the development of IH at the suture joint, WSS of the whole anastomosis model under steady flow was calculated and presented in this section.

Figures 6-4 (a) and (b) show the WSS distributions of the proximal anastomosis. Note that for the ease of presentation, two arbitrary coordinates were used to present the results. The origin of x_1 is the point selected approximately at the end of the straight aortic wall and is going along the direction of the graft inner wall, while the annotation x_2 is used to indicate the spatial location along the graft outer wall, as shown schematically at the corner of the figures. It can be observed in Figure 6-4 (a) that when approaching the heel, the WSS decreased slightly along the aorta and then increased sharply until reaching the peak value at $x_1=0\text{mm}$. After that the WSS decreased drastically and stayed about the same level to form a low WSS region, which was due to the low velocity region occurred there. Along the graft outer wall, as demonstrated in Figure 6-4 (b), the WSS remained negative at the downstream of aorta which was due to the definition of the x_2 coordinate and the flow direction. At the toe region a stagnation point was found which was indicated by zero WSS. After the stagnation point the WSS was found to increase along the graft outer wall and decrease at further graft downstream due to the skewed velocity vector shifted slowly toward the graft centerline.

Figure 6-4 WSS distribution at the proximal anastomosis of the whole anastomosis model
(a) along the graft inner wall (b) along the graft outer wall

Figures 6-5 (a), (b) and (c) show the WSS distributions along the graft inner wall, graft outer wall and coronary artery floor at the distal anastomosis respectively. Similarly, as shown at the upper right corner of the each figure, arbitrary coordinates were assigned to present the WSS. For WSS distributions along the inner wall and outer wall of graft, the origins of x_3 and x_4 were selected as shown in Figure 6-5 (a) and (b), with positive direction toward the occlusion end and antegrade end of coronary artery respectively. For the WSS distribution along the coronary artery bed, the origin of x_5 was selected at the point just below the toe of the anastomosis with positive direction toward the DOS of the coronary artery, as demonstrated in Figure 6-5 (c). Along the graft inner wall as shown in Figure 6-5 (a), the WSS was kept at a low level, which is due to the low velocity at the heel region. Since the coronary artery is fully occluded and the fluid was found almost stationary near the occlusion, the wall shear stress is nearly zero. The existence of recirculation region inside the anastomosis formed a flow separation point near the heel, which was indicated as zero WSS.

Along the graft outer wall, the WSS was maintained at a relatively low level as shown in Figure 6-5 (b) and increased slightly when approaching the toe, which was corresponding to the relatively low velocity along the smooth curvature of the graft outer wall. The WSS increased steeply after $x_4 = -2\text{mm}$ and reached the peak value at $x_4 = 1.3\text{mm}$. After that the WSS has decreased in magnitude but maintained at a relatively high level with small variations, as demonstrated in Figure 6-5 (b). The drastic change of the WSS at the toe should be due to the geometrical shape variation around the anastomosis and is a reflection of the great variation in flow field.

As shown in Figure 6-5 (c), the WSS along the coronary artery bed was around zero near the occluded end of the coronary artery, which was due to weak recirculation in the region. The WSS increased dramatically from $x_5 = -3.5\text{mm}$ onwards and reached a peak value of 19 Pa at $x_5 = 5.0\text{mm}$ due to the flow impinged on the coronary artery floor from the graft. Meanwhile the WSS was also high at the further downstream of the artery. The distinguished high WSS on the artery bed at and after the toe region 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 6-5 WSS distribution at the distal anastomosis of the whole anastomosis model (a) along graft inner wall (b) along graft outer wall (c) along artery bed

Figure 6-6 showed the WSS distributions of the whole anastomosis model obtained numerically by Zhang (2005) using the same geometrical and flow conditions. Similar trend has been found when comparing the WSS distributions of present study with those of the numerical simulation, that is higher WSS was also found in the toe and heel of proximal anastomosis than its surrounding and much higher WSS values were found along the graft outer wall and artery bed of the distal anastomosis. Although present study has only focused on the flow field and WSS distributions within the model center plane, the good agreement between the experimental study and numerical simulation indicated that present PIV measurement not only could validate the numerical result but also could reveal the flow characteristics of the complete model and provide sufficient information in evaluating the hemodynamic effect on the bypass system. Lee et al (2001) studied a complete bypass tube model under steady flow condition and found that the highest WSS at the toe and the WSS along the coronary artery bed after the toe was also high. WSS distribution obtained by Kute and Vorp (2001), when one end of distal anastomosis was occluded, indicated that although high WSS was observed at the toe of distal anastomosis, a region of high WSS was also observed at the bed. All these findings are in line with the present PIV measurements.

Figure 6-6 WSS distributions along the whole anastomosis model (Obtained from Zhang 2005)

6.3 Hemodynamics of the Whole Anastomosis Model under Pulsatile Flow

6.3.1 Flow Characteristics

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

6.3.1.1 Flow Characteristics of Proximal Anastomosis

Figure 6-7 shows the flow fields at different time interval within a flow cycle of the proximal anastomosis. As observed in Figure 6-7 (a), when flow just began to accelerate ($t_1=0.1s$), part of the main flow from aorta diverted into the graft smoothly. With the evolution of the acceleration ($t_2=0.25s$), flow separation was observed near the heel of the proximal anastomosis as shown in Figure 6-7 (b). The size of the low velocity region was found to increase by 300% immediately after the proximal anastomosis when the inlet flow reached its peak at $t_3=0.3s$, as shown in Figure 6-7 (c). In addition, the flow separation point was also found to move further downstream along the graft with time. Flow field during early deceleration ($t_4=0.35s$) showed that the flow separation moved further downstream. Furthermore, due to the flow separation and the decrease in momentum, some blood in the graft flowed back toward the aorta along the inner wall before flowing back to the graft, as shown in Figure 6-7 (d).

With further deceleration, the backflow along the graft inner wall became stronger and formed a large elliptic recirculation region near the heel as shown in Figure 6-7 (e) at

$t_5=0.45s$. The streamlines show the recirculating flow near the heel region merged with the inlet flow from the upstream of aorta and entered into the graft again along the graft outer wall. At further downstream the flow skewed toward graft inner wall and reattached at further downstream. With the evolution of deceleration, backflow along the graft inner wall became stronger, while the inlet flow from aorta decreased sharply. As shown in Figure 6-7 (f), at $t_6=0.55s$ backflow along the graft inner wall rotated inside the anastomosis and flowed back into the graft along the graft outer wall. Big recirculation flow region was formed inside the anastomosis and a stripe of low velocity region occupied the center of the graft. At $t_7=0.60s$, as shown in Figure 6-7 (g), backflow along the graft inner wall merged with the inlet flow from upstream aorta near the heel and caused reverse flow along the ceiling of aorta. The reverse flow along the graft inner wall and the positive core flow of the upstream aorta formed a complex flow pattern near the toe region. The nodal point viewed as source in the streamlines inside the anastomosis was the attachment point of three dimensional flow separation (Filippone, 2004). Buchanan et al. (1999) also reported that 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 $t_8=0.70s$, the net flow rate was in the reverse direction dominated by the backflow along the upper wall of aorta. Flow separation occurred along the graft outer wall as shown in Figure 6-7 (h). At $t_9=0.85s$, the flow was accelerating again with a low positive flow rate. From Figure 6-7 (i) it was found that along the aorta upper wall backflow still dominated at this time interval. Although the flow velocity magnitude was quite small, the flow pattern was found to be more complicated than that of $t_8=0.70s$

especially at the anastomotic joint. At the heel a nodal point was detected and a recirculation region was found at the toe region.

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

(a) $t_1=0.1\text{ s}$

(b) $t_2=0.25\text{ s}$

(c) $t_3=0.30\text{ s}$

(d) $t_4=0.35\text{s}$

(e) $t_5=0.45\text{s}$

(f) $t_6=0.55\text{s}$

Figure 6-7 Velocity fields of proximal anastomosis part at different time intervals

6.3.1.2 Flow Characteristics of Graft

Comparing with the proximal anastomosis, the flow patterns in graft section (as indicated in Figure 6-1) at different time intervals were much simple, however, some variations during the flow cycle can also be observed in Figure 6-8. At acceleration ($t_1=0.1s$) the flow in the graft was quite smooth and nearly parallel to the graft axis, and it was approximately parabola in shape as shown in Figure 6-8 (a). When reaching the peak flow phase ($t_2=0.3s$), the flow field in the graft was remained relatively smooth with much higher magnitude, the flow nevertheless skewed toward graft outer wall, which was due to the curvature of the graft under acceleration. At the deceleration phase ($t_3=0.50s$), because of the decrease of momentum and the complex flow characteristics at the proximal anastomosis, some of the blood along graft inner wall reversed the flow direction, however, the flow rate was dominated by the positive flow along the graft outer wall as shown in Figure 6-8 (c). With the further deceleration ($t_4=0.55s$), more blood reversed the flow direction along the graft inner wall and formed a recirculation region at the center of the graft as demonstrated in Figure 6-8 (d), which was consistent with the results of proximal anastomosis at this time interval. At $t_5=0.70s$, when the net flow rate was negative, the flow in graft was dominated by the backflow, as shown in Figure 6-8(e). This observation was consistent with results of proximal anastomosis and those of Buchanan et al. (1999) for flow in the celiac branch at T_3 . The flow field became positive at $t_6=0.85s$, this is due to the inlet flow was accelerating again.

Although some disturbances can also be observed, the flow fields in the graft were found to be much less complicated when comparing them with those of proximal anastomosis. In addition, the results were consistent with corresponding results at proximal anastomosis.

Figure 6-8 Velocity fields of graft at different time intervals

6.3.1.3 Flow Characteristics of Distal Anastomosis

Figure 6-9 shows the flow field of distal anastomosis. At the beginning of the acceleration ($t_1=0.10s$), the flow field was quite smooth and a stagnation point on the coronary artery bed opposite the heel of distal anastomosis was observed. At the graft the flow was mainly parallel to the graft axis but skewed slightly toward the toe when approaching the anastomosis which was due to the graft curvature and the fully occlusion at POS. The velocity is higher in the coronary artery due to the conservation of flow, as the cross sectional area of coronary artery is smaller than the graft cross sectional area. A zone of low momentum, weak recirculating fluid was contained between the junction and the blockage in the right end of the coronary artery, as seen in Figure 6-9 (a). At $t_2=0.25s$, the stagnation point on the artery bed was found moving towards the DOS slightly as shown in Figure 6-9 (b). Meanwhile the graft flow impacted more strongly on the toe and the coronary artery bed. With the evolution of acceleration, the impact of the graft flow on the toe and the artery bed became stronger than before. When the inlet flow accelerated to the peak flow phase ($t_3=0.30s$), the inlet graft flow skewed toward the toe region and formed a relatively low momentum region along the graft inner wall. Inside the junction area near the POS, the recirculation flow is also reduced in size while the flow in DOS is greatly increased in magnitude, as demonstrated in Figure 6-9 (c). During the early deceleration phase ($t_4=0.35s$), the main stream of the flow did not change much when comparing with the peak flow phase, however, an apparent flow separation started to generate near the occluded end due to the loss of momentum of graft inlet flow, as shown in Figure 6-9 (d). With further deceleration ($t_5=0.45s$) the flow separation region had shifted slightly from the occluded end and increased in size, however, graft inlet flow still dominated the main stream, as shown in Figure 6-9 (e).

The vortex caused by the flow separation continued to develop with the evolution of deceleration. At $t_6=0.55s$ a large vortex has formed within the anastomosis near the heel region, as shown in Figure 6-9 (f). Furthermore, part of blood flowed back to the graft along the graft inner wall due to the vortex, and this is consistent with the flow fields at proximal anastomosis as illustrated earlier. The vortex formed inside the anastomosis was observed to grow with time, and it can be found that most of the separated flow was merged with the graft flow into the DOS with very small portion flow back along the graft inner wall. At $t_7=0.60s$, as shown in Figure 6-9 (g), the vortex has dominated almost half of the junction area. More backflow along the graft inner wall was found, although forward flow still existed along the graft outer wall to the DOS at this time interval. All these observations were in agreement with those of Cole et al. (2002b) at distal anastomosis of Taylor bypass model. At $t_8=0.70s$, when the net flow rate was in the reverse direction, the flow in the graft was dominated by the backflow along the inner wall as shown in Figure 6-9 (h). The flow in the coronary artery was also dominated by the backflow and the streamlines were curved and skewed toward the heel at the middle part of the junction because of the existence of large recirculation region. When flow was acceleration again with small net positive flow rate at $t_9=0.85s$, the flow patterns became more complex when comparing with those of $t_1=0.10s$. Recirculation regions occupied almost half of the junction of distal anastomosis close to the heel. Backflow along the graft inner wall still existed although the main flow along the graft outer wall and in the coronary artery have been dominated by forward flow.

In general, sever flow skewed toward the toe and impinged on the artery floor, while near the heel, a large, low momentum recirculation region persisted within the cycle. The disturbed flow patterns subsequently resulted in nonuniform distributions in WSS with

high values on the toe and artery floor, which increase transmural filtration and elevated LDL influx (Perktold et al., 2002), and extremely low values near the heel which could increase 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. Therefore the results have provided strong evidence that the flow conditions at the heel and toe of the distal anastomosis might initiate the progression of IH.

Figure 6-9 Velocity fields of distal anastomosis at different time intervals

6.3.2 Distributions of Hemodynamic Parameters

“Disturbed flow” which resulted in abnormal hemodynamic parameters (HP), may trigger a cascade of abnormal biological processes leading to intimal thickening and/or thrombi formation, therefore sufficiently high and sustained HP values can be employed to determine susceptible sites for the onset of blood vessel diseases (Kleinstreuer et al., 2001). 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 more vulnerable to the formation of plaques. Since in this study the flow fields in the graft were found to be much less complicated when comparing them with those of proximal and distal anastomoses, the hemodynamic parameters in the graft are relatively small in magnitude with less variation and not shown here. Numerical study on the whole anastomosis model under pulsatile flow carried out by Zhang (2005) also indicated that the hemodynamic parameters in graft section are almost uniform without causing any severe problems.

6.3.2.1 Hemodynamic Parameters of Proximal Anastomosis

Figures 6-10 (a) and (b) show the contour maps of the WSS distribution of the proximal anastomosis along the graft inner and outer walls respectively. Note that the x -axis represents the distance along the graft, as defined earlier in Section 6.2.2 and the y -axis represents the time interval of the flow cycle. Lines on Figures 6-10 (a) and (b) represent the paths of stagnation/reattachment/separation point movements along the graft inner and outer walls respectively. From Figure 6-10 (a) it can be observed that the WSS along the graft inner wall was relatively small at the beginning of the flow cycle because the flow just began to accelerate. The WSS increased in magnitude with the time and reached the peak value at $t=0.3s$ near the heel. Low and negative WSS region after the heel was found

from $t=0.1s$ onwards and increased in size with time until the reverse flow phase $t=0.7s$. This is due to the recirculating flow occurred there, as demonstrated in the flow fields of Figure 6-7 earlier. Note that the sign of WSS is determined by the flow direction and the definition of the coordinate. The WSS was found to maintain low and negative at the reverse flow phase until the inlet flow reached acceleration phase again. Flow reattachment was found on the graft inner wall during the systolic flow phase and the locations of flow reattachment were found to shift further downstream of the graft inner wall during the early acceleration phase till $t=0.16s$ and move toward aorta thereafter till the late deceleration phase $t=0.55s$.

The WSS distributions along the graft outer wall were found to be higher in magnitude in general, as indicated in Figure 6-10 (b), which is due to the flow skewed toward the graft outer wall. Note that the presentation of x_2 coordinate is opposite to the usual convention, that is x_2 is increased from right to left for the flow from aorta to graft outer wall. The same presentation of x_2 , x_4 and x_5 was used in Figure 6-11 (b), Figure 6-13 (b) and (c) (also Figure 6-14 (b) and (c)) respectively. WSS along the graft outer wall was relatively small at the beginning of the flow cycle and increased in magnitude with the time and reached the peak value at $t=0.3s$. Note that negative WSS found on the ceiling of aorta near the toe was due to the flow direction and definition of x_2 coordinate. Stagnation point was found on the graft outer wall indicated by the zero WSS from the beginning of the flow cycle until the reverse flow phase ($t=0.6s$). From Figure 6-10 (b) it can be observed that the stagnation point moved toward graft downstream slightly during the acceleration phase and moved back along the graft outer wall toward the aorta from the late acceleration phase to the deceleration phase. At the end of deceleration, when the flow reversed, flow separation point emerged at the downstream of graft outer wall and

moved toward the toe. It then shifted slightly to graft downstream until the end of the reverse flow. At the diastolic flow phase (from $t=0.8$ onwards), the stagnation point re-emerged at aorta and moved upstream toward graft outer wall. The WSS was found to be relatively low in magnitude during the reverse flow and diastolic flow phase which was due to the low inlet flow rate during the time interval.

Figure 6-10 Contour maps of the WSS distribution of the proximal anastomosis (a) along the graft inner wall (b) along the graft outer wall (Lines on the plots indicated the locations of the stagnation/reattachment/separation point on the graft walls)

Figures 6-11 (a) and (b) show the contour maps of the spatial wall shear stress gradient (SWSSG) of proximal anastomosis along the graft inner and outer walls respectively. As shown in Figure 6-11 (a), SWSSG near the heel region was found to have more variation with time and larger in magnitude due to the low flow velocity near the heel, however, before and after the heel region the SWSSG distribution was relatively smooth. On the other hand, larger SWSSG was found along the graft outer wall and peak SWSSG was

attained at the peak flow phase ($t=0.3\text{s}$ at $x_2=1.8\text{mm}$) around the stagnation point region due to the bifurcation flow, as shown in Figure 6-11 (b).

Figure 6-11 Contour maps of the SWSSG distribution of the proximal anastomosis (a) along the graft inner wall (b) along the graft outer wall

Figures 6-12 (a) and (b) show the time-averaged WSS, OSI and WSSG distributions of the proximal anastomosis along the graft inner wall and outer wall respectively. High time-averaged WSS region were found at the heel, toe and the region downstream of the toe as shown in Figure 6-12, and these regions experienced relatively less reverse flow as demonstrated by the low OSI values. There were also two significant areas with low time-averaged WSS, after the heel along the graft inner wall (around $x_1 = 1.0\text{mm}$) and after the toe along the graft outer wall (around $x_2 = 2.0\text{mm}$), as demonstrated in Figures 6-12 (a) and (b) respectively. These low time-averaged WSS regions were areas of flow separation/stagnation throughout the whole cycle with high oscillating flow as indicated by high OSI at the same regions. In addition, high time-averaged WSSG regions were

associated with the low-WSS-high-OSI regions near the heel and toe as observed in the figure. Buchanan et al. (1999 and 2003) also reported the similar HPs distribution for aorto-celiac junction and an abdomina 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 low-WSS-high-OSI or high-WSS-low-OSI. The continued growth of the lesions was likely due to modifications in the permeability of endothelium as can be related to the increase in the WSSG. Therefore, regions of heel, toe and region along the graft inner wall after the heel would be more prone to disease at the proximal anastomosis.

Figure 6-12 Time-averaged WSS, WSSG and OSI distributions of the proximal anastomosis along (a) graft inner wall (b) graft outer wall

6.3.2.2 Hemodynamic Parameters of Distal Anastomosis

Figures 6-13 (a), (b) and (c) show the contour maps of the WSS distributions along the graft inner wall, graft outer wall and the arterial floor of the distal anastomosis respectively. At the beginning of flow cycle the WSS maintained a relatively low value and then increased with time at the acceleration phase. Low and negative WSS was found at the deceleration phase when reverse flow occurred. The WSS along the graft inner wall, as shown in Figure 6-13 (a), was found to be much less than those along the graft outer wall and arterial floor. This is because the inlet flow skewed toward graft outer wall and DOS caused by the curvature of the graft and the occlusion of the proximal coronary artery when approaching the distal anastomosis. After the heel the WSS was found to be relatively small in magnitude along the coronary artery ceiling, which was because the fluid near the occlusion was almost kept stationary except weak recirculation within the whole flow cycle.

Along the graft outer wall the WSS increased drastically when approaching the anastomosis at acceleration phase and reached its peak value ($t=0.3s$) at the toe. After the toe the WSS decreased slightly because the flow skewed toward the bottom of coronary artery, as shown in Figure 6-13 (b). Along the arterial floor the WSS reached its peak value at the downstream of distal coronary artery at $t=0.3s$, as shown in Figure 6-13 (c). Stagnation point on the artery floor was indicated by zero WSS and it was found to move toward proximal artery end at the acceleration phase and move back toward the distal artery end during flow deceleration. The stagnation point was found to mainly oscillate within the proximal half of the arterial floor near the heel, which is due to the occlusion of the proximal coronary artery, as shown in Figure 6-13 (c).

Figure 6-13 Contour maps of the WSS distribution of the distal anastomosis (a) along the graft inner wall (b) along the graft outer wall (c) along arterial floor

Figures 6-14 (a), (b) and (c) show the contour maps of the SWSSG distributions along the graft inner wall, graft outer wall and the arterial floor of the distal anastomosis respectively. Along the graft inner wall, the SWSSG was found to be small except a relatively high SWSSG region near the heel during the systolic flow phase, which was due to the occlusion of proximal outlet of the distal anastomosis, as shown in Figure 6-14(a). Along the graft outer wall, the SWSSG were observed to have much higher in magnitude than those along the graft inner wall. The SWSSG were found to be higher

during the systolic flow phase ($t=0.1s$ to $t=0.6s$) than those of the reverse flow phase and diastolic flow phase, as demonstrated in Figure 6-14 (b). In addition, the SWSSG was found to increase when approaching the toe and reached its peak of 35.6 Pa/mm at $x_4 = -1.8mm$ and $x_4 = -0.8mm$. The SWSSG dropped sharply to a relatively low value after the toe and increase again until reaching another peak at $x_4 = 2.8mm$.

As shown in Figure 6-14 (c), the SWSSG was small in magnitude near the proximal outlet of the distal anastomosis and only minor variation was observed within this region, which was due to the occlusion at this end. Similarly, the SWSSG during the systolic flow phase was also found to be higher than those of the other time intervals. During the systolic flow phase, the SWSSG increased from the proximal outlet to the distal outlet of the anastomosis and reached a peak of 29.2 Pa/mm at $x_5 = -0.8mm$. After that the SWSSG decreased sharply and increased again to another peak of 32.1 Pa/mm at $x_5 = 2.6mm$, the SWSSG then decreased again and increased at further downstream of the coronary artery.

Figure 6-14 Contour maps of the SWSSG distribution of the distal anastomosis (a) along the graft inner wall (b) along the graft outer wall (c) along arterial floor

Figures 6-15 (a), (b) and (c) show the time-averaged WSS, WSSG and OSI distributions of the distal anastomosis along the graft inner wall, outer wall and arterial floor respectively. It can be found in Figure 6-15 (b) and (c) that high time-averaged WSS regions were observed at the toe along the graft outer wall and downstream of the coronary arterial floor respectively, due to the skewing of the flow through the

anastomosis and the reduction of lumen area when approaching the downstream of coronary artery. These regions were experienced less reverse flow as shown by low OSI. However, low time-averaged WSS were found at the heel along the graft inner wall and the occluded end of the coronary arterial floor in Figure 6-15 (a). The low momentum recirculating flow region at the heel had high OSI values as demonstrated in Figures 6-15 (a) and (c). In addition, high time-averaged WSSG variation regions with few distinct peaks were observed near the heel along the graft inner wall (Figure 6-15 (a)), and near the toe along the graft outer wall (Figure 6-15(b)). Along the arterial floor high time-averaged WSSG regions were found opposite the toe and further downstream of coronary artery, as shown in Figure 6-15 (c). These distributions of hemodynamic parameters were similar with the case A of Longest and Kleinstreuer (2003), when proximal end of the coronary artery was totally occluded. As regions with low-WSS-high-OSI and high-WSS-low-OSI 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.

In summary, the susceptible sites of IH and/or atherosclerotic lesion formation in the whole CABG model were the toe, heel, the region along the graft inner wall of proximal anastomosis together with the toe, downstream of the coronary artery bed, the heel and the coronary artery bed near the occluded end of the distal anastomosis.

Figure 6-15 Time-averaged WSS, WSSG and OSI distributions of the distal anastomosis along (a) graft inner wall (b) graft outer wall and (c) artery floor

6.4 Comparisons with Other Published Works

Zhang (2005) numerically investigated the complete bypass grafting model under the pulsatile flow conditions. Generally, a fair match can be found between the flow characteristics of the experimental investigation and numerical simulations. Disturbed flows (flow separation/reattachment, vortical and secondary flow) were 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 time 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. However, the flow fields inside the graft were found to be relatively smoother than those at the anastomoses (Zhang 2005). Figures 6-16 (a) and (b) show the typical flow fields obtained by Zhang (2005) at the proximal and distal anastomoses at the peak flow phase respectively. Comparing Figures 6-16 (a) and (b) with the corresponding flow fields obtained in present PIV study (as shown in Figures 6-7 (c) and 6-9 (c)), it can be observed the numerical results share a similar trend with the experimental ones. At the proximal anastomosis for both studies, flow separation was observed near the heel of the proximal anastomosis, and along the graft inner wall the velocities were relatively lower than those along the graft outer wall, as shown in Figure 6-16 (a). At the distal anastomosis, inlet graft flow skewed toward the toe region and formed a relatively low momentum region along the graft inner wall for both studies. A zone of low momentum, weak recirculating fluids was observed near the fully blocked coronary artery at the right end, as shown in Figure 6-16 (b).

Figure 6-16 Flow characteristics of the whole anastomosis model at peak flow phase (a) the proximal anastomosis (b) the distal anastomosis (obtained from Zhang, 2005)

To compare the hemodynamics of the experimental results with the numerical simulations, Figure 6-17 shows the contour map of the time-averaged wall shear stress obtained by Zhang (2005). When compared Figure 6-17 with Figures 6-12 and 6-13 it can be observed that the time-averaged wall shear stress distributed in the similar pattern at both proximal and distal anastomoses. As shown in Figure 6-17 (a), at the proximal anastomosis the wall shear stress increased to the peak value at the heel and then decreased into the low wall shear stress region along the graft inner wall. The wall shear stress experienced the peak value at the toe and then decreased down to almost zero at the stagnation point. The wall

shear stress increased again toward the graft downstream. For the distal anastomosis, peak wall shear stress occurred at the toe and further downstream of the artery floor. Along the graft inner wall and near the occlusion end, the wall shear stress is low for both results of numerical simulation and experimental measurements as demonstrated in Figures 6-17 (b) and 6-13 respectively.

Figure 6-17 Time-averaged wall shear stress distributions of the whole anastomosis model (a) proximal anastomosis (b) distal anastomosis (obtained from Zhang, 2005)

Discrepancy was also found in the flow field comparison, especially at the deceleration phase and reverse flow phase. This is because the flow waveform applied in the experiment, which has a gently deceleration, is slightly different to that used in simulation. Another possible reason for the discrepancy is the experimental model may not be perfectly the same as that used in numerical simulation, which would definitely affect the flow fields in detailed variation. In addition, for both proximal and distal anastomoses, the numerical simulation was found to have relatively higher magnitude in the peak time-averaged wall shear stress. As stated earlier, one reason for lower experimental wall shear stress is the underestimation trend of the PIV measurements, and another one is the limited spatial resolution of the PIV system which cannot provide enough spatial resolution to capture the detailed variation as the simulation.

Generally, the present experimental results in the whole bypass grafting model match quite well with the numerical studied by Zhang (2005), although with some discrepancy in the flow fields and hemodynamics. The present results suggested that proximal and distal anastomoses, especially at the toe and heel regions of distal anastomosis are the areas suspected to initiate the atherosclerotic lesion, which was consistent with the numerical results obtained by Zhang (2005).

6.5 A Summery for the Chapter

The experimental results obtained for the whole anastomosis model under steady and pulsatile flow conditions were presented in the chapter. Disturbed flow (flow separation/reattachment, vortical and secondary flow) was found at proximal and distal anastomoses, especially at the distal anastomosis. Near 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.

Furthermore, hemodynamic parameters, such as WSS, SWSSG and time-averaged WSS, WSSG, OSI were investigated. The results indicated that the low-WSS-high-OSI and high-WSS-low-OSI regions were found occurred at 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 increase of WSSG. As 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 the most significant along the suture line of distal anastomosis (Bassiouny et al., 1992; Loth et al., 2002).

CHAPTER 7

MEASUREMENTS AND COMPARISON OF TWO DISTAL ANASTOMOSIS MODELS

7.1 Introduction

Nonuniform hemodynamics is believed to play an initiating role in early bypass graft thrombosis and more frequently in graft failure caused by intimal hyperplasia. Intimal thickening that occurs at and near the toe, heel, and arterial wall in the anastomotic bed of distal anastomosis may be accelerated or modified by nonuniform hemodynamics (Depaola et al., 1992; He and Ku, 1996; Henry et al., 1996; Kleinstreuer et al., 1996). From the results of the whole anastomosis model in Chapter 6, it is noted that disturbed flow patterns occurred most seriously at the distal anastomosis and elevated WSSG was found near the toe and the arterial floor of the distal anastomosis where the intimal hyperplasia were shown to be more susceptible to occur. Therefore in order to maintain the long-term bypass patency, it is necessary to reduce the nonuniformity of hemodynamics at the distal anastomosis by improving its geometrical configuration.

Many studies have recognized that bypass configurations, including anastomotic geometry, graft/artery diameter ratio, graft/artery angle, etc., are the primary factors that strongly alter anastomotic hemodynamics and thus long-term bypass graft patency (Keynton et al., 1991; Lei et al., 1995; Jackson et al., 2001). As a consequence, restenosis and thrombosis may be greatly mitigated if specific junction geometries could be determined such that nonuniformity of hemodynamics are avoided or reduced. Many studies have been performed to optimize the anastomotic configuration for better

hemodynamic performance (Lei et al., 1996; Jackson et al., 2001; Rachev et al., 2000). Currently two types of popular geometries used in peripheral bypass operation, Miller cuff and Taylor patch were reported to have favorable performance (Taylor et al., 1992; Harris et al., 1993; Perktold et al., 2002), but only limited to below-keen popliteal bypasses. Lei et al. (1997) developed optimal femoral bypass geometry with a large hood and much smoother transition at the toe and heel compared to the conventional and Taylor patch geometry that minimizes WSS gradient. The study indicated that graft geometry profoundly affects the degree of nonuniform flow and the magnitude of the WSS gradients generated, and it is feasible to obtain an optimal design so that the chance of development of IH and the incident of thrombosis can be greatly reduced if not totally eliminated.

However, most of the studies are focused on the peripheral bypasses and little has been done for coronary artery regions. Therefore it is necessary to consider whether a hemodynamic advantage is also promoted by the revised geometry for coronary bypasses and evaluate the hemodynamic performances under typical physiological flow conditions.

7.1.1 Test Models

It is well known that the hemodynamic environment depends heavily on the anastomotic geometry. The primary geometric feature that influence the hemodynamic environment in the conventional end-to-side anastomosis includes the graft angle (Fei et al. 1994) and graft-to-host diameter ratio (DR) (Moore et al. 1999), while other features, such as out-of-plane curvature and surface feature have much less influence (Sherwin et al. 2000). In addition, the proximal outlet segment (POS) and the distal outlet segment (DOS) may also be one of the factors that influence the hemodynamic environment in the distal anastomosis and that may, in turn, influence the subsequent development of IH (Li and

Rittgers., 2001). Based upon the hypothesis that sustained wall shear stress gradients would increase restenosis, the specific graft-artery parameters including cross sectional area ratios, bifurcation angles and wall curvatures could be designed to minimize local wall shear stress gradients.

Since the average size of a saphenous vein of an Asian adult varies from 3 to 5 mm in diameter and the coronary artery diameter varies around 2mm, the conventional distal anastomosis model where was used as a baseline model was designed to have a bifurcation angle of $\alpha = 30^\circ$ and a graft-to-artery diameter ratio of 1.5:1, as shown in Figure 7-1 (a). The diameters of graft and host artery were set as 3mm and 2mm respectively. According to the studies carried out by Kleinstreuer et al. (1996) and Lei et al. (1997), the baseline model was also designed to have a relatively sharp connecting edges and the geometry of the graft-artery intersection following closely conventional suturing of a distal anastomosis. The improved model was designed to have a larger graft-to-artery diameter ratio, i.e. $d_{\text{graft}} : d_{\text{artery}} = 2:1$, as shown in Figure 7-1 (b). Note that in the improved model, the anastomosis that joint the graft and the host artery is modified so that the flow would be more streamline with smoother connection without sharp edges.

Figure 7-1 Geometric configurations of the distal anastomosis models (a) baseline model ($d_{\text{graft}} : d_{\text{artery}} = 1.5:1$) (b) improved model ($d_{\text{graft}} : d_{\text{artery}} = 2:1$)

7.1.2 Flow Conditions

According to Kute and Vorp (2001), the nature of the flow in the proximal outlet segment of artery at the distal anastomosis varies from case to case depending on the clinical situation presented. A partial stenosis of a bypass arterial segment may allow residual prograde flow through the proximal artery to the distal anastomosis of the graft. However this flow condition is relatively rare that most bypass operations would not been done unless the coronary arteries had at least 70% of diameter been occluded (Eagle et al., 1999). A serious stenosis would result in zero flow in the proximal artery segment, however, retrograde flow could be occurred due to the presence of small collateral vessels between the blockage and the anastomosis, especially under certain geometrical circumstances, that the location of distal anastomosis is done at a longer distance from the occluded site of the coronary artery. Since the proximal artery flow may affect the hemodynamics of the anastomosis greatly (Kute and Vorp, 2001), therefore in this study two different proximal artery flow conditions, retrograde and zero flow, were applied to the test models to investigate the flow patterns and evaluate their hemodynamic performances.

As shown in Figure 7-1 (b), the flow rates through the graft, POS and DOS are represented by Q_g , Q_p and Q_d respectively. Two different mean flow rate ratios $Q_p:Q_d$ of (1) 20:80 and (2) 0:100 were investigated for both anastomosis models. Note that the retrograde proximal flow case (1) $Q_p:Q_d=20:80$ was used to evaluate the effect of the improved anastomosis geometry on the local hemodynamics and the zero proximal flow case (2) $Q_p:Q_d=0:100$ was used to examine the effect of the proximal flow on the hemodynamics of the distal anastomosis. Figure 7-2 shows the waveform measured at the

graft inlet (Q_g) for both flow rate ratio conditions, however, flow rate waveforms at the proximal outlet (Q_p) and distal outlet (Q_d) are only for mean flow rate ratio of 20:80. The Womersley number of the waveform (Q_g) is 1.3 and the Reynolds number has a maximum value of 538 and mean value of 162. There is also a small reverse flow portion with a maximum Reynolds number of 81. Six typical time steps representing the acceleration ($t_1=0.1s$), peak flow ($t_2=0.3s$), deceleration ($t_3=0.5s$, $t_4=0.6s$), reverse flow ($t_5=0.7s$) and diastolic peak flow ($t_6=0.85s$) were chosen to show the flow characteristics.

Figure 7-2 Physiological flow waveform at the graft inlet (Q_g), proximal artery outlet (Q_p) and distal artery outlet (Q_d)

7.2 Effect of the Geometry on the Local Hemodynamics

7.2.1 Flow Characteristics of Baseline Model at Retrograde Flow (20:80)

At the beginning of acceleration ($t_1=0.1s$) the inlet flow was diverted smoothly into two streams toward the POS and DOS respectively, as shown in Figure 7-3 (a). A stagnation point was found on the arterial floor opposite the heel region at $x = 11.6mm$. When the inlet flow accelerated to the peak flow phase ($t_2=0.3s$), the inlet graft flow skewed toward

the toe with larger angle, as shown in Figure 7-3 (b). The flow hits the artery floor hard with the maximum flow slightly below the artery centerline and adjusted back to the centerline along the DOS artery downstream. At the early deceleration phase ($t_3=0.5s$) the flow field was similar comparing to that of the acceleration phase, however, a relatively low velocity region was found near the heel region, as shown in Figure 7-3 (c). In addition, at the hood region the velocity was small along the graft outer wall due to the skewing flow toward the arterial floor and loss of momentum during the deceleration.

With the evolution of deceleration, the low velocity region near the heel was found to increase in size with time. At $t_4=0.6s$ a recirculation flow was found near the heel, as shown in Figure 7-3 (d). In addition, the low velocity region along the graft outer wall increased in size and flow separation and reattachment points were found on the hood. When the inlet flow reached the reverse flow phase ($t_5=0.7s$), backflows from both POS and DOS closed to the artery ceiling were observed, however, positive flow was found at the center of graft and along the DOS artery floor, as shown in Figure 7-3 (e). A large vortex inside the anastomosis, flow separation ($x=13mm$) and reattachment ($x=8mm$) points were formed on the arterial floor when backflows met with the inlet graft flow. When the inlet flow reached its diastolic peak ($t_6=0.85s$) the flow field was similar to that of the acceleration ($t_1=0.1s$), but in smaller magnitude, as shown in Figure 7-3 (f).

Chapter 7

Measurements and Comparison of Two Distal Anastomosis Models

(a) $t_1 = 0.1 \text{ s}$

(b) $t_2 = 0.3 \text{ s}$

(c) $t_3=0.5\text{s}$

(d) $t_4 = 0.6 \text{ s}$

Figure 7-3 Velocity fields of the baseline model at different time intervals under retrograde proximal artery flow condition (POS: DOS=20:80)

7.2.2 Flow Characteristics of Improved Model at Retrograde Flow (20:80)

Figure 7-4 shows the flow fields in the symmetry plane of the improved model at six typical time steps under retrograde proximal artery flow condition (POS: DOS=20:80). As shown in Figure 7-4 (a), the inlet flow diverted into two streams toward the POS and DOS respectively when approaching the anastomosis. It was found that most of the fluid was channeled into the DOS due to the specified experimental flow condition. A stagnation point was found on the arterial floor at $x = 9.6mm$ which is slightly closer to the heel than to the toe. When the inlet flow reached its peak flow phase at $t_2=0.3s$, the flow was found to be skewed more toward the arterial floor, as shown in Figure 7-4 (b). At the deceleration phase ($t_3=0.5s$) the mainstream of the flow did not change much when

comparing with the peak flow phase except smaller in velocity magnitude, however, a recirculation flow region was found near the heel, as shown in Figure 7-4 (c). The stagnation point ($x = 10.2\text{mm}$) on the arterial floor was observed to have shifted toward the POS slightly.

The recirculation region near the heel was found to have grown in size with the evolution of deceleration and occupied almost 40% of the anastomotic area at $t_4=0.6\text{s}$, as demonstrated in Figure 7-4 (d). The stagnation point on the arterial floor was found moving further toward the DOS of the anastomosis ($x = 7.9\text{mm}$). Figure 7-4 (e) shows the flow field at the reverse flow phase ($t_5=0.7\text{s}$). Backflows from both POS and DOS were met inside the anastomosis and a recirculation region near the toe was formed. The flow inside the graft was found in reverse direction and skewed toward the graft outer wall and resulted in a relatively low velocity region formed along the graft inner wall. When the inlet flow reached its diastolic peak ($t_6=0.85\text{s}$) the flow field was similar to that of the acceleration ($t_1=0.1\text{s}$), as shown in Figure 7-4 (f), except smaller in velocity magnitude.

Figure 7-4 Velocity fields of the improved model at different time intervals under retrograde proximal artery flow condition (POS: DOS=20:80))

7.2.3 Hemodynamic Parameters of Distal Anastomosis Models

The wall shear stress distributions along the graft inner wall-artery ceiling toward the POS, along the graft outer wall-artery ceiling toward the DOS and along the coronary artery floor were calculated and presented in Figures 7-5, 7-6 and 7-7 respectively. Note that for the ease of presentation, three arbitrary coordinates were used to present the results. For WSS distributions along the inner wall and outer wall of graft, the origins of x_3 and x_4 were selected as shown in the figure, with positive direction toward the POS and DOS respectively. For the WSS distribution along the coronary artery bed, the origin of x_5 was selected at the point just below the toe of the anastomosis with positive direction toward DOS. Note that same color code was applied in plotting the contour maps of the WSS distributions of the two models for the ease of comparison.

Figures 7-5 (a) and (b) show the contour map of the WSS distributions along the graft inner wall-artery ceiling of the baseline model and improved model respectively. For the two models, the general characteristics of the WSS distributions are similar. Relatively low WSS is observed around the heel at the acceleration and early deceleration phase ($t=0.1-0.4s$). Before the heel relatively high WSS is found along the graft inner wall and peak WSS is attained. After the heel the WSS was found to increase along the artery ceiling and reached the second peak at further downstream. At the late deceleration and reverse flow phase the WSS was small in magnitude and increased at the diastolic flow phase. Comparing Figures 7-5 (b) with (a) it can be found that the WSS magnitudes of the improved model were generally smaller than those of the baseline model and the peak value of WSS of the improved model (7.52 Pa) was smaller than that of the baseline model (11.1 Pa). This is expected as the improved model has a rounded heel and the results obtained have demonstrated that the geometry has great influence on the WSS distribution.

WSS distributions along the graft outer wall-artery ceiling of baseline model and improved model were shown in Figure 7-6 (a) and (b) respectively. Generally the WSS distributed in the similar pattern for the two models. The WSS was relatively low at the early acceleration and increased with the evolution of acceleration and attained the highest value when the inlet flow reached the systolic peak. After that the WSS decreased and became negative when entered the reverse flow phase. As shown in Figure 7-6 (a) it was found that the WSS was relatively high during 0.2-0.5s compared with other time intervals. High WSS region was found around the toe (from $x_4 = -0.46mm$ to $x_4 = 0.46mm$), the artery ceiling close to the toe (from $x_4 = 1.53mm$ to $x_4 = 2.6mm$) and the further downstream of DOS ($x_4 = 4.38mm$ to $x_4 = 5.2mm$). In addition, a

relatively small WSS region was found before the toe ranged from $x_4 = -5.15\text{mm}$ to $x_4 = -2.4\text{mm}$, however, the WSS was higher at further upstream of the graft inlet. Comparing the WSS distribution of the baseline model and the improved model, it was found that the WSS distributed with much less variation in the improved model. Extreme WSS disappeared in the improved model, although around the toe the WSS was also high but was almost half of that in the baseline model (17.8 Pa versus 33 Pa). The low WSS region before the toe of the improved model was found shifted further upstream along the graft outer wall and the magnitude was also higher than that of the baseline model. This is because the improved model increased the hood length and the anastomotic area, which would be advantageous in providing more uniform flow condition and avoiding too much disturbance when the inlet flow approaching the anastomosis.

Figures 7-7 (a) and (b) show the WSS distribution along the artery floor of baseline model and improved model respectively. Stagnation points on the artery floor were found for the two models and indicated on the contour maps. The stagnation point moved toward the POS slightly at the acceleration phase and shifted toward the DOS at the deceleration phase. This is because during the deceleration the adverse pressure gradient would cause the slower, near-wall fluid to reverse its flow direction. Since the near-wall velocity increased progressively along the artery floor toward the DOS, therefore the position where the fluid reversed its direction has resulted in the stagnation point, which shifted distally during deceleration. At the reverse flow phase, the reversed flow in the POS opposed the backflow from the DOS to the heel and formed an separation point on the artery floor, hence there is an apparent discontinuity at $t=0.6\text{s}$. For the improved model the WSS on the artery floor distributed in a similar trend as that of baseline model, however, with less variation. For the baseline model the peak value of WSS was found

on the DOS artery floor (37Pa, $t=0.3s$) and sustained almost the same value in the region opposite to the toe. On the other hand, the WSS peak value of the improved model was found to be much smaller (26Pa, $t=0.3s$), due to the relatively uniform flow field and less disturbance due to the increased hood size, natural intersection and larger anastomotic area of the improved model.

In general, the WSS distributed more uniformly in the improved model, which would benefit in avoiding extreme spatial WSSG, and the extreme WSS magnitude was greatly reduced especially on the toe, heel and the artery floor. Since extreme in WSS could increase transmural filtration and elevate LDL influx (Perktold et al, 2002, Stangeby et al., 2002, Wada and Karino, 2002) and elevated spatial WSSG was believed to contribute the high LDL permeability (Buchanan et al., 1999) and intimal hyperplasia (Lei et al., 1995), therefore the improved model has a much better hemodynamic performance.

Figure 7-5 Contour maps of the WSS distribution along the graft inner wall-artery ceiling (a) baseline model (b) improved model

Figure 7-6 Contour maps of the WSS distribution along the graft outer wall-artery ceiling (a) baseline model (b) improved model

Figure 7-7 Contour maps of the WSS distribution along the artery floor (a) baseline model (b) improved model (Lines on the plots indicated the locations of the stagnation/separation point on the artery floor)

Figures 7-8, 7-9 and 7-10 show the spatial wall shear stress gradients along the graft inner wall-artery ceiling, graft outer wall-artery ceiling and artery floor respectively. Generally the patterns of the SWSSG distribution of the baseline model and the improved model were found to be similar. Relatively low SWSSG were observed in both models except the characterized time interval of acceleration phase and early deceleration phase ($t=0.1s$ to $t=0.4s$), where high SWSSG existed due to the much more complicated flow field. Along the graft inner wall-artery ceiling, as shown in Figure 7-8 (a), high SWSSG existed almost all the locations under investigation in the baseline model and a peak value of 24.5 Pa/mm occurred at $x_3 = -0.75mm$. However at the improved model (Figure 7-8 (b)), the relatively high SWSSG region was only found along the graft inner wall proximal to the heel (ranging from $x_3 = -0.67mm$ to $x_3 = -1.1mm$) and the peak value was also found to be smaller than that of the baseline model (17.5Pa/mm at $x_3 = -0.94mm$).

As shown in Figure 7-9 (a), along the graft outer wall-artery ceiling, high SWSSG occurred and sustained from the hood at $x_4 = -2.6mm$ to further distal artery ceiling at $x_4 = 5.7mm$ with a peak value of 26.4 Pa/mm on the hood at $x_4 = -0.5mm$ and several second peaks on the artery ceiling at $x_4 = 0.5mm$, $1.8mm$, $2.6mm$ and $5.3mm$. Additionally, relatively high SWSSG was also found at the further upstream on the graft outer wall ranging from $x_4 = -8.5mm$ to $x_4 = -4.6mm$. For the improved model, relatively high SWSSG region with peak value of 13.9Pa/mm at $x_4 = -1.4mm$ on the hood was also found, however, generally the magnitude was much smaller than that of the baseline model in general, as shown in Figure 7-9 (b).

Along the artery floor a large high SWSSG region occupied the whole anastomotic area in the baseline model ranging from $x_5 = -7\text{mm}$ to $x_5 = -1.0\text{mm}$ with peak value of 18.5Pa/mm at $x_5 = -1.2\text{mm}$ as shown in Figure 7-10 (a). Several small regions with relatively high SWSSG were also found at the POS and DOS in the baseline model. Similarly, within the anastomotic area the SWSSG was also found to be relatively high in the improved model and have a peak value of 7.9 Pa/mm at $x_5 = -7.6\text{mm}$, but the magnitude was generally smaller than that of baseline model, as shown in Figure 7-10 (b).

Figure 7-8 Contour maps of the SWSSG along the graft outer wall-artery ceiling (a) baseline model (b) improved model

Figure 7-9 Contour maps of the SWSSG along the graft outer wall-artery ceiling (a) baseline model (b) improved model

Figure 7-10 Contour maps of the SWSSG along artery floor (a) baseline model (b) improved model

In order to compare the hemodynamics of the baseline model and the improved model quantitatively, time-averaged WSS, WSSG and OSI along the graft inner wall-artery ceiling, graft outer wall-artery ceiling and artery floor for the two models were shown in Figures 7-11 and 7-12 respectively. For the ease of comparison and locating the susceptible intimal thickening sites, the hemodynamic parameters at the same region were presenting with different symbol in the same figure for each model. For the baseline model, high OSI was found around the heel whereas at other locations the OSI was almost zero. Relatively low time-averaged WSS was also found at the vicinity of the heel and WSSG has great variation with 3 peaks found at $x_3 = -0.75\text{mm}$, -0.25mm , and 0.5mm , as shown in Figure 7-11 (a). Along the graft outer wall-artery ceiling, the OSI was kept at a very low level with minor variation due to the dominated forward flow. The time-averaged WSS was moderate in magnitude at the upstream of graft outer wall and decreased into a low WSS region at the hood, which was coincide with the low velocity region found earlier (Figure 7-3). When approaching the toe the time-averaged WSS increased sharply to a peak and then slightly decreased along the artery ceiling with minor variation. The time-averaged WSSG distributed in the similar pattern as WSS except that the peak WSSG occurred earlier at $x_4 = -0.75\text{mm}$, and decreased at a faster rate than those of the time-averaged WSS, as shown in Figure 7-11 (b).

Along the arterial floor, from POS the time-averaged WSS decreased steadily to almost zero when accessing the stagnation point, as shown in Figure 7-11 (c). After that the WSS increased and maintained a high value at further downstream of DOS. The time-averaged WSSG was found extremely high at the region where WSS varied drastically with three peaks ($x_5 = -6\text{mm}$, $x_5 = -3.2\text{mm}$, and $x_5 = -1\text{mm}$), whereas it was kept low with minor variations at other places. The OSI value kept almost zero at most of the artery

floor except at the stagnation point (zero WSS at $x_5 = -4.7\text{mm}$,) has a peak value of 0.49, as demonstrated in Figure 7-11 (c). Although WSSG is not at its peak, it has a relatively high value of 7.5 Pa/mm at the stagnation point.

In order to examine the improvement of the hemodynamics performance of the improved model, the same scale of OSI, WSS and WSSG were used in Figure 7-12 as those of baseline model. As shown in Figure 7-12 (a), hemodynamic parameters were distributed in a similar trend as those of the baseline model along the graft inner wall. High OSI and low time-averaged WSS was found around the heel, however, the WSSG at this region was much smaller than that of the baseline model. Along the graft outer wall-artery ceiling, as shown in Figure 7-12 (b), both the WSS and the WSSG were found to be smaller than those of the baseline model, although the general distribution pattern was the same. The hemodynamics parameters distribution along the artery floor was found to have same general pattern as the baseline model, as shown in Figure 7-12 (c). High OSI and zero WSS were found at $x_5 = -8.0\text{mm}$, and at further downstream of DOS the time-averaged WSS was almost the same as that of the baseline model. However, the time-averaged WSSG of the improved model was much smaller with the peak value of WSSG was about only half of the peak WSSG of the baseline model.

In general high-OSI-low-WSS regions were found around the heel and stagnation point on the artery floor at both the baseline model and the improved model. Around the toe low-OSI-high-WSS region was also found in the two models. However, for the improved model the WSS field was reduced in magnitude and distributed more evenly throughout the anastomotic area when compared with that of the baseline model. Furthermore, the baseline model exhibited distinctive high SWSSG regions around the heel, toe and the

floor of the junction, whereas the SWSSG was reduced drastically in magnitude in the improved model, especially around the toe, stagnation point on artery floor and distal coronary artery. It was believed that high time-averaged WSSG triggers abnormal biological processes leading to rapid restenosis, i.e. excessive tissue overgrowth and renewed plaque formation, and hence early graft failure. As regions with high-OSI-low-WSS and low-OSI-high-WSS combinations were suspected to initiate the atherosclerotic lesion (Buchanan et al, 1999 and 2003), which were further worsened by modifications in permeability with the increases of WSSG (Buchanan et al., 1999, Lei et al., 1995), the improved model would provide better hemodynamics environments for the distal anastomosis. In summary, with respect to the baseline model, significant flow field improvements leading to measurable reductions in WSSG magnitude have been achieved in the improved model via the following geometrical improvement: larger diameter ratio ($d_{graft} : d_{artery} = 2:1$), increased anastomotic area and smooth junction curvatures (increased hood length).

Figure 7-11 Time-averaged WSS, WSSG and OSI distributions of the baseline model along (a) graft inner wall-artery ceiling (b) graft outer wall-artery ceiling (c) artery floor

Figure 7-12 Time-averaged WSS, WSSG and OSI distributions of the improved model along (a) graft inner wall-artery ceiling (b) graft outer wall-artery ceiling (c) artery floor

7.3 Effect of the Proximal Artery Flow Condition on the Local Hemodynamics

The improved model was designed and evaluated by the hemodynamic performance under the retrograde flow condition, however, when the distal anastomosis is close to the fully occluded location of the artery, there will be no retrograde flow. Hence it is necessary to validate the performance of the improved model under zero proximal artery flow condition, which would affect the hemodynamics of the anastomosis greatly (Kute and Vorp, 2001). Therefore both the baseline model and the improved model were studied further under the zero proximal artery flow condition to validate the performance of the geometrical improvement.

7.3.1 Flow Characteristics of Baseline Model at Zero Proximal Artery Flow

At the beginning of the acceleration ($t_1=0.10s$), the flow field was quite smooth and a stagnation point on the coronary artery bed ($x=11.5mm$) close the heel of distal anastomosis was observed. At the graft the flow was mainly along the graft axis but skewed slightly toward the toe when approaching the anastomosis. it can be seen that the flow to DOS is much higher in magnitude due to the smaller diameter of coronary artery and the flow at the proximal outlet segment was much small in magnitude due to its fully blockage, as shown in Figure 7-13 (a). When the inlet flow accelerated to the peak flow phase ($t_2=0.30s$), the inlet graft flow skewed toward the toe region with much larger angle and formed a relatively low momentum region along the graft inner wall, as demonstrated in Figure 7-13 (b). The stagnation point on the artery floor moved toward the distal outlet segment ($x=10.2mm$) and a low recirculation region was formed and increased in size with the evolution of acceleration.

At the deceleration phase of $t_3=0.5$ and $t_4=0.6$ s, the main stream of the flow did not change much when comparing with the peak flow phase, however, an apparent flow separation generated near the proximal arterial end due to the fully occlusion of POS and the incoming flow has lost the momentum, as shown in Figures 7-13 (c) and (d) respectively. When the inlet flow reached the reverse flow phase ($t_5=0.7$ s), backflow from the host artery toward the graft was found, as shown in Figure 7-13 (e). From the figure it was found that inlet flow still existed in the graft along the graft outer wall. When the backflow and the graft inlet flow met a recirculation region was formed in the graft and a flow separation point was found on the hood. At the diastolic peak flow phase ($t_6=0.85$ s), the flow field was similar to that of the acceleration ($t_1=0.1$ s) except smaller in velocity magnitude, as shown in Figure 7-13 (f).

(a) $t_1=0.1$ s (b) $t_2=0.3$ s

Figure 7-13 Velocity fields of the baseline model at different time intervals under zero proximal artery flow condition (POS: DOS=0:100)

7.3.2 Flow Characteristics of Improved Model at Zero Proximal Artery Flow

Figure 7-14 shows the flow field of the improved distal anastomosis model at different time intervals when the proximal outlet segment was totally occluded. As shown in Figure 7-14 (a), the blood was channeled smoothly from the graft into the host artery at the beginning of acceleration. A stagnation point was found on the arterial floor at $x=14\text{mm}$ and low velocity region was observed at the POS. When the inlet flow reached its peak flow phase ($t_2=0.3\text{s}$), the smooth flow field still could be found along the graft outer wall and the arterial ceiling as shown in Figure 7-14 (b). This is because the improved distal anastomosis was designed to have a smooth (as streamlining) connection between the graft and the coronary artery to avoid drastic variation when the flow approaching the anastomosis. Noted that the stagnation point on the arterial floor was found to move further downstream toward the DOS ($x=11\text{mm}$) and a low velocity recirculation region was formed and increased in size with the evolution of acceleration, which was also found in the baseline model. When the inlet flow reached the deceleration phase ($t_3=0.5\text{s}$), the mainstream flow field did not change much compared with that of the acceleration phase, as shown in Figure 7-14 (c). However, near the POS a flow separation region was formed on the arterial floor during the deceleration and increased in size with the further deceleration due to the backflow from POS and interaction with the down wash graft flow at the anastomosis area near the heel, as shown in Figure 7-14 (d). When the inlet flow became negative ($t_5=0.7\text{s}$), backflows from both POS and DOS were found at this time interval, as shown in Figure 7-14 (e). At $t_6=0.85\text{s}$ the inlet flow reached the diastolic peak flow phase, the flow field was found similar to that of the early acceleration ($t_1=0.1\text{s}$), but in relatively small magnitude and a low velocity recirculation region was observed at this time interval, as shown in Figure 7-14 (f).

Figure 7-14 Velocity fields of the improved model at different time intervals under zero proximal artery flow condition (POS: DOS=0:100))

7.3.3 Hemodynamic Parameters of Distal Anastomosis Models

For baseline model and improved model under zero proximal artery flow condition, the contour maps of the wall shear stress distribution along the graft inner wall-artery ceiling, graft outer wall-artery ceiling and artery floor were shown in Figures 7-15, 7-16 and 7-17 respectively. For the ease of comparison, same color code was used in presenting the hemodynamic parameters (WSS and WSSG in Figure 7-18, 7-19 and 7-20) in both baseline and improved models.

Generally the WSS distributed in a similar general pattern for the two models; that is the WSS was high from the acceleration phase to early deceleration phase ($t=0.1s$ to $t=0.32s$) whereas the WSS was low at other time intervals. However, distinguished difference was found in the peak and mean WSS magnitude for the two models. Along the graft inner

wall-artery ceiling, the WSS was much smaller in magnitude than those along graft outer wall-artery ceiling and artery floor, which was due to skewed flow toward the toe and relatively low velocity caused by the occluded proximal outlet, as shown in Figures 7-15 (a) and (b). Relatively high WSS was observed at upstream of graft in the baseline model (with peak value of 6.8 Pa at $x_3 = -1.2\text{mm}$,) and improved model (with peak value of 2.1Pa at $x_3 = -1.1\text{mm}$,). For WSS along graft outer wall-artery ceiling, around the toe region a significant elevated WSS region (peak value of 37.8 Pa at $x_4 = -0.3\text{mm}$,) was found at the baseline model, whereas, the WSS of the improved model was distributed in a much smoother way (with a peak value of 22 Pa at $x_4 = -0.5\text{mm}$,), as shown in Figures 7-16 (a) and (b) respectively. This distinction was also found between the baseline model and the improved model under the retrograde proximal artery flow condition as discussed earlier.

Along the artery floor large low-WSS region was found at the vicinity opposite to the heel and the proximal artery for both models due to the totally occluded POS. For the baseline model, within the anastomotic area the WSS increased progressively from the POS toward the distal coronary artery and reached the peak value when reaching $x_5 = 0\text{mm}$, and maintained at a relatively high level with minor variation throughout the DOS of the model, as shown in Figure 7-17 (a). For the improved model the WSS distributed in a similar trend as that of the baseline model, except that the magnitude of WSS (with peak value of 29 Pa at $x_5 = 1.2\text{mm}$,) was generally smaller than the corresponding baseline value (with peak value of 41.9 Pa at $x_5 = 3.1\text{mm}$,) as shown in Figure 7-17 (b). In general, the WSS distributed more uniformly in the improved model

under the zero proximal flow condition, which would benefit in avoiding extreme WSSG, and the extreme WSS was greatly reduced especially on the toe, heel and the artery floor.

Figure 7-15 Contour maps of the WSS along the graft inner wall-artery ceiling under zero proximal artery flow condition (a) baseline model (b) improved model

Figure 7-16 Contour maps of the WSS along the graft outer wall-artery ceiling under zero proximal artery flow condition (a) baseline model (b) improved model

Figure 7-17 Contour maps of the WSS along the artery floor under zero proximal artery flow condition (a) baseline model (b) improved model

Figures 7-18, 7-19 and 7-20 show the contour maps of the spatial WSSG along the graft inner wall-artery ceiling, outer wall-artery ceiling and artery floor respectively. For the baseline model, SWSSG was small near the occluded artery and elevated SWSSG region occurred just before the heel (with peak value of 13.9 Pa/mm at $x_3 = -0.53$ mm), whereas it has much smaller size and magnitude (with peak value of 9.2 Pa/mm at $x_3 = -0.57$ mm) in the improved model. Along the graft outer wall-artery ceiling, distinct elevated SWSSG region was found around the toe at the baseline model with a peak value of 23.2Pa/mm on the hood ($x_4 = -0.68$ mm). On the further upstream of graft or downstream of coronary artery ceiling the SWSSG was generally low except several minor peaks can be observed in Figure 7-19 (a). For the improved model the extreme high WSSG region disappeared and only several locations with small peak WSSG were found along the graft outer wall-artery ceiling, as shown in Figure 7-19 (b).

More obvious difference was found between the SWSSG distribution on the artery floor of the baseline model and the improved model. As shown in Figure 7-20 (a), a large elevated SWSSG region (with peak value of 21.6 Pa/mm at $x_5 = -2.1\text{mm}$) was found on half of the artery floor within the anastomotic area close to the DOS (ranging from $x_5 = -3.8\text{mm}$ to $x_5 = 0\text{mm}$). Near the proximal outlet of the anastomosis the SWSSG was low whereas the SWSSG was relatively high on the distal coronary floor with several small peaks formed. On the other hand, the magnitude of the SWSSG in the improved model was generally smaller than those of the baseline model, as shown in Figure 7-20 (b). Although a region with relatively elevated SWSSG was also found within the anastomotic area (ranging from $x_5 = -8.1\text{mm}$ to $x_5 = -3.8\text{mm}$), only small amplitude with a much smaller peak value of 8.02 Pa/mm at $x_5 = -6.0\text{mm}$ was found at this region.

Figure 7-18 Contour maps of the SWSSG along the graft outer wall-artery ceiling under zero proximal artery flow condition (a) baseline model (b) improved model

Figure 7-19 Contour maps of the SWSSG along the graft outer wall-artery ceiling under zero proximal artery flow condition (a) baseline model (b) improved model

Figure 7-20 Contour maps of the SWSSG along the artery floor under zero proximal artery flow condition (a) baseline model (b) improved model

Figures 7-21 7-22 and 7-23 show the time-averaged WSS, WSSG and OSI distributions along the graft inner wall-artery ceiling, graft outer wall-artery ceiling and the artery floor respectively for the two models. For the ease of comparison, same scale of vertical ordinate was used in presenting the hemodynamic parameters (OSI, WSS and WSSG) for the same regions in both models.

Along the graft inner wall-artery ceiling, the OSI was low in the graft but increased drastically when accessing the heel and maintained at high value due to the recirculating flow near the occluded proximal artery, as shown in Figures 7-21 (a) and (b). The time-averaged WSS was relatively high at the graft and decreased to nearly zero when approaching the heel and thereafter. Elevated time-averaged WSSG region occurred at the vicinity of heel whereas small in magnitude at other locations. Comparing the two models, regions of low-WSS-high-OSI were both found near the occluded artery but the OSI value in the baseline model has higher value. In the baseline model, peak time-averaged WSSG (6.1 Pa/mm) was found at $x_3 = -0.47\text{mm}$ which located the low-WSS-high-OSI region, and second peak (4.7 Pa/mm at $x_3 = -1.0\text{mm}$) was found to be located in the high-WSS-low-OSI region. However, there is no such elevated time-averaged WSSG region found in the improved model and the time-averaged WSSG was generally smaller in magnitude (with peak of 4.3 Pa/mm at $x_3 = -0.54\text{mm}$).

Figure 7-21 Time-averaged WSS, WSSG and OSI distributions along the graft inner wall-artery ceiling (a) baseline model (b) improved model

As shown in Figures 7-22 (a) and (b), the OSI was kept low along the graft outer wall-artery ceiling in two models, which is due to the dominant forward flow. For the baseline model the time-averaged WSS increased slowly when approaching the toe from upstream graft outer wall and reached the peak value of 10.7 Pa at $x_4 = -0.3$ mm. After the toe the time-averaged WSS decreased steadily and then varied gently on the further downstream of artery ceiling, as shown in Figure 7-22 (a). In addition, elevated time-averaged WSSG was also found around the toe region. For the improved model the time-averaged WSS was also increased to the peak value around the toe but in a smaller magnitude (7.12 Pa at

$x_4 = -0.33\text{mm}$). The time-averaged WSSG was generally low with small variations throughout the graft outer wall-artery ceiling, as shown in Figure 7-22 (b).

Figure 7-22 Time-averaged WSS, WSSG and OSI distributions along the graft outer wall-artery ceiling (a) baseline model (b) improved model

The OSI distribution along the artery floor was found to be much more complicated for both the baseline model and the improved model. As shown in Figure 7-23 (a), the OSI was almost zero at the DOS and extended to $x_5 = -2\text{mm}$ opposite to the toe. A sharply increase in OSI value was found at $x_5 = -4\text{mm}$ where the WSS dropped sharply to zero (i.e. stagnation point) and then the OSI was kept in relatively high level with minor variation along arterial floor to POS. Note that the time-averaged WSS was initially high at DOS. In addition, elevated WSSG was associated with the increase in OSI and

decrease in WSS. For the improved model, the OSI was also almost zero at the DOS and increased sharply to the peak value at $x_5 = -8.2\text{mm}$ where the stagnation point located. However, the OSI decreased drastically to almost zero after the stagnation point and increased again at further proximal locations. The time-averaged WSS was low at the vicinity opposite to the heel and increased to a relatively high level at the DOS, but in smaller magnitude (8.8 Pa) as compared with that of the baseline model (11.7Pa), as shown in Figure 7-23 (b). In addition, the time-averaged WSSG distributed more smoothly with minor variations and the magnitude was much smaller than that of the base model (peak value of 2.55Pa/mm of improved model versus 9.8Pa/mm at baseline model).

Figure 7-23 Time-averaged WSS, WSSG and OSI distributions along the artery floor (a) baseline model (b) improved model

The general pattern of the WSS distribution was similar in the two models but the WSS field was small in magnitude and distributed more evenly throughout the anastomotic area in the improved model. As a consequence, the spatial WSSG was reduced tremendously in magnitude in the improved model, especially around the toe, stagnation point on artery floor and distal coronary artery. At the heel, toe, stagnation point on artery floor and distal coronary artery, sites susceptible to intimal hyperplasia, overlapping of low-WSS-high-OSI/high-WSS-low-OSI regions and elevated time-averaged WSSG were found in the baseline model whereas no such sites or its combinations sites can be observed in the improved model. As regions with high-OSI-low-WSS and low-OSI-high-WSS combinations were suspected to initiate the atherosclerotic lesion (Buchanan et al, 1999 and 2003), and elevated time-averaged WSSG was believed to trigger excessive tissue overgrowth, renewed plaque formation, and hence rapid restenosis and early graft failure, the improved model may work well under the zero proximal artery flow condition and provide better hemodynamic environments.

7.4 A Summery for the Chapter

In this Chapter geometrical improvement for the distal anastomosis was carried out in order to minimize the hemodynamics nonuniformity of the bypasses. According to previous studies about the geometrical optimization of distal anastomosis, an improved model was designed and fabricated based on the baseline model with geometrical improvements of larger diameter ratio (from $d_{graft} : d_{artery} = 1.5 : 1$ to $d_{graft} : d_{artery} = 2 : 1$), increased anastomotic area and smooth junction curvatures (increased hood length). Under retrograde proximal artery flows condition, experimental study was done to examine and evaluate the hemodynamic performance of the improved and baseline

models and further experimental investigation under the zero proximal artery flow condition was to validate the better performance of the improved model.

Disturbed flows (flow separation/stagnation/reattachment, vortical) were found at two models near the heel, toe and artery floor under retrograde flow condition. High-OSI-low-WSS regions were found around the heel and stagnation point on the artery floor at both the baseline model and the improved model. Around the toe low-OSI-high-WSS region was also found in the two models. However, at the retrograde flow condition of the improved model the WSS distributed more evenly throughout the anastomotic area; the peak WSS magnitude reduced about 69% at the heel (2.1 Pa vs 6.8 Pa), 42% at the toe (22 Pa vs 37.8 Pa) and 31% at the floor (29 Pa vs 41.9 Pa) when compared with those of the baseline model. In addition, the baseline model exhibited distinctive high SWSSG regions around the heel, toe and the floor of the junction, whereas the SWSSG was reduced tremendously in the improved model, especially around the heel (17.5 Pa/mm vs 24.5 Pa/mm, reduced about 28.5%), toe (13.9 Pa/mm vs 26.4 Pa/mm, reduced about 47.3%) and stagnation point on artery floor (7.9 Pa/mm vs 18.5 Pa/mm, reduced about 57.2%).

Similarly the experimental results under zero proximal artery flow condition also showed distinctive high SWSSG regions in the baseline model. At the heel, toe, stagnation point on artery floor and distal coronary artery, sites susceptible to intimal hyperplasia, overlapping of low-WSS-high-OSI/high-WSS-low-OSI regions and elevated time-averaged WSSG were found in the baseline model whereas no such sites were found in the improved model. The improved model was shown to work well indicated by the reduction in SWSSG magnitude as comparing with that of the baseline model (9.2 Pa/mm vs 13.9 Pa/mm at the heel, reduced about 33.8%; 10.8 Pa/mm vs 23.2 Pa/mm, reduced

about 53.4%; 8.02 Pa/mm vs 21.6 Pa/mm, reduced about 62.8%). In summary, with respect to the baseline model, significant flow field improvements leading to measurable reductions in SWSSG magnitude have been achieved in the improved model, which would be able to enhance the long-term hemodynamic performance and patency of coronary bypass graft.

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CHAPTER 8

CONCLUSIONS AND SUGGESTIONS FOR FUTURE WORK

8.1 Conclusions

In this study, pulsatile flow test rig was specifically designed and constructed to investigate the hemodynamic performance of the coronary artery bypass graft system using PIV measurement technique. Test rig was fine-tuned so that the flow rate waveform in the test section resembled the corresponding physiological flow rate waveform. Test models representing proximal anastomosis, whole anastomosis, and distal anastomosis were designed and fabricated, based on the clinical data from Singapore National Heart Centre. Blood analogues were used in the measurement to match the refractive index of the test model as well as the blood properties such as density and viscosity.

At the first stage, the effects of proximal anastomotic angle on local hemodynamics were studied to provide useful information for medical doctors and serve as the basis for the design of whole anastomosis model, with emphasis on identifying site-specific hemodynamic features that could reasonably be expected to trigger the initiation and further development of anastomotic intimal hyperplasia. PIV measurement revealed that the flow field in the proximal anastomosis was strongly influenced by the anastomotic angle. Under pulsatile flow condition, large size of flow separation region was found along the graft inner wall just after the heel and decreased in size with the decreasing of graft angle except the 30° model. This disturbed flow could prolong the resident time of blood elements, thus increasing the likelihood of adhesion of platelets and leukocytes to

local endothelium and leading to the stimulation of smooth muscle cell proliferation and intimal thickening. Notable movement of the location of stagnation point at the outer graft wall was found at all models except the 90° model. The existence of flow separation, vortex and the nearly stationary stagnating point throughout the pulsatile flow cycle may accelerate the formation of IH.

The wall shear stress distributions in the pulsatile flow also demonstrate significant variations in time and space. Elevated spatial wall shear stress gradients, which were believed to correspond to the elevated LDL permeability (Buchanan et al., 1999), were found around the anastomotic joints. Along the graft inner wall the size of the elevated SWSSG region and the maximum value of SWSSG were increased with the increasing anastomotic angle except the 30° model, which had the highest SWSSG and biggest elevated SWSSG region at the vicinity of heel. Along the graft outer wall, both the size of the elevated SWSSG region and maximum value of SWSSG were amplified notably with the increasing of anastomotic angle. Regions of low-WSS-high-OSI and high-WSS-low-OSI were found around the anastomotic joints, where elevated time-averaged SWSSG was also noticed for all models. The size of the region of low-WSS-high-OSI along the graft inner wall varied drastically at different anastomotic model. The 45° model has the smallest such region whereas the 90° model has the largest.

Considered all models together, hemodynamic performances at both graft inner and outer walls deteriorated with increasing anastomotic angle except the 30° model, which has a good performance along graft outer wall but the worst performance along the graft inner wall. In contrast to the other models, the 45° proximal anastomotic model is recognized to have higher patency rate as it had the smallest flow separation region along graft inner

wall. In addition, the 45° model had the smallest region of low-WSS-high-OSI and high-WSS-low-OSI around the anastomotic joint, which were believed to correlate with early atherosclerotic lesion growth (Buchanan et al., 1999), and insignificant elevation of SWSSG, which further affirmed its superiority.

In order to enhance the understanding of the stenosis pathophysiological process in CABG, whole anastomosis model was designed and fabricated based on the result that 45° is the optimized proximal anastomotic angle. The experimental results revealed that disturbed flow (flow separation/reattachment, vortical and secondary flow) was found at proximal and distal anastomoses, especially at the distal anastomosis. Near the heel of distal anastomosis, a large recirculation region with low momentum persisted within the cycle, which augmented the resident 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. High-OSI-low-WSS and low-OSI-high-WSS regions were found occurring at 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. As 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).

In order to ensure the long-term patency as well as to avoid early failure of coronary bypasses, geometrical improvement for the distal anastomosis was carried out in order to

minimize the hemodynamics nonuniformity of the bypasses. According to previous studies about the geometrical optimization of distal anastomosis, an improved model was designed and fabricated based on the baseline model with geometrical improvements of larger diameter ratio (from $d_{graft} : d_{artery} = 1.5 : 1$ to $d_{graft} : d_{artery} = 2 : 1$), increased anastomotic area and smooth junction curvatures (increased hood length). PIV measurement was done to examine and compare the hemodynamic performance of the improved and baseline models under retrograde proximal artery flow condition. Generally high-OSI-low-WSS regions were found around the heel and stagnation point on the artery floor at both the baseline model and the improved model. Around the toe low-OSI-high-WSS region was also found in the two models. However, for the improved model the WSS was low in magnitude and distributed more evenly throughout the anastomotic area when compared with those of the baseline model. In addition the baseline model exhibited distinctive high SWSSG regions around the heel, toe and the floor of the junction, whereas the SWSSG was reduced drastically in magnitude in the improved model, especially around the toe, stagnation point on artery floor and distal coronary artery.

Further experimental investigation under the zero proximal artery flow condition was done to evaluate and compare the hemodynamic performance of the baseline and improved models since the proximal artery flow may affect the hemodynamics of the anastomosis greatly (Kute and Vorp, 2001). Similar with the retrograde flow condition, around the toe low-OSI-high-WSS region was also found in the two models under zero flow condition. However, for the improved model the WSS was low in magnitude and distributed more uniformly than those of the baseline model. In addition, the SWSSG was reduced tremendously in magnitude in the improved model, especially around the toe,

stagnation point on artery floor and distal coronary artery. Elevated time-averaged WSSG was believed to trigger excessive tissue overgrowth, renewed plaque formation, and hence rapid restenosis and early graft failure, therefore the improved model was found to work well under the zero proximal artery flow condition and provided better hemodynamic environments. In summary, with respect to the baseline model, significant flow field improvements leading to measurable reductions in SWSSG magnitude have been achieved in the improved model. The improved model was shown to be less flow condition sensitive and would be able to enhance the long-term hemodynamic performance and patency of coronary bypass graft.

8.2 Suggestions for Future Work

Although present experimental works have successfully investigated the complex hemodynamics of proximal anastomoses, a complete CABG model and improved model, there are still areas of interest for further study. As an extension to the current work, the followings are suggested:

1. Further investigations on a CABG model with more realistic feature, such as aorta/graft and graft/artery non-planarity and compliance of blood vessel, could enhance the understanding of pathophysiological process. The realistic CABG model can be fabricated employing casting techniques such as Computed Tomography (CT) using e.g. porcine heart with coronary bypass. Based on the data of CT obtained CAD/CAM software can be used in replicating and constructing the 3-D model. The defined CAD geometry can be exported to CAM system (STL or CNC machining) to produce the male or female modules. Either of these can be used to fabricate a clear silicone rubber model through a series of casting processes as described in Section

- 3.3.3. Then the three-dimensional PIV system can be used in exploring the hemodynamic performance of the realistic CABG model.
2. Further optimization of the improved geometry for both proximal and distal anastomoses. The blood flow waveform varies from one location to another in the arterial system and varies from resting to exercise following human activities. It is also different from person to person and would be complicated through the progress of the disease. In order to accommodate these situations, the effect of input flow waveform on hemodynamic performance of the anastomosis will be examined by varying the frequency, mean Reynolds number and the shape of the flow waveform. The optimized improved anastomosis should be less sensitive to the flow waveform so it can work well under different flow condition.
 3. Further investigation on distal anastomosis with different percentages of stenosed coronary artery would provide the surgeon the necessary information in deciding at which percentage of stenosis the surgery should be done. This is because the hemodynamics would become much more complicated due to the competition flow from the partially stenosed artery with the flow from the graft in the first two weeks after CABG operation (Bertolotti and Deplano, 2000). In addition, investigations on the effects of the location of anastomosis would provide surgeon useful and important information about the optimal distance to place the graft away from the stenosed coronary artery.

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APPENDIX A:

SUPPLEMENT OF EXPERIMENTAL RESULTS

Appendix A

Supplement of Experimental Results

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APPENDIX B:

CONFIGURATIONS OF THE ANASTOMOSIS MODELS

Figure B-1 Drawing of the 45° proximal anastomosis model

Figure B-2 Drawing of the whole anastomosis model

Figure B-3 Drawing of the baseline distal anastomosis model

Figure B-4 Drawing of the improved distal anastomosis model