Flow simulations and measurements of a novel coronary arterial bypass graft design of sequential anastomoses

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**FLOW SIMULATIONS AND MEASUREMENTS OF A
NOVEL CORONARY ARTERIAL BYPASS GRAFT
DESIGN OF SEQUENTIAL ANASTOMOSES**

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Abstract

Coronary artery bypass grafting (CABG), the primary treatment for high-risk coronary artery disease patients, has a limited long-term patency mainly due to anastomotic intimal hyperplasia (IH). It is well proven that hemodynamic factors are implicated in the initiation and progression of IH. Therefore, in order to further improve the hemodynamics at the downstream anastomosis and alleviate the drawbacks of the available CABG anastomosis designs so as to attain higher patency rates in bypass grafts, a novel coupled sequential anastomoses (SQA) configuration design is developed in the present study, based on the beneficial flow characteristics and higher patency rates observed in the side-to-side (STS) anastomosis of sequential bypass grafts, as compared to the ETS anastomosis. In this distal SQA design, there is initially a STS anastomosis, located distal to the stenosis, and then the graft end is anastomosed to the same coronary artery further downstream in an ETS fashion.

Firstly, the flow fields and distributions of various WSS parameters are studied in this CABG design, and compared to those of the conventional distal ETS anastomosis, by means of computational fluid dynamics (CFD) simulations of pulsatile Newtonian blood flow, assuming the blood vessels as rigid tubes. The simulation results demonstrate that the new SQA model provides: (i) a more uniform and smooth flow at the ETS anastomosis, without any stagnation point on the artery bed and vortex formation in the heel region of the ETS anastomosis within the coronary artery; (ii) a spare route for the blood flow to the coronary

artery, to avoid re-operation in case of re-stenosis in either of the anastomoses; and (iii) improved distribution of HPs at the coronary artery bed and in the heel region of the ETS anastomosis, with more moderate shear stress indices. These advantages of the SQA design over the conventional ETS anastomosis are influenced by the occlusion ratio of the native coronary artery, and are most prominent when the proximal segment of the coronary artery is fully occluded. Upon varying the design parameters of the anastomotic angle and distance between the two anastomoses within a physiological range, the superior coupled STS-ETS anastomoses design is found to have the anastomotic angle of 30° and 30mm distance between the two (STS and ETS) components. Subsequently, the beneficial flow-simulation results of the novel SQA design are validated in vitro by experimental flow measurements, utilizing Particle Image Velocimetry (PIV) technique. Finally, the effects of wall compliance and non-Newtonian rheology on the local flow field and HPs distribution are investigated by a two-way coupled fluid–structure interaction (FSI) analysis in conjunction with the shear thinning property of blood. The time-averaged wall shear stress (TAWSS) is reduced up to 32% while the oscillatory nature of the flow is somewhat increased in the compliant model. The effect of non-Newtonian rheology on the HPs is found to be heterogeneous.

In conclusion, although the coupled SQA design does involve one additional anastomosis, it brings about some positive features and provides distinct advantages in the flow field and distribution of HPs, which motivates the use of this design instead of the conventional ETS configuration. However, prior to clinical adoption of this novel SQA design, it is necessary to conduct animal studies, in order to find out the biological response and consequences of the employment of this suggested design in vivo.

Dedication

To my dearest parents and my beloved sisters, and to my dear uncle, Dr. Rahimi Kazerouni, who has always believed in me and encouraged me to take up this field of research.

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Nomenclature

a	Yasuda exponent
B_n	Fourier coefficients
d	Distance between the two anastomoses of the novel design, m
D_a	Aperture diameter of the camera, m
D_A	Coronary artery diameter, m
D_G	Graft diameter, m
d_{image}	Image diameter, m
d_p	Particle diameter, m
d_{pitch}	Pixel pitch, m
d_s	Airy function diameter, m
E_θ	Young's (elastic) modulus in peripheral direction, Pa
f	Focal length, m
F	F-number of the camera lens
i	Imaginary unit
J_0 and J_1	The first kind Bessel functions of order zero and one, respectively
L_D	Length of the distal section of the host artery, m
L_{ETS}	Length of the end-to-side anastomosis, m
l_{int}	Length of interrogation window side, m
L_P	Length of the proximal section of the host artery, m
L_{STS}	Length of the side-to-side anastomosis, m
M	Magnification coefficient
n	Power law index in Carreau-Yasuda model
N_{int}	Number of pixels on each interrogation window side
P	Pressure, Pa
Q	Volume flow rate, $m^3 \cdot s^{-1}$
r	Radius, m

R	Lumen radius, m
R^*	Radius of the tube plus half the thickness of the tube wall, m
Re	Reynolds number
St	Strouhal number
t	Time, s
T	Time period, s
$t_{separation}$	Laser pulse separation time, s
u_{∞}	Free-stream velocity, $m \cdot s^{-1}$
U	Flow velocity, $m \cdot s^{-1}$
V_p	Particle velocity, $m \cdot s^{-1}$
W	Velocity of the control volume boundary (mesh velocity), $m \cdot s^{-1}$

Greek Symbols

α	Womersley number
$\dot{\gamma}$	Rate of shear, s^{-1}
η	Dynamic viscosity (non-Newtonian), $Pa \cdot s$; Wall-oriented coordinate, m
η_0	Low shear viscosity, $Pa \cdot s$
η_{∞}	High shear viscosity, $Pa \cdot s$
λ	Wavelength of the laser sheet, m; Carreau-Yasuda time constant, s
μ	Dynamic viscosity (Newtonian), $Pa \cdot s$
ζ	Wall-oriented coordinate, m
ν	Kinematic viscosity, $m^2 \cdot s^{-1}$; Poisson's ratio
ρ	Density, $kg \cdot m^{-3}$
τ_0	Wall shear stress for Poiseuille flow, Pa
τ_w	Wall shear stress, Pa
τ_x, τ_y, τ_z	Shear stress components in x, y, and z directions, respectively, Pa
ω	Angular frequency, $rad \cdot s^{-1}$

List of Abbreviations

AVG	Arteriovenous graft
CABG	Coronary arterial bypass grafting
CAD	Coronary artery disease
CCD	Charge coupled device
CFD	Computational fluid dynamic
CNC	Computer numerical control
COV	Coefficient of variation
CVD	Cardiovascular disease
DAIH	Distal anastomotic intimal hyperplasia
DOS	Distal outlet segment
DV	Diameter variation
EC	Endothelial cell
ETE	End-to-end
ETS	End-to-side
FSI	Fluid–structure interaction
HP	Hemodynamic parameter
IH	Intimal Hyperplasia
IT	Intimal thickening
LAD	Left anterior descending coronary artery
LCA	Left coronary artery
LCx	Left circumflex coronary artery
LDL	Low-density lipoprotein
LDV	Laser Doppler velocimetry
LMCA	Left main coronary artery
OM	Obtuse marginal
OSI	Oscillatory shear index

PCI	Percutaneous coronary intervention
PDMS	Polydimethylsiloxane
PIV	Particle image velocimetry
POS	Proximal outlet segment
RCA	Right coronary artery
SIMPLEC	Semi-implicit method for pressure-linked equations - consistent
SMC	Smooth muscle cell
SNR	Signal-to-noise ratio
SQA	Sequential anastomoses
STS	Side-to-side
SV	Saphenous vein
TAWSS	Time-averaged wall shear stress
TAWSSG	Time-averaged wall shear stress gradient
TTL	Transistor-Transistor-Logic
UDF	User defined function
WSS	Wall shear stress
WSSG	Wall shear stress gradient

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Chapter 1

1 Introduction

1.1 Coronary artery disease (CAD)

According to the statistics from American Heart Association [109], an estimated 81,100,000 American adults (more than 1 in 3) have one or more types of cardiovascular disease (CVD). Mortality data show that CVD, as the underlying cause of death, accounted for 34.3% of all (1 of every 2.9) deaths, and in particular, coronary heart disease caused approximately 1 of every 6 deaths in 2006 in the United States.

Arteriosclerosis, coming from the Greek for “hardening of the arteries”, refers to several diseases in which the arterial wall thickens and loses its elasticity. Commonly confused with atherosclerosis, which is the formation of plaques consisting of cholesterol and other substances on the arterial walls, arteriosclerosis is the thickening and stiffening of the artery walls from too much pressure. Atherosclerosis can lead to arteriosclerosis. In 2004, coronary atherosclerosis was estimated to be responsible for 1.2 million hospital stays and was the most expensive condition treated in the United States [109].

When a coronary artery is blocked (typically due to coronary atherosclerosis), the cardiac muscle (myocardium) tissue supplied by the coronary artery beyond the point of the blockage is deprived of oxygen and nutrients, as illustrated in Figure 1.1. Persistence of the obstruction causes the affected myocardium tissue to begin to die, known as myocardial infarction (heart attack).

Figure 1.1: Diseased coronary artery causing heart attack (taken from [74]).

Several alternative treatments exist for CAD, including medical therapy, rotablation, endarterectomy, percutaneous coronary intervention (PCI) or balloon angioplasty, stenting, and coronary arterial bypass grafting (CABG). Depending on the severity, number, and position of atherosclerotic lesions and the clinical history of the patient, any of the above mentioned treatments may be chosen. For high-risk patients, such as those with left main coronary artery (LMCA) disease, severe three-coronary vessel (left anterior descending

(LAD), left circumflex (LCx), and right coronary artery (RCA)) disease, severe ventricular dysfunction (i.e. low ejection fraction), and diabetes mellitus, CABG is preferred [146]. In general, the greater the extent of coronary atherosclerosis and its diffuseness, the more compelling the choice of CABG, particularly if left ventricle function is depressed [160].

1.2 Coronary arterial bypass grafting and its complications

CABG is a surgical procedure performed to graft arteries or veins from patient's body or synthetic conduits to the coronary arteries in order to bypass atherosclerotic narrowing and improve the blood supply to the coronary circulation, nourishing the myocardium, as shown in Figure 1.2.

Figure 1.2: Illustration of coronary arterial bypass grafting (taken from [75]).

Although CABG is extremely effective for symptomatic relief and prognostic improvement in CAD and is the preferred remedy for high-risk patients, it is not devoid of complications and the long-term benefits are directly related to continuing conduit patency. Approximately 10–15% of vein grafts occlude during the first year after operation. About half of the vein grafts are only effective for a period of 5 to 10 years [36, 80]. By 10 years after surgery, about 60% of vein grafts are patent, only 50% of which remain free of significant stenosis [18, 23, 48].

Early graft failure (within 30 days) of bypass grafts is attributable to technical errors or thrombosis, while late graft failures are mainly caused by progression of atherosclerosis and intimal hyperplasia (IH) [171, 186]. Various studies have found IH to be the major cause of graft stenosis [22, 40, 171]. IH is the abnormal, continued proliferation and overgrowth of smooth muscle cells (SMCs) in response to endothelial injury or dysfunction [43]. Although many theories have been hypothesized, the exact mechanism of IH remains uncertain, with indications that both biological and mechanical factors are involved, which include endothelial injury [30, 32], platelet activation [108, 120], disturbed local hemodynamics [9, 79, 89, 93, 124, 185], compliance mismatch between graft and host vessel [1, 7], and interactions between blood and graft material [31].

It has been shown that in end-to-side (ETS) graft–artery configurations, IH develops predominantly on the suture-line (mainly at the toe and heel of the anastomosis) and on the artery bed across the junction [11, 163, 175], as shown in Figure 1.3. On the basis of this focal distribution of intimal thickening (IT), investigators have suggested that disturbed flow

patterns and hemodynamic factors are correlated with and play a key role in the onset and progression of atherosclerosis and distal anastomotic intimal hyperplasia (DAIH) [110, 121, 129, 130, 163]. Thus, hemodynamic parameters (HPs) are believed to be highly important among the aforementioned factors [11, 63, 71], and are the focus of this dissertation.

Accordingly, several investigations have been conducted and different anastomotic geometries and devices have been designed to improve the flow fields and HPs distribution at ETS anastomosis, in order to enhance the graft patency. These investigations include studies on the effects of geometrical factors, such as anastomotic angle [46, 165], modified configuration of distal anastomosis [33, 72, 98, 100, 101, 105, 111, 168], graft-to-host artery diameter ratio [17, 142], and out-of-plane graft [133, 158], and effects of stenosis severity and proximal artery flow [27, 39, 95, 141] and distance of grafting [14, 15, 159]. However, these available designs generally do not exhibit large variation in terms of general flow characteristics, such as the vortex formation at the heel, or the impingement of blood on the artery floor which can be observed in almost all the available distal anastomosis models.

Figure 1.3: Outline of the spatial distribution of IH in an ETS anastomosis (taken from [128]).

1.3 Objectives

The overall aim of this thesis is to design and develop a superior configuration for the distal anastomosis of CABGs, in order to considerably improve the blood flow patterns and HPs distribution to enhance the graft patency. For this purpose, the following stage-targets are addressed:

- Design a basic geometry for CABG and compare its hemodynamic performance with that of the conventional ETS anastomosis, using computational fluid dynamics (CFD) simulation method.
- Optimize the designed CABG configuration, and improve its performance by modification of the geometrical parameters involved.
- Validate the CFD simulation results experimentally, by in vitro flow measurements, using Particle Image Velocimetry (PIV) technique.
- Incorporate the effects of vessel wall elasticity and non-Newtonian blood rheology into the superior designed CABG anastomotic configuration model simulations, in order to compare its hemodynamic performance with that of the conventional ETS anastomosis in a more realistic biomechanical environment and verify the advantages of this configuration, observed in the first-stage preliminary study.

1.4 Significance

Patent CABGs result in a considerable improvement in global ejection fraction of patients with CAD [70]. Based on the correlation between hemodynamic factors and IH progression,

improved anastomotic configurations have been designed, and somewhat longer survival times for bypass grafts have been attained. Further enhancement of longevity and patency rate of CABGs and elimination of the need for re-operation by the design of an optimal anastomotic configuration can lower morbidity and reduce medical costs for patients suffering from cardiovascular diseases. Hence, the design of a novel CABG configuration which provides considerably improved hemodynamics can be of a high importance.

1.5 Outline of the report

After the introduction and presentation of the research objectives in Chapter 1, a background study is presented in Chapter 2 on bypass graft failure modes, causative biological and mechanical factors, and relevant hypothesized theories. A novel CABG design of sequential anastomoses (SQA) is introduced in Chapter 3; computational simulation of blood flow and study of HPs distribution in this novel CABG SQA configuration is carried out, involving comparison of the flow field and HPs in the new design with existing ETS and side-to-side (STS) anastomotic models, and sensitivity analysis of the design parameters to obtain the superior configuration. The experimental validation of the simulation results by PIV measurements is described in Chapter 4. In Chapter 5, the effects of wall elasticity and non-Newtonian blood rheology on the SQA CABG hemodynamics are studied, by a two-way fluid–structure interaction (FSI) analysis. Finally, the conclusions, future works, and directions are presented in Chapter 6.

Chapter 2

2 Background

2.1 Theories on bypass graft failure

According to angiography and histological examinations, common graft failure modes include acute thrombosis, IH, and onset of progressive atherosclerosis [156]. Thrombosis is the formation of a blood clot (thrombus) in arteries or veins. Atherosclerosis is a disease of the arteries in which fatty material and plaque are deposited in the wall of an artery, resulting in narrowing of the arterial lumen and eventual impairment of blood flow. The predominant theory suggests that atherosclerosis develops in response to injury [148]; however, there is no consensus as to whether this injury is mechanical, chemical, immunological, or a combination of these and other factors.

Artery walls consist of three concentric sections: The tunica intima (innermost section), the tunica media (middle section), and the tunica adventitia (outermost section), as shown in Figure 2.1. The media contains SMCs and elastic tissues, and intima contains endothelial cells (ECs) which line the inner surface of vessels. IH, the major cause of late graft failure, is the abnormal increase in the number of cells and thickening of the tunica intima of a blood vessel. IH was first described by Carrel and Guthrie [25], who observed that within a few

days after arterial vein graft implantation, the anastomotic stitches happened to be covered with a material similar to the normal endothelium.

Although the pathological mechanisms responsible for the development of thrombosis, IH, and atherosclerosis have not been fully elucidated, many theories have been hypothesized, indicating the involvement of both biological and mechanical factors, some of which are briefly discussed in the following sections.

Figure 2.1: Structure of a muscular artery (taken from [73]).

2.1.1 Biological Factors

The endothelial cells sense the mechanical forces acting on them through mechanotransducers [37]. The presence of abnormal mechanical forces on the endothelium leads to some biological effects, which can trigger excessive release of mitogens and growth factors and lead to subsequent SMC proliferation and excessive platelet aggregation [28]. Monocytes and cholesterol accumulate in the intima, creating foam cells. Monocytes become macrophages within the intima, resulting in formation of an atherosclerotic plaque

[177]. 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. The artery with a rigid matrix 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 and consequent restenosis.

2.1.2 Vascular Injury

During the surgery, endothelium and SMCs of the recipient artery and the autogenous graft are injured in several ways: grasping of the instruments used to harvest the graft; routinely applied high intra-luminal pressure to check for the graft leakage; and sutures for the construction of the anastomoses. In addition, due to implantation of the vein graft in the arterial circulation, the grafted vein is exposed to high pressures and high blood flow causing further damage to the venous endothelium [35]. The injured endothelium is less capable of producing anti-proliferative products [36], and the physiological balance in the vessel wall is further disturbed by the release of intracellular growth factors from injured medial SMCs [36, 80]. It has been demonstrated that acute injury to the intima and media can produce hyperplasia and SMCs proliferation, which occur at a rate proportional to the degree of the injury [28, 32]. It is also observed that IH forms around the injury sites after balloon angioplasty [4]. These suggest the involvement of a wound healing process in IH formation.

2.1.3 Compliance Mismatch

It has been shown in vivo that a higher degree of compliance mismatch between the graft and the artery results in a greater amount of suture-line IH formation [1, 11]. As high intramural stresses have been observed at suture-lines in both ETS and end-to-end (ETE) junctions, it has been suggested that elevated suture-line intramural stresses might be an important proliferative stimulus for IH formation in vascular reconstructions [7]. Consequently, since increased compliance mismatch causes stress concentration and leads to increased intramural stresses [7, 105, 137], the proliferative influence of increased compliance mismatch on suture-line hyperplasia in ETS anastomoses has been correlated to the resulting increase in intramural stresses [7].

However, computational studies of ETS anastomosis models have illustrated that compliance mismatch has only minor effects on local hemodynamic factors [71, 167].

2.1.4 Hemodynamic factors

In vivo observations indicate that in an ETS graft-artery anastomotic configuration, IH occurs preferentially around the suture-line (especially at the toe and heel of the anastomosis), and also develops on the bed of the host artery across the junction [11, 161-163, 165, 175].

Arterial floor IT is attributable to altered flow conditions [11]. It has been suggested that suture-line IT might be related to vascular healing; nevertheless, an in vivo study by Sottuirai [161] has shown opposing results. He investigated the role of anastomotic

configuration, using autogenous femoro-femoral bypass with ETS configuration and ETE interposition graft in canine models. Since compliance mismatch is not an issue in the autogenous femoro-femoral bypass, for DAIH which exclusively occurred in the ETS (and not in the ETE) distal anastomoses, the geometry of the distal anastomosis has been concluded to be the logical causal factor. Moreover, creation of an arbitrary stricture on an extended hood of the arterial graft, to function as the “physiologic toe”, resulted in transferring DAIH to the site of the graft stricture (see Figure 2.2), which attests to the fact that it is the ETS anastomotic configuration and its unnatural flow conditions, and not the trauma along the suture-line, that contributes to DAIH formation.

Figure 2.2: (a) ETS distal anastomosis with a vein patch (b) a section of distal ETS anastomosis; creation of an arbitrary stricture at the hood to simulate the toe (*) results in transferring the IH from the suture-line at the anastomotic toe to the stricture at the hood (physiologic toe); arrows indicate direction of blood flow (taken from [161]).

Several investigations have been conducted to better understand the relationship between blood flow-based stresses acting on the walls and IT in bypass grafts [11, 47, 61, 89, 115, 147, 163]. Subsequently, multiple HPs have been associated with occlusive formations in arterial bypass grafts and other branching blood vessel configurations.

2.1.4.1 High WSS

Based on in vivo experiments on dogs, it has been suggested that ECs seem to be normal when the time-average shear stresses are below a specific value, suggesting that high shear stresses erode the endothelium [54]. Besides, an investigation of the effect of blood flow rates on the accumulation of thrombotic materials within arteries has illustrated that the regions of high shear rate appear to be most prone to thrombus growth [132]. Moreover, laser Doppler velocimetry (LDV) measurements in models of human aortic bifurcation have indicated that the intima is thicker at sites exposed to higher shear rates [52].

2.1.4.2 Safe bandwidth of WSS

The existence of a safe bandwidth of WSS has been suggested, based on the postulate that (i) very low, oscillating wall shear initiates atherosclerotic lesions, and (ii) both low and high shear stresses contribute to the growth of plaque formation [122, 123]. This idea has successfully determined the sites and growth patterns of atherosclerotic lesions and IH in several arterial bifurcations and bypass graft configurations, respectively.

Moreover, study of numerical results of simulation of blood flow in the human aortic arch has broadly suggested preferential development of early atherosclerotic lesions in regions of extreme (either maxima or minima) WSS and pressure [157]. In addition, it has been reported that the ECs in both low and high shear regions experience structural and functional abnormalities [124], thereby supporting the hypothesis of a safe bandwidth of WSS.

2.1.4.3 Low magnitude-high oscillatory WSS

Caro et al. [24] observed that atherosclerotic lesions occur along the inner wall of arterial curvature, where low shear stress exists. Hence, they proposed that, due to low WSS and enhanced particle residence time in flow separation and flow recirculation zones, excess cholesterol is deposited on the surface of the lumen, initiating atheroma growth, while in the regions of high WSS, more cholesterol is washed away by the blood flow. Based on their theory, it is the “shear-dependent mass transfer” which is responsible for atheroma development and IT.

Low shear stress acting on the vessel wall has been introduced as the key hemodynamic factor involved in the localization of IT, due to significant correlations found between the preferred sites of IT and the regions of slow recirculation flow (i.e. long particle residence time) with low WSS [81, 147, 170, 185].

Morinaga et al. [121] investigated IT occurrence in autogenous vein grafts in dogs, by comparing the conditions of high flow rate and low WSS with low flow rate and high WSS. A comparatively significant intimal thickness was observed in high flow rate and low WSS condition, revealing that WSS, and not the rate of flow, is the essential hemodynamic factor related to IH.

Ku et al. [94] found a positive correlation between plaque location and low oscillating shear stress, indicating that marked oscillations in the direction of wall shear may enhance atherogenesis. Consequently, they put forward the concept of “oscillatory shear index”

(OSI) to quantify the oscillatory nature of WSS. The modified definition of OSI is given as [68]:

$$OSI = \frac{1}{2} \left(1 - \frac{\left| \int_0^T \vec{\tau}_w dt \right|}{\int_0^T |\vec{\tau}_w| dt} \right) \quad (2.1)$$

where T is the time period of a cardiac cycle and $\vec{\tau}_w$ is the WSS vector (traction). This definition takes into account not only the reverse (180 degree) direction but also any direction changes (0 to 180 degrees) of the WSS in three-dimensional space. The OSI value varies between 0 and 0.5, where 0 corresponds to the regions experiencing no reverse flow, and 0.5 is for the case of fully oscillatory flow without net forward flow [99].

Li and Rittgers [106, 107] compared the mechanical factors, obtained from study of pulsatile flow in vitro model of the distal ETS anastomosis of an arterial bypass graft, with histological findings of IH formation from earlier canine studies. Their results suggest that regions exposed to a combination of low mean WSS and high OSI may be most prone to IH formation. The same conclusion was obtained using in vitro preconditioned human umbilical vein ECs [134].

2.1.4.4 High gradient of WSS

In an ETS graft-artery anastomosis, the floor typically experiences low oscillating WSS, due to the presence of a moving stagnation point during the cardiac cycle, as shown in Figure 2.3. However, this low WSS–high OSI hypothesis does not explain IH formation at the toe

of the anastomosis. Consequently, it has been postulated that the large spatial WSS gradient (WSSG), which is mainly observed at the toe of the anastomosis, induces morphological and functional changes in the endothelium that contribute to elevated wall permeability and hence possible atherosclerotic lesions [38]. The spatial WSSG represents the non-uniformity of the force distribution [128], and implies a stretching force applied on the ECs, which may lead to IH [33].

Figure 2.3: Typical distribution of HPs and IT (a) and flow patterns (b) in the distal anastomosis of arterial bypass grafts (adopted from [66, 114]).

Moreover, the local WSSG is suggested as the single best indicator of non-uniform flow fields leading to atherogenesis [102]. By employing the aorto-celiac junction of rabbits as a representative atherosclerotic model, an experimentally validated computer simulation model for convection mass transfer has shown that the WSSG is a reliable predictor of critical atherogenic sites in branching arteries [103]. It is seen that IH tends to develop at sites having high spatial and temporal gradients in WSS [128].

2.2 Disturbed flow patterns associated with distal ETS anastomosis

The configuration of distal ETS anastomosis is not naturally present in the arterial system (except for the patent ductus arteriosus). A distal ETS anastomosis is characterized by

abnormal flow conditions, including flow oscillation at the heel, impact on the artery floor, and flow separation at the toe.

Typically, there is a low WSS region at the heel, where a vortex forms due to the interaction of the flow from the graft with the relatively slow flow in the occluded proximal artery, whose size changes with the flow phase, as shown in Figure 2.3. The presence of a slow recirculation flow (i.e. a vortex) increases the near-wall residence time and results in platelet activation [76] and fibrin thrombus formation [53, 145], which leads to IH development [11, 81, 147, 161, 170, 185].

Along with this vortex, there is a stagnation point on the artery bed, where the graft flow impinges the floor, whose location oscillates (with the size of the vortex) during the cardiac cycle. This moving stagnation point provides a low magnitude-high oscillatory WSS condition on the artery bed which is prone to enhancement of atherogenesis [94] and IH formation [106, 107]. In addition, the flow impact on the artery floor is known to be injurious to the endothelium and is believed to be a contributing factor to the graft failure, as there is evidence of change in the flow character once it impacts against the junction floor [12].

In a conventional ETS configuration, there are high flow shear rates at the toe of the anastomosis (causing high WSS at the toe), usually with a flow separation region just distal to the toe at the inner wall of the coronary artery (causing flow recirculation and low WSS at this area). This results in a high spatial gradient of WSS at the toe of the anastomosis, which

induces morphological and functional changes in the endothelium that contribute to elevated wall permeability and consequent atherosclerotic lesions [38, 102, 103] and IH development [128]. Moreover, in flow separation and flow recirculation zones, due to low WSS and enhanced particle residence time, excess cholesterol is deposited on the surface of the lumen, initiating atheroma growth [24] and IH [76, 77].

Although an ETS anastomosis is essentially a bifurcation [114], surgically created anastomoses can be modified to yield a flow environment that improves graft longevity, in contrast to arterial bifurcations. As briefly reviewed above, investigations of blood flow and HPs and their comparison with focal locations of IT and IH formation in CABGs have resulted in correlation of some HPs to initiation and progression of IH. Consequently, HPs can, in turn, be utilized as indicators to show susceptible sites of IT and favorable conditions for thrombi and IH formation. Accordingly, using these indicators, extensive efforts have been put to obtain an optimal graft design, which is an end point for the study of correlations between hemodynamics and graft failure.

2.3 Attempts to design an optimal anastomotic configuration

First efforts towards attaining an optimal anastomosis have been made by changing the anastomotic angle. It has been shown that tissue remodeling at ETS arterial anastomoses is highly sensitive to graft angle [82], and graft patency rates vary according to anastomotic angle. The anastomotic angle affects the flow regime and shear stress [19, 140]. It is shown that flow separation and disturbances at the toe increase with anastomotic angle [46, 77, 165,

166]. Hence, a smaller distal ETS anastomotic angle ($\leq 30^\circ$) seems to bring about a less disturbed and more uniform, smooth flow from the graft into the coronary artery.

The effect of graft-to-host diameter ratio on the hemodynamics of CABGs has also been examined. It is observed that larger graft-to-host diameter ratios (5:3) have better hemodynamic performance than smaller ones (1:1) [17, 142]. Likewise, results of a recent computational study, using mesh-less CFD and genetic algorithms optimization, indicate that the graft caliber should be always maximized [192].

Further efforts have been put to obtain a more favorable CABG anastomosis by design of cuffed and patched anastomotic configurations. Miller et al. [119] introduced a vein cuff design that produced good patency in femoral-distal grafts (see Figure 2.4). However, the utility of this technique is somewhat controversial. While some studies found that grafts implanted with vein cuffs resulted in decreased developments of IH [90, 169] and had better patency than those with a non-cuffed anastomosis [20], other investigations showed that (i) the use of a Miller cuff caused no difference in IH thickness [126], (ii) the improved patency was only in below-knee grafts (and not in above-knee popliteal bypasses) [119, 144, 168], and (iii) the use of a cuff has adverse effects on hemodynamic factors around the anastomosis, such as large variations in shear stress on the artery floor, low-momentum recirculation within the cuff, and prominent separation at the cuff toe [34, 69, 112]. It is hence suggested that the improved patency rates achieved with cuffed anastomoses are due not to a decrease in IH but to an increased ability to accommodate IH before it causes significant stenosis (owing to the increased anastomotic volume) [126, 188].

Figure 2.4: Miller cuff construction: (a) vein cuff is sewn longitudinally around arteriotomy (b) graft is then sutured end-to-cuff (taken from [168]).

The Taylor vein-patch technique [173] (see Figure 2.5) has been found to decrease IH [59], diminish flow disturbances and undesirable flow separation at the toe of the anastomosis [33], and slightly reduce the WSSG in the anastomotic region [98]. However, it causes only a small improvement in hemodynamic factors. Besides, patched and non-patched grafts have shown similar primary patency rates [59].

Figure 2.5: Schematic drawing of Taylor-patched anastomosis (taken from [59]).

Lei et al. [98] further improved the geometric design of the Taylor patch, which yielded a significant reduction (ranging from two to six fold decrease, compared with standard and Taylor hooded configurations) in local time-averaged WSSG (TAWSSG) both at the toe and on the floor, due to the gradual transition in wall curvature and cross-sectional area at the toe region, as shown in Figure 2.6.

Figure 2.6: Improved anastomotic geometry with gradual transition in wall curvature and cross-sectional area at the toe region (adopted from [98, 114]).

Tyrrell collar has been developed in attempts to incorporate the advantages of the Miller and Taylor anastomotic designs, by avoiding direct suturing of the graft and artery (which can cause high compliance mismatch in case a synthetic graft is used), and providing a more streamlined shape at the toe [176] (see Figure 2.7). However, trials of Tyrrell collar venous anastomosis in arteriovenous grafts (AVGs) not only showed no improvements in graft patency [104], but also indicated that the use of the collar at the venous anastomosis of forearm loop AVGs resulted in early graft failure [56].

Figure 2.7: Diagram of a Tyrrell vein collar (a) without and (b) with a PTFE graft (taken from [56]).

Longest and Kleinstreuer [111] numerically simulated the haemodynamics for a conventional ETS base case, the VenafloTM graft, and an improved cuffed graft-end configuration, which are shown in Figure 2.8. Considering the critical toe region, the VenafloTM graft demonstrated considerable improvements over the base case in predictive

computer simulations as well as in clinical trials. The performance showed further improvement in the modified graft-end design, due to smoother wall curvatures and the elimination of the graft bulges.

Figure 2.8: Geometric surface models of the base case, Venaflo™ graft, and modified graft-end design (adopted from [111]).

A streamlined anastomotic configuration in which the distal outlet segment (DOS) is aligned with the graft has been developed by Longest et al. [113]. This configuration, shown in Figure 2.9(a), resulted in an advantageous reduction of the peak WSSG values in the vicinity of the toe (to 1.7 from 11.8 in a conventional ETS model); however, particle-wall interactions remained significant throughout the anastomosis, which can result in platelet activation, and may lead to IH.

O'Brien et al. [127] have designed a configuration to replace the anastomosis with a synthetic bifurcation connected in an ETE fashion with the proximal outlet segment (POS) and DOS (see Figure 2.9(b)). Their numerical simulations indicate that the smoothly curving bifurcation improves the WSS environment by reducing flow separation and stagnation.

Figure 2.9: (a) Streamlined arterial bypass graft (b) Arterial bypass graft configuration designed to reduce stagnation and separation zones (adopted from [113, 114, 127]).

Walsh et al. [182] have designed a novel vascular grafting device with a bifurcating configuration, in order to eliminate the flow impingement on the interior wall of the artery at the distal anastomosis, as shown in Figure 2.10. In this vascular device, the flow from the proximal anastomosis is bifurcated into two branches and these branch flows impinge upon each other at a central region of the lumen at the distal anastomosis. By avoiding arterial bed impingement, the possibility of disease formation is reduced.

Figure 2.10: Vascular grafting device (1) flow from the proximal anastomosis (2,3) suture-lines of the end-to-end anastomoses of the distal section (4) the host artery (adopted from [182]).

Optimal anastomosis design must take into account practical issues such as surgical construction. As reviewed above, the designed anastomotic configurations which are feasible to be constructed during operation using autogenous materials, including Miller cuff, Taylor patch, and Tyrrell collar, have not shown a remarkable enhancement in patency of bypass grafts. On the other hand, those configurations which have shown considerable improvement in HPs distribution are made of synthetic materials due to their complex geometry. This results in high compliance mismatch at the synthetic graft-blood vessel interface leading to increased intramural stresses which has been suggested as a cause for IT formation [11].

Moreover, although several configurations are suggested for the distal anastomosis, they have not changed the general problematic flow characteristics, such as the vortex formed at the heel (especially in the case of a fully stenosed proximal segment of the host vessel) or the impact of the blood on the artery bed (except for the Walsh's vascular grafting device). The presence of a vortex results in an increase of local particle residence time which has been associated with general qualitative sites of IH development [11, 161, 185] and fibrin thrombus formation [53, 145], and the impact on the floor is believed to be a contributing factor to the graft failure, as there is evidence of the change in the flow character once it has impacted against the junction floor [12].

Therefore, there exists the dilemma of designing an optimal anastomotic configuration that can bring about considerable improvements in the flow regime, HPs distribution, and graft patency, which remains unsolved.

2.4 Hypothesis

The failure mechanism addressed in this dissertation is the DAIH. Although the exact underlying mechanism for IH has not yet been fully understood, hemodynamics is believed to be critical in serving as a regulator and modifier of cellular biology and in the development of the disease process. A number of research studies have correlated the formation of DAIH to multiple HPs, such as high WSS, low WSS, high WSSG, oscillatory shear, and also extreme shear resulting in a safe bandwidth of WSS.

However, as indicated in this background study, the majority of evidences witness that low, oscillating WSS and high spatial WSSG have significant association with regions of IH formation and IT. Hence, the current assumption is that the IH develops at sites of low magnitude-high oscillatory WSS and regions of elevated spatial WSSG.

Consequently, a novel CABG configuration is proposed and is hypothesized to have superior blood flow patterns and HP distributions for enhanced graft patency. The goal of this dissertation is to evaluate this hypothesis, based on the abovementioned assumption.

Chapter 3

3 Novel CABG design of sequential anastomoses [83]

3.1 Sequential bypass grafting

The sequential bypass grafting technique, first described by Flemma et al. [49] and Bartley et al. [10], is a technique in which two or more coronary artery anastomoses are made with a single graft, usually the saphenous vein (SV). Figure 3.1 illustrates a typical sequential anastomoses configuration.

Figure 3.1: Geometry of a sequential aorto-left coronary bypass graft model. The SV is originated from the aorta at point A and anastomosed to the branches of the LCx artery (OM1 and OM2) at points B and C in STS and ETS fashions, respectively (taken from [150]).

Intra-operative studies have demonstrated a higher blood flow [64] and a higher velocity [131] in the proximal (pre-anastomotic) segment of a sequential graft than in a single coronary graft with an ETS anastomosis. It has been shown that the STS anastomosis has a smoother flow with smaller spatial gradients of WSS as compared to the ETS anastomosis [150]. Moreover, Higher patency rates have been observed through post angiograms in the STS anastomoses than in the ETS anastomoses [179].

Patient-specific post-surgical blood flow simulations in ETS and STS anastomoses has illustrated that (i) flow stagnation zones exist in ETS but not in STS anastomosis, and (ii) the STS configuration has smoother stream divisions of mass flow throughout the cardiac cycle than the ETS configuration [50].

These advantages of the STS anastomosis may motivate the use of sequential bypass grafting over multiple bypass grafting, and are the impetus for the design of the novel CABG coupled SQA in this dissertation.

3.2 New Coupled STS-ETS Anastomoses Bypass Graft Configuration

Based on the abovementioned beneficial results of sequential bypass grafting, a new configuration for the CABG is proposed to improve the flow field and HPs distribution of the conventional ETS anastomosis. This configuration replaces a conventional ETS anastomosis by a coupled STS-ETS SQA. In this distal SQA design, there is initially a STS anastomosis distal to the stenosis, and then the graft end is anastomosed to the same coronary artery further downstream in an ETS fashion, as shown in Figure 3.2(a). It is

expected that the partial flow through the STS anastomosis and the coronary artery segment between the two anastomoses, by merging with the flow from the graft at the ETS anastomosis and redirecting that into the distal segment of the coronary artery, smoothens the flow field at the ETS anastomosis and vanishes the vortex and the floor impact. This is assumed to provide a combination of two (a STS and a modified ETS) anastomoses, each of which has a better performance and a higher patency than a conventional ETS anastomosis.

This configuration is supposed to benefit the flow field in different ways including uniform, smooth flow in the anastomotic region, less impact on the artery bed, less or even no vortex at the heel region of the ETS anastomosis, and providing a spare route for the blood flow to the coronary artery in case of re-stenosis in either of the (STS or ETS) anastomoses, to avoid re-operation.

Therefore, in order to evaluate and compare the advantages and disadvantages of the suggested design over a conventional ETS configuration, a CFD study is conducted and flow field and HPs are investigated accordingly.

3.2.1 Base models

In order to evaluate and compare the advantages and disadvantages of the suggested SQA design over a conventional ETS anastomosis configuration, three base CFD models are designed and evaluated: (i) the new coupled anastomoses configuration, shown in Figure 3.2(a), (ii) a parallel STS anastomosis (Figure 3.2(b)), and (iii) a conventional ETS anastomosis (Figure 3.2(c)). The latter two are the reference models to be compared,

respectively, with the STS component of the new design (in order to study the possible effects of the ETS anastomosis of the new design on its STS component) and with its ETS component.

Figure 3.2: Three base anastomotic models: (a) the new proposed coupled STS-ETS SQA model (b) parallel STS anastomosis model (c) conventional ETS anastomosis model with an anastomotic angle of 45°.

3.2.2 Geometric parameter values

The dimensions of the three base models are listed in Table 3.1, where D_G , D_A , L_P , L_{STS} , L_{ETS} , L_D , and d stand, respectively, for the graft diameter, coronary artery diameter, length of the proximal section of the host artery, length of the STS anastomosis, length of the ETS anastomosis, length of the distal section of the host artery, and distance between the two anastomoses in the new SQA model, as shown in Figure 3.2.

The base models are considered to have an ETS anastomotic angle of 45° with the proximal segment of the coronary artery fully occluded. The models are designed to be planar, based on the study of Galjee et al. [58] who demonstrated that the typical location and course of SV in RCA bypass graft can be assumed to be approximately planar.

Geometric models are built in Pro-Engineer software and transferred to Gambit software to be finalized and meshed.

Table 3.1: Dimensions of the three base models (all dimensions are given in mm).

Model	D_G	D_A	L_P	L_{STS}	L_{ETS}	L_D	d
New SQA design	4	2	6.5	8	7	48	30
Conventional ETS	4	2	10	N.A.	7	48	N.A.
Parallel STS	4	2	6.5	8	N.A.	48	N.A.

3.3 Mesh generation and validation

Since generating structured mesh for complex geometries such as the anastomotic region of the present models could be extremely time consuming, if not impossible, each model is divided into small sections including graft, anastomosis, and distal host artery, and each section is meshed separately as shown in Figure 3.3.

As quadrilateral/hexahedral elements permit a much larger aspect ratio than triangular/tetrahedral cells in relatively simple geometries in which the flow conforms well to its shape, such as the graft and host artery sections in the present models, a structured mesh of quadrilateral/hexahedral cells is applied in the graft and distal host artery of each

model, in order to reduce the computational cost. However, the anastomosis sections are meshed by prism and triangular/tetrahedral elements.

Figure 3.3: Generated mesh for the new SQA model.

Flow in a cylindrical conduit has high velocity gradient in near-wall region and smaller one in central region. Hence, in order to obtain sufficient information to characterize the gradients in both regions, and minimize the total number of mesh elements at the same time, a boundary layer mesh is applied in radial direction, whose density is increased near the wall according to an exponential distribution. Resolution of the boundary layer (i.e. mesh spacing near walls) plays a significant role in the accuracy of the computed WSS, especially in the case of laminar flows where the grid adjacent to the wall should obey Equation (3.1) which is proposed based upon the Blasius solution for laminar flow over a flat plate at zero incidence [154].

$$y_p \sqrt{\frac{u_\infty}{\nu x}} \leq 1 \quad (3.1)$$

where

y_p = distance to the wall from the adjacent cell centroid;

u_{∞} = free-stream velocity;

ν = kinematic viscosity of the fluid;

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

In this study, the velocity is smaller than 0.74m/s and the kinematic viscosity of the blood is $3.885 \times 10^{-6} \text{m}^2/\text{s}$; therefore, assuming $x=1\text{mm}$, the maximum distance of the most adjacent cell centroid to the wall should be 0.07mm; while in the present meshed models, all the near wall elements' centroids have a distance less than 0.04mm, satisfying the criterion.

A computational model is assumed to be mesh-independent if further refinement yields no significant improvement in results. Therefore, the mesh sensitivity is tested on the velocity and WSS, by increasing the number of grid cells. The spatial resolution of the computational domain is considered to be sufficient for this study when further mesh refinements could only result in less than 3% change in velocity and 1% change in WSS at some examined sections. The final models of the new SQA, parallel STS, and conventional ETS anastomoses consist of 196331, 150645, and 88701 elements, respectively.

3.4 Assumptions and boundary conditions

For the preliminary study of the suggested design at this stage, the vein and arteries are considered as rigid tubes and blood is assumed as a Newtonian fluid (i.e. the effects of vessel wall elasticity and FSI and non-Newtonian rheology of blood are not taken into account).

3.4.1 Laminar flow

Peacock et al. [136] correlated the critical peak Reynolds number with Womersley number (α) and Strouhal number (St) in pulsatile flow through a straight tube by Equation (3.2). They, accordingly, predicted the critical peak Reynolds number for the human coronary arteries to range from 1650 to 2650. However, actual coronary peak Reynolds number varies from 550 (at rest) to 2275 (with exercise). Thus, assuming the coronary arteries as straight tubes, they concluded that coronary flow is unlikely to be disturbed. Thereby, laminar flow is usually assumed for blood flow simulations in coronary arteries.

$$Re_{\text{peak(critical)}} = 169 \alpha^{0.83} St^{-0.27} \quad (3.2)$$

In the present study, $Re_{\text{peak(critical)}}$ is calculated to be 853.7 and 865.5 in the coronary artery and graft respectively, while Re_{peak} is obtained as 187.4 and 93.7 correspondingly, which is far below the critical value, validating the assumption of laminar flow for this study.

3.4.2 The inlet length

The inlet length for oscillatory flow is shorter than that for a steady flow at the same Reynolds number (the higher the value of α , the shorter the oscillatory inlet length is). The inlet length for steady flow can be calculated by Equation (3.3), where $\bar{U}$ is the average velocity, R is the tube radius, ν is the kinematic viscosity, and k is a derived constant [125].

$$L = \frac{2k\bar{U}R^2}{\nu} \quad (3.3)$$

The highest value for k is quoted by Chang and Atabek [26] as $k=0.13$. They have determined $k=0.08$ for oscillatory flow which is used in this study. Substituting the

numerical values of the abovementioned parameters for the current study ($\bar{U}=0.0586\text{m/s}$, $R=0.002\text{m}$, $\nu=3.89\times 10^{-6}\text{m}^2/\text{s}$) in Equation (3.3), the inlet length is obtained as $L = 9.7\text{mm}$ for both the graft and the coronary artery. Hence, the exit flow is assumed to be in a fully developed condition due to 48mm long distal section of the host artery (L_D). Thereby, a traction-free boundary condition is imposed at the coronary artery outlet (i.e. the outflow boundary condition is set to assume a zero normal gradient for all flow variables except pressure).

3.4.3 Flow waveform and velocity profile at the graft inlet

The proximal anastomosis of the graft to the aorta is not analyzed in this study, and the focus is only on the distal anastomosis. Hence, a fully-developed pulsatile flow is applied at the graft inlet (assuming that the length of the proximal part of the graft, which is not modeled here, is more than the calculated entrance length of 9.7mm). The flow waveform and the velocity profile are based on measurements by magnetic resonance phase velocity mapping within a CABG [57]. The original waveform has been measured in grafts with an average diameter of 6mm; hence, the corresponding cross sectional average velocity values for a graft diameter of 4mm are calculated by similitude so as to have the same Reynolds number. Also, some modifications are made to obtain the smoothened waveform with the time period of 0.9s, adapted for this study, as demonstrated in Figure 3.4.

Figure 3.4: Average velocity values of the waveform used in the present study (labels indicate times at which flow is studied).

The systolic peak flow rate is $Q_{\max}=70\text{ml/min}$, and the maximum Reynolds and Womersley numbers are calculated to be $Re_{\max}=79$ and $\alpha_{\max}=2.45$, respectively, based on the graft diameter of 4mm.

The Womersley solution [190] is assumed for the inlet axial velocity profile, which is derived as a fully-developed pulsatile flow and expressed as

$$U_z(r,t) = \bar{U}(t) \left(1 - \frac{J_0\left(i^{\frac{3}{2}} \frac{\alpha r}{R}\right)}{J_0\left(i^{\frac{3}{2}} \alpha\right)} \right) / \left(1 - \frac{2J_1\left(i^{\frac{3}{2}} \alpha\right)}{i^{\frac{3}{2}} \alpha J_0\left(i^{\frac{3}{2}} \alpha\right)} \right) \quad (3.4)$$

where $\bar{U}(t)$ is the average velocity waveform, i is the imaginary unit, R is the tube radius, J_0 and J_1 are the first kind Bessel functions of order zero and one respectively, and α is the Womersley number. Using fast Fourier transform, the frequency content of the waveform

for its fundamental angular frequency (ω) is extracted [45, 51] to compute a complex Fourier series with Fourier coefficients B_n as

$$\bar{U}(t) = \sum_{n=-N}^{n=N} B_n e^{in\omega t} \quad (3.5)$$

From Equations (3.4) and (3.5), the axial velocity is obtained as

$$U_z(r, t) = \sum_{n=-N}^{n=N} B_n \left\{ \frac{\left(1 - \frac{J_0\left(i^{\frac{3}{2}} \frac{\alpha_n r}{R}\right)}{J_0\left(i^{\frac{3}{2}} \alpha_n\right)} \right)}{\left(1 - \frac{2J_1\left(i^{\frac{3}{2}} \alpha_n\right)}{i^{\frac{3}{2}} \alpha_n J_0\left(i^{\frac{3}{2}} \alpha_n\right)} \right)} \right\} e^{in\omega t} \quad (3.6)$$

where $\alpha_n = R\sqrt{\omega_n/\nu}$. Equation (3.6) can be further simplified to

$$U_z(r, t) = 2B_0 \left[1 - \left(\frac{r}{R} \right)^2 \right] + 2 \times \text{Real} \left\{ \sum_{n=1}^{n=N} B_n \frac{\left(1 - \frac{J_0\left(i^{\frac{3}{2}} \frac{\alpha_n r}{R}\right)}{J_0\left(i^{\frac{3}{2}} \alpha_n\right)} \right)}{\left(1 - \frac{2J_1\left(i^{\frac{3}{2}} \alpha_n\right)}{i^{\frac{3}{2}} \alpha_n J_0\left(i^{\frac{3}{2}} \alpha_n\right)} \right)} e^{in\omega t} \right\} \quad (3.7)$$

where $\text{Real}\{\}$ represents the real part of the complex expression. Subsequently, a user defined function (UDF) is provided (enclosed in Appendix A) to implement the above time-varying velocity profile as the inlet boundary condition within FLUENT (the commercial CFD package used in this study).

In the parallel STS model, 15% of the blood flow is set to pass through the STS anastomosis into the coronary artery, and the remaining 85% is assumed to pass through the graft (to the assumptive distally located ETS anastomotic junction). The above percentage is adjusted to have the parallel STS model consistent with the new coupled SQA model, since the flow is found to be bifurcated with the same proportion through the coronary artery and the graft at the STS component of the SQA model (on average within each cycle), as observed in the simulation results of the SQA model and is reported for some time instants in Section 3.6.

Finally, the no-slip boundary condition is specified on all walls.

3.5 Numerical solution

The governing equations for blood flow through the coronary artery bypass, which is assumed as a three-dimensional, time-dependent, incompressible, isothermal, Newtonian, laminar flow, are

$$\text{Continuity equation, } \nabla \cdot \mathbf{U} = 0 \quad (3.8)$$

and

$$\text{Navier-Stokes equation, } \rho \frac{\partial \mathbf{U}}{\partial t} + \rho(\mathbf{U} \cdot \nabla) \mathbf{U} = -\nabla P + \mu \nabla^2 \mathbf{U} \quad (3.9)$$

where $\mathbf{U}$ is the velocity vector, t is the time, and P is the pressure. The density (ρ) and dynamic viscosity (μ) of blood are assumed to be 1050 kg/m^3 and $0.00408 \text{ Pa}\cdot\text{s}$ respectively.

The governing equations are solved numerically by a finite volume method and the commercial CFD package, FLUENT (Fluent User's Guide, Fluent, Lebanon, NH), using the

segregated solver. The semi-implicit SIMPLEC algorithm is used as the pressure-velocity coupling scheme.

Convergence is achieved when the scaled residual is decreased to 5×10^{-5} in this study. The scaled residual for the continuity equation is the total absolute rate of mass creation in all the computational cells divided by its maximum value obtained in the first five iterations. For the Navier-Stokes equation, the residual for the FLUENT's segregated solver is defined as the imbalance in the momentum conservation equation for each discretized cell, summed over all the computational cells.

Although there is no Courant stability restriction on the time-step size due to the use of a fully implicit scheme by segregated solver, in order to fully exploit the transient phenomena, the time-step is chosen to be as small as 0.01s, and the results are recorded at the end of each time-step. Besides, in order to eliminate the start-up effects of transient flow, the computation is carried out for 5 periods, and the fifth period results are presented.

3.6 Simulation results

3.6.1 Flow behavior and patterns at the symmetry plane

The flow field in all the three base models is studied at 12 instants of time (as shown on the waveform in Figure 3.4), and the velocity vectors and streamlines are presented in Figures 3.5 to 3.28, wherein the new SQA design, parallel STS, and conventional ETS models are labeled as (a), (b), and (c), respectively.

3.6.1.1 Acceleration phase

As the flow accelerates from t_1 to t_3 (the peak flow rate), in the conventional ETS anastomosis model, a vortex forms at the heel region, with a stagnation point on the artery floor moving from $x=0.050\text{m}$ to $x=0.052\text{m}$ due to the graft flow impacting the artery bed, as shown in Figures 3.5 to 3.10. However, in the new SQA model (Panel (a) of the figures), the flow at the distal ETS anastomosis is very smooth without any vortex formation; and there is no impingement on the artery floor. This is because the partial flow from the STS anastomosis along the coronary artery changes the velocity components of the ETS anastomosis flow toward the toe and the coronary artery axis rather than to the artery floor. This results in having no stagnation point formed on the bed.

At the STS anastomosis of the new SQA model (Panel (a)), a vortex forms at the heel region along with a stagnation point on the artery bed, due to the interaction of the flow from the graft with the relatively slow flow in the occluded proximal segment of the host artery. This is consistent with the parallel STS anastomosis model (Panel (b)); Bonert et al. [17] have also shown similar results. At the peak flow rate (t_3) in the new design, 11% of the graft flow goes through the STS anastomosis, and 89% of that passes through the ETS anastomosis. The diversion of 11% of graft flow into the coronary artery at the STS anastomosis has the effect of smoothing the flow at the distal ETS anastomosis.

Figure 3.5: Velocity vectors at the symmetry plane of the base models at time $t_1=0.03s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model

Figure 3.6: Flow streamlines at the symmetry plane of the base models at time $t_1=0.03s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.7: Velocity vectors at the symmetry plane of the base models at time $t_2=0.06s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.8: Flow streamlines at the symmetry plane of the base models at time $t_2=0.06s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. A vortex forms at the heel region with a stagnation point on the artery bed of the anastomoses with occluded proximal segment.

Figure 3.9: Velocity vectors at the symmetry plane of the base models at time $t_3=0.13s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.10: Flow streamlines at the symmetry plane of the base models at time $t_3=0.13s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. Strong impact on the artery floor in the conventional ETS anastomosis at the peak flow rate.

3.6.1.2 Deceleration and reversed flow phases

As the flow decelerates, as shown in Figure 3.12 at $t_4=0.26s$, each of the above mentioned vortices initially split into two, and with further deceleration of flow (at t_5) they merge into one larger vortex, stretched towards the center of the anastomosis as demonstrated in Figure 3.14, while the overall flow field in general does not change considerably. However, at the first valley of the velocity cycle (t_6), partial recirculation and backflow appear in the graft in all the models, particularly at the inner wall of the graft curvatures where the blood flow has low inertia, and exhibits oscillatory characteristics, as shown in Figures 3.15 and 3.16. At this time (t_6), the blood near the heel of the ETS anastomosis of the new design flows back along the graft inner wall to about 2 graft diameters in length, and into the coronary artery in between the two anastomoses. The backflow is so strong that not only is there no flow from the graft into the coronary artery at the STS anastomosis, but there is partial flow from the coronary artery into the graft towards the ETS anastomosis. Comparing the ETS anastomosis of the new design with the conventional ETS anastomosis, it is observed that the vortex of the latter model is broken into two and increased in size. The bigger vortex at the conventional ETS model has shifted further downstream to cover the whole heel region and occupy part of the graft. Yet, all these are not found in the new design.

On the other hand, at the heel of the parallel STS anastomosis, the original vortex has been split into two with the bigger vortex shifted further downstream, covering about 60% of the anastomosis; but, flow from the graft to the artery can be observed. Comparison of the STS anastomosis of the new design with the parallel STS anastomosis demonstrates that the backflow in the coronary artery of the new design reduces the size of the vortex at the STS

anastomosis remarkably and shifts it up to the center of the anastomosis, eliminating the stagnation point on the artery bed as demonstrated in Figure 3.16(a).

During the second (diastolic) acceleration phase (t_7 and t_8), the flow field and streamlines are exactly the same as the first (systolic) acceleration phase (t_1 to t_3), and also throughout the early diastolic deceleration phase (t_9 and t_{10}) the flow field and streamlines are similar to the time interval from t_4 to t_6 (systolic deceleration phase) as long as the net flow rate is positive (forward net flow), as demonstrated in Figures 3.17 to 3.24.

Figure 3.11: Velocity vectors at the symmetry plane of the base models at time $t_4=0.26$ s, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.12: Flow streamlines at the symmetry plane of the base models at time $t_4=0.26$ s, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. Each vortex splits into two at this time instant in all the models.

Figure 3.13: Velocity vectors at the symmetry plane of the base models at time $t_5=0.28s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.14: Flow streamlines at the symmetry plane of the base models at time $t_5=0.28s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. The two vortices are merged into a large vortex at this time instant in all the models.

Figure 3.15: Velocity vectors at the symmetry plane of the base models at time $t_6=0.32s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. No flow from the graft into the coronary artery at the STS anastomosis of the new SQA model.

Figure 3.16: Flow streamlines at the symmetry plane of the base models at time $t_6=0.32s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. Partial recirculation and backflow appear in all the models. The size of the vortex at the STS anastomosis of the new design is reduced due to the backflow from the ETS component along the coronary artery.

Figure 3.17: Velocity vectors at the symmetry plane of the base models at time $t_7=0.37s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.18: Flow streamlines at the symmetry plane of the base models at time $t_7=0.37s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.19: Velocity vectors at the symmetry plane of the base models at time $t_8=0.45s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.20: Flow streamlines at the symmetry plane of the base models at time $t_8=0.45s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. A vortex forms at the heel region with a stagnation point on the artery bed of the anastomoses with occluded proximal segment.

Figure 3.21: Velocity vectors at the symmetry plane of the base models at time $t_9=0.76s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.22: Flow streamlines at the symmetry plane of the base models at time $t_9=0.76s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.23: Velocity vectors at the symmetry plane of the base models at time $t_{10}=0.81s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

Figure 3.24: Flow streamlines at the symmetry plane of the base models at time $t_{10}=0.81s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model.

As the net flow rate just becomes negative (t_{11}), the blood flows back towards the aorta through the graft at near wall regions, while it still flows forward at the central regions near the graft axis, as shown in Figure 3.25. This is due to the high inertia of the fluid in the central region compared to the fluid near the wall having low inertia, as a result of the friction between the layers of the fluid within the boundary layer. At this time instant (t_{11}), there are large vortices and recirculation areas in all the models. At the ETS anastomosis of the new SQA model, there is a vortex at the graft inner wall, upstream of the distal anastomosis as shown in Figure 3.26(a). However, in the conventional ETS anastomosis (Figure 3.26(c)), the vortex is much larger and occupies most of the anastomosis region and half of the graft near the inner wall. In the parallel STS anastomosis model (Figure 3.26(b)), a large vortex occupies the entire anastomosis region. On the other hand, in the STS anastomosis of the new SQA model, the size of the vortex is remarkably reduced and shifted over the toe of the anastomosis. This is due to the blood flow from the ETS component circulating within the vascular loop of the new SQA model, which eliminates the stagnation point on the artery bed as illustrated in Figure 3.26(a).

At the peak reversed flow (t_{12}), the vortex at the heel region of the conventional ETS anastomosis shifts into the occluded proximal segment of the coronary artery. Although there is no vortex at the ETS anastomosis of the new design, a stagnation point is formed at the heel region where the backward flow bifurcates into the graft and the coronary artery as shown in Figure 3.28(a). At the STS anastomosis of the new design, the flow field is a bit smoother than that of the parallel STS anastomosis where the blood flows back from the graft with a small dip at the anastomosis and then flows passing the heel towards the aorta

(Figure 3.28(b)). At this time instant in the new design, 68% of the flow passes through the ETS anastomosis and the rest 32% flows through the coronary artery merging at the STS anastomosis towards aorta.

Figure 3.25: Velocity vectors at the symmetry plane of the base models at time $t_{11}=0.84s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. At this time instant in all the models, the blood flows back towards the aorta through the graft at near wall regions, while it still flows forward at the central regions near the graft axis, due to the high inertia of the fluid in the central region compared to the fluid near the wall having low inertia.

Figure 3.26: Flow streamlines at the symmetry plane of the base models at time $t_{11}=0.84s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. Large vortices are formed in the anastomotic region of the conventional ETS and parallel STS models. The corresponding vortices in the new SQA model are reduced in size and shifted over the heel of the ETS and toe of the STS anastomoses, respectively, due to the flow circulation in the vascular loop of the new design model.

Figure 3.27: Velocity vectors at the symmetry plane of the base models at time $t_{12}=0.87s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. At this time instant in the heel region of the new SQA design model, the backward flow bifurcates into the graft and the coronary artery with the percentage ratio of 68% and 32%, respectively, merging at the STS anastomosis towards aorta.

Figure 3.28: Flow streamlines at the symmetry plane of the base models at time $t_{12}=0.87s$, (a) new SQA design model, (b) parallel side-to-side model, (c) conventional ETS model. The backflow from the coronary artery at the STS component of the new design smoothens the flow field in this region compared to that in the parallel STS model.

3.6.2 Hemodynamic parameters distribution

It has been shown that (i) localized distribution of low-WSS and high-OSI strongly correlates with the focal locations of atheroma [68], (ii) large spatial WSSG contributes to the elevated wall permeability and atherosclerotic lesions [38], and (iii) prevailing development of these lesions and growth of plaque formation occur in regions of extreme (either maxima or minima) WSS [91, 157]. Hence, in this study, the distributions of HPs, including OSI [68], time-averaged WSS (TAWSS), and non-dimensional TAWSSG [21], are calculated according to their expressions in Equations (2.1), (3.10), and (3.11), respectively, and compared in all the models.

$$TAWSS = \frac{1}{T} \int_0^T |\vec{\tau}_w| dt \quad (3.10)$$

$$TAWSSG = \frac{D_G}{\tau_0} \frac{1}{T} \int_0^T \sqrt{\left(\frac{\partial \tau_x}{\partial x}\right)^2 + \left(\frac{\partial \tau_y}{\partial y}\right)^2 + \left(\frac{\partial \tau_z}{\partial z}\right)^2} dt \quad (3.11)$$

where τ_0 is the WSS for Poiseuille flow at the mean flow Reynolds number, which is calculated as 0.48Pa for the present study. The contours of the abovementioned HPs are presented in Figures 3.29 to 3.31, respectively.

In order to compare the distribution of HPs quantitatively at the critical sites of the anastomosis such as the toe, heel, bed, and suture-line (see Figure 3.32), the segmental averages of the HPs are calculated and listed in Table 3.2. In this table, the above mentioned calculated parameters are also presented for a few more studied models, which will be introduced later in the following sections.

Figure 3.29: TAWSS distribution at the anastomotic regions of the base models.

Figure 3.30: TAWSSG distribution at the anastomotic regions of the base models. Qualitative distribution of TAWSSG is the same in all the models, with larger high-TAWSSG area in the parallel STS model than in the STS component of the new design.

Figure 3.31: OSI distribution at the anastomotic regions of the base models. The OSI is generally low, due to the flow having mostly a forward direction within the cycle.

Figure 3.32: Critical regions of ETS and STS anastomoses, which are the susceptible sites of IH and atherosclerotic lesion formation: 1,5. Suture line, 2,6. Toe, 3,7. Heel, 4,8. Bed

Table 3.2: Comparison of segmental average of <HP>s in models with fully occluded host artery.

ETS anastomotic angle:			30°			45°			60°		
Model		Location	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>
Conventional ETS model*		1- Suture line	0.03	2.59	20.1	0.02	3.08	44.8	0.02	3.49	64.4
		2- Toe	0.01	6.37	40.1	0.01	6.37	74.2	0.01	6.87	111.4
		3- Heel	0.07	0.54	7.0	0.05	0.59	9.0	0.05	0.63	10.7
		4- Bed	0.12	1.42	5.0	0.11	1.40	7.5	0.10	1.39	9.8
New design model with d=30mm	ETS component	1- Suture line	0.02	2.59	17.5	0.02	3.05	40.5	0.02	3.43	57.8
		2- Toe	0.01	6.40	40.7	0.01	6.43	78.6	0.01	6.91	109.4
		3- Heel	0.05	0.53	4.7	0.05	0.56	6.6	0.05	0.57	7.0
		4- Bed	0.05	1.60	4.1	0.05	1.63	6.2	0.05	1.66	7.6
	STS component	5- Suture line-sts	0.05	0.66	11.5	0.04	0.63	10.6	0.05	0.67	13.3
		6- Toe-sts	0.04	0.66	10.5	0.04	0.65	11.2	0.04	0.65	10.2
		7- Heel-sts	0.07	0.43	5.8	0.07	0.43	6.6	0.07	0.43	6.3
		8- Bed-sts	0.21	0.17	0.4	0.20	0.18	0.4	0.20	0.18	0.4
New design model with d=20mm	ETS component	1- Suture line	0.02	2.58	21.5	0.02	3.05	40.2	0.02	3.43	57.6
		2- Toe	0.01	6.40	55.9	0.01	6.44	79.0	0.01	6.21	87.3
		3- Heel	0.05	0.53	5.3	0.05	0.55	6.2	0.05	0.57	6.9
		4- Bed	0.05	1.62	4.3	0.05	1.65	6.4	0.05	1.68	7.6
	STS component	5- Suture line-sts	0.04	0.64	11.0	0.04	0.64	11.1	0.04	0.65	10.6
		6- Toe-sts	0.03	0.66	11.9	0.03	0.66	12.1	0.03	0.66	10.9
		7- Heel-sts	0.07	0.43	6.8	0.07	0.43	6.8	0.07	0.43	6.3
		8- Bed-sts	0.20	0.18	0.4	0.20	0.19	0.4	0.19	0.19	0.5
Non-planar new design model (with diamond STS component and d=20mm)	ETS component	1- Suture line	0.02	2.58	18.9	Isolated STS models					
		2- Toe	0.01	6.38	43.4						
		3- Heel	0.05	0.54	4.7						
		4- Bed	0.05	1.63	4.2						
	STS component	5- Suture line-sts	0.09	0.49	9.4	0.05	0.68	1.9	0.03	0.69	14.0
		6- Toe-sts	-	-	-	-	-	-	0.01	0.76	15.6
		7- Heel-sts	-	-	-	-	-	-	0.07	0.44	6.7
		8- Bed-sts	0.09	0.23	1.3	0.03	0.35	0.4	0.15	0.24	0.6

* Reference models

3.6.2.1 TAWSS

General distribution of TAWSS is qualitatively the same at the ETS anastomoses of the new design and the conventional ETS anastomosis model, as shown in Figure 3.29. However, at the STS anastomosis region of the new design, the maximum TAWSS on the host artery wall happens near the toe region, while TAWSS is increasing along the artery wall from the heel to the toe of the parallel STS model, except for a small low-TAWSS region at the top surface of the coronary artery. The maximum TAWSS is higher in the parallel STS model and is located at the toe of the STS anastomosis as compared to that of the new design.

As shown in Table 3.2 for the base models (with anastomotic angle of 45° and $d=30\text{mm}$), TAWSS is increased on the artery bed of the ETS anastomosis of the new SQA model to 1.63Pa, from 1.40Pa in the conventional ETS model. The TAWSS in the STS anastomoses is generally low, with its peak located at the toe; the TAWSS is lower in the STS component of the new SQA model than in the parallel STS model.

3.6.2.2 TAWSSG

TAWSSG distributions at both the ETS and STS components of the new design are qualitatively the same as those in the conventional ETS and parallel STS anastomosis models, respectively, as shown in Figure 3.30. Nevertheless, the high-TAWSSG area is larger in the parallel STS anastomosis.

As shown in Table 3.2, TAWSSG at the heel and bed of the ETS component as well as at the toe and suture-line of the STS component of the new SQA model is reduced, compared

to the conventional ETS and parallel STS anastomoses, respectively. This manifests a more uniform distribution of WSS in the new SQA design at these critical locations, which can lessen the vessel wall permeability and the probability of atherosclerotic lesion development.

3.6.2.3 OSI

The OSI at the ETS anastomosis of the new SQA model is lower on the artery wall and bed opposite to the heel, than in the conventional ETS anastomosis model (0.05 versus 0.11), as demonstrated in Figure 3.31 and Table 3.2 for the base models.

As shown in Figure 3.31, the OSI is generally low within the graft, due to the flow having mostly a forward direction within the cycle; yet, there is a high-OSI area on the artery bed and wall just distal to the heel of the STS anastomosis, due to the vortex forming there and the moving stagnation point. The OSI is also high at the occluded segment of the host artery; but, this is due to the very small mean WSS in this area rather than due to large changes in WSS over the cardiac cycle as reported by Bonert et al. [17]. The OSI distribution in the segment of the coronary artery between the two anastomoses of the new SQA model differs from that of the distal segment of the coronary artery in the parallel STS anastomosis model. In this segment, the OSI value increases up to 0.15 in the new design, while it is below 0.05 in the parallel STS model. This increase in OSI can be due to the circulation of blood flow in the vascular loop in the new design. At the STS anastomosis region of the new SQA model and in the parallel STS model, the OSI distribution is almost the same in the graft, at the heel, and the proximal part of the artery wall, as shown in Figure 3.31 and Table 3.2.

However, the OSI is increased on the artery bed and at the toe of the STS component of the new design compared to those of the parallel STS model (from 0.15 and 0.01 to 0.20 and 0.04, respectively).

3.6.3 Effects of the design parameters on hemodynamic parameters distribution

There are two types of parameters involved in the design of the suggested configuration. One group of parameters can be controlled by the surgeon such as the anastomotic angle at the ETS component, and the distance between the two anastomoses (d), albeit there are anatomical restrictions. The other group of parameters cannot be controlled, while they are different from one patient to another, such as the diameter of the SV and coronary arteries, and the percentage and location of stenosis; the latter can result in having parallel configuration (where the graft and host artery centerlines are approximately in plane) or diamond configuration (where the centerlines of the host artery and graft cross at approximately 90°) at the STS component.

3.6.3.1 Adjustable parameters

In order to obtain a better flow field and HP distributions, a number of models are simulated for a range of the adjustable parameters, involving anastomotic angle (of 30, 45, and 60 degrees) at the ETS component and the distance ($d = 20$ and 30mm) between the two (STS and ETS) components of the new design. Comprehensive information of the flow regime dependence on the design parameters (including the graft and coronary artery diameter) can enable tailoring an optimal design for a specific patient.

3.6.3.2 Non-planar model

In order to verify the advantage of the suggested design for the left coronary artery (LCA) bypasses (where the graft and coronary arteries cannot be assumed to be in the same plane), a non-planar model with a diamond configuration at the STS component is studied, whose TAWSS contour is illustrated in Figure 3.33.

Figure 3.33: TAWSS distribution in the non-planar model. TAWSS is low in the graft and proximal segments of the coronary artery, and it is increased at the ETS component and downstream of the coronary artery, with its peak occurring at the toe of the ETS anastomosis.

3.6.3.3 Variation in occlusion ratio

Anastomosis models with different percentages of coronary artery stenosis are simulated in order to evaluate the performance of the new SQA graft design in the early post-operative stage. It is well known that during the first weeks following grafting (at least until two weeks [14]) a non-negligible residual flow remains through the stenosed host artery, which will progressively decrease until the stenosed vessel is completely occluded [86]. Hence,

anastomosis models with two stenosis severity of 75% and 91% (equivalent to 50% and 70% diameter stenosis, respectively) are investigated in this study. For this purpose, an axisymmetric stenosis with a Gaussian profile [159] is considered to be located 6mm upstream from the heel in the models (with the ETS anastomotic angle of 30° and $d=30\text{mm}$). At the coronary artery inlet, Berne and Levy [13] flow waveform (shown by the red line in Figure 3.34) is imposed. According to Speziale [164] who indicated that the flow rate in an internal thoracic artery graft increases with progressing stenosis of the native coronary artery, the distribution percentage of the flow rates issued from the graft and stenosed coronary artery are allocated to be 75 versus 25 and 91 versus 9 in the two studied cases, respectively, to simulate the progressive decrease of residual blood flow from a constricted host artery following the bypass surgery.

Figure 3.34: (a) The OSI distribution of the new SQA model with stenosis severity of 75%: a high-OSI region observed distal to the narrowing due to the presence of a vortex tube and a moving stagnation ring, wrapping the vessel (b) Flow streamlines and contour of velocity magnitude at the symmetry plane of the model at $t=0.09\text{s}$: the cross-section of the vortex tube is illustrated; the graft and coronary artery waveforms are shown in blue and red, respectively.

The segmental averages of the calculated HPs for the studied models with (i) fully occluded and (ii) partially stenosed coronary arteries are, respectively, presented in Table 3.2 and Table 3.3.

Table 3.3: Comparison of segmental average of <HP>s in models with partially occluded host artery and ETS anastomotic angle of 30°.

Occlusion ratio:			75%			91%		
Model		Location	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>
Conventional ETS model*		1- Suture line	0.01	2.29	12.4	0.02	2.35	15.0
		2- Toe	0.004	5.59	28.8	0.01	5.78	29.8
		3- Heel	0.03	0.56	4.4	0.04	0.49	5.8
		4- Bed	0.003	1.55	3.5	0.02	1.32	4.0
New design model with d=30mm	ETS component	1- Suture line	0.01	2.25	12.9	0.02	2.34	13.6
		2- Toe	0.004	5.57	28.6	0.01	5.80	30.1
		3- Heel	0.04	0.47	4.0	0.05	0.49	4.4
		4- Bed	0.04	1.39	3.6	0.05	1.46	3.7
	STS component	5- Suture line-sts	0.02	0.64	7.2	0.04	0.60	8.0
		6- Toe-sts	0.03	0.52	5.4	0.04	0.59	7.4
		7- Heel-sts	0.02	0.52	4.4	0.03	0.41	4.1
		8- Bed-sts	0.03	0.38	0.4	0.11	0.18	0.3
Parallel STS model*		1- Suture line	0.01	0.93	16.5	0.02	0.67	10.5
		2- Toe	0.01	0.85	20.8	0.01	0.75	14.4
		3- Heel	0.02	0.52	4.9	0.03	0.41	4.7
		4- Bed	0.005	0.69	1.1	0.05	0.32	0.7

* Reference models

3.6.3.4 Inferences drawn from the results in Tables 3.2 and 3.3:

The following can be inferred from the results in Tables 3.2 and 3.3:

From Table 3.2, comparison of the conventional ETS models with different anastomotic angles indicates that the TAWSSG is considerably increased with the anastomotic angle, while the TAWSS is marginally increased (except on the artery bed where it is slightly decreased), and the OSI is almost remained constant. Therefore, a smaller anastomotic angle results in a more favorable HP distribution. This is in agreement with the results reported by Fei et al. [46] who studied the flow in distal ETS anastomoses with anastomotic angles of 20, 30, 40, 45, 50, 60 and 70 degrees, and suggested that grafts should be placed with a minimal distal anastomotic angle.

Comparing the six planar SQA design models:

As shown in Table 3.2, when the anastomotic angle is changed from 30° to 60°, the TAWSSG is drastically increased mainly at the toe and suture-line of the ETS component (by 169 and 230%, respectively), while generally the TAWSS is negligibly increased (8 and 32%, respectively) and OSI is not changed. This implies that the TAWSSG is the overriding factor in the selection of the preferred anastomotic angle, which makes the case for the smaller anastomotic angle for the new design.

A change in the distance between the two components (d), has affected the TAWSSG mainly at the toe of the ETS component, with a different trend in each model depending on the anastomotic angle. A decrease in d (from 30mm to 20mm), has caused the TAWSSG

(primarily at the toe) to (i) increase in the model with the anastomotic angle of 30° , (ii) decrease in the model with the anastomotic angle of 60° , and (iii) stay almost unchanged in the model with the anastomotic angle of 45° .

Neither the anastomotic angle, nor the distance between the two components has any obvious effect on the HP distribution at the STS component of the new design.

The non-planar model with a diamond configuration at the STS component (with ETS anastomotic angle of 30° and $d=20\text{mm}$):

This non-planar model (whose TAWSS contour is illustrated in Figure 3.33) depicts a lower TAWSSG distribution at the ETS component than the corresponding planar model, as shown in Table 3.2. On the artery bed of the STS component of this non-planar model, while the TAWSS and TAWSSG are slightly increased (to 0.23 and 1.3 from 0.18 and 0.4, respectively), the OSI is reduced to half (from 0.2 to 0.09) as compared to that of the corresponding planar model; this is beneficial to prevent the coincidence of low-WSS and high-OSI on the bed. However, on the suture-line of the STS component of the non-planar model, the OSI becomes almost double (from 0.04 to 0.09), while TAWSS and TAWSSG are slightly decreased (from 0.64 and 11 to 0.49 and 9.4, respectively) compared to the corresponding planar model. In addition, the segmental average of TAWSSG on the graft wall across the STS anastomosis of the non-planar model is calculated and found to be increased to 1.6 from 1.0 in the corresponding planar model (these latter values are not given in Table 3.2).

This is in agreement with the results reported by Bonert et al. [17], who demonstrated that the parallel configuration is more favorable than the diamond configuration for maintaining the graft patency at the STS anastomosis, while the diamond one is favorable for maintaining the host artery patency. Since graft patency is vital for the STS anastomosis of the new design, this design can be more beneficially applicable for the right CABG, wherein the graft and the coronary artery are approximately in the same plane. This fact is further proven by comparing the HP distributions in the STS component of the non-planar SQA model with the isolated diamond STS model, where all the HP distributions are more favorable both on the suture-line and bed of the anastomosis, as shown in Table 3.2.

The models with partially stenosed coronary arteries:

Comparison of the STS component of each new design model with the corresponding parallel STS model (in Table 3.3) indicates that the suggested SQA design configuration affects the distribution of HPs at the STS anastomosis of the partially occluded models with exactly the same trend as in the fully occluded models.

Comparison of the ETS component of each new design model with the corresponding conventional ETS model (in Table 3.3) indicates that in the case of 91% stenosed coronary artery, the change in the TAWSSG and TAWSS distributions due to the new design configuration has the same trend as in the fully stenosed models. Yet, it does not hold for the OSI at the heel and on the bed of the coronary artery.

In the case of 75% stenosed coronary artery, none of the advantages which were observed in the distribution of HPs in the fully occluded and 91% stenosed models of the new design are present anymore. The TAWSSG on the bed and suture-line, and the TAWSS and OSI on the heel and bed of the ETS component of the new design are inferior compared to those of the corresponding conventional ETS model.

This suggests that if the occlusion percentage of the stenosed artery is below a certain level, the overall advantages of the new configuration might be affected during the first few days following the bypass surgery, due to the competitive flows problem. This is in agreement with the results of the earlier studies [44, 55, 187, 191], which have confirmed the existence of a critical value for stenosis severity, below which the graft failure is expected, and above that, the recipient artery will be progressively occluded.

3.6.3.5 Summary

The effects of the above studied parameters can be summarized as follows:

Comparison of each new SQA model with the corresponding conventional ETS model depicts that in all the new design models the HP distribution is improved on the bed, heel, and (in most of the models) suture-line of the ETS component.

The variation of the design parameters of the new SQA graft design demonstrates that the combination of a smaller anastomotic angle at the ETS component and a longer distance between the two components results in a better flow field and distribution of HPs. Yet, there

are restrictions which inhibit surgeons from implementing a very acute anastomotic angle and adopting a long distance between the two components practically. Although some innovative suturing methods are proposed to obtain an acute anastomotic angle using prosthetic grafts [65], it is impractical in the standard clinical practice to perform a very small anastomotic angle due to the large cross sectional area of the graft section resulted in such an anastomosis.

Moreover, the lengths of coronary arteries are limited: the LAD coronary artery measures from 10 to 13cm in length, whereas the LCx artery measures about 6 to 8cm, and the dominant RCA is about 12 to 14cm in length [180]. Therefore, taking into account the length of the coronary artery, located proximal to the stenosis, plus the distance of grafting (required distance between the stenosis and the STS anastomosis), in addition to the lengths of the two anastomoses of the new SQA design, there would be a restricted length of the coronary artery left to be adopted as the distance between the two STS and ETS components of the new graft design practically.

Hence, in this study, the minimum anastomotic angle and maximum distance between the two components are adopted to be 30° and 30mm, respectively, which result in a better flow field and distribution of HPs than the other models investigated.

The simulation results for the models with partially stenosed coronary arteries further confirm the existence of a critical value for stenosis severity, below which graft failure is expected due to the competitive flows problem. Note that the effect of the partial flow

through the coronary artery is only studied on the models with anastomotic angle of 30° and $d=30\text{mm}$, whose results are shown to be the most favorable amongst the investigated models.

3.7 Discussion

In this chapter, a new SQA model design for the distal CABG anastomoses is suggested based on the advantageous flow characteristics observed within the STS anastomosis in sequential bypass grafts. The flow fields and HPs are studied within the model, and compared to those of the conventional ETS distal anastomosis by means of CFD simulation. Finally, sensitivity analysis for the suggested SQA design is conducted by simulation and comparison of several models within the physiological range of the parameters involved.

3.7.1 Evaluation of model assumptions, methods and limitations

The effects of the elasticity of the vessel walls and FSI and non-Newtonian rheology of blood are not yet investigated at this stage of the study.

The wall motion is ignored in this investigation, as it is shown that the motion of the RCA has minor effect on TAWSS patterns, and hemodynamic aspects of the cardiac motion are dominated by the effects of flow pulsatility [195]. In addition, it is indicated that the use of a static geometry to predict the mean wall shear rates would yield reasonably accurate results and the dynamic behavior is not significant at the base cardiac frequency of 1Hz [151].

3.7.2 Evaluation of results: novelty and features of the coupled STS-ETS graft design

In the new design, during the acceleration and early deceleration phases, part of the graft flow is diverted into the coronary artery at the STS anastomosis. When this flow in the coronary artery reaches the ETS anastomosis, it lifts up the flow coming from the graft and helps to direct the graft flow smoothly into the coronary artery, as shown in Figures 3.5 to 3.14. Thereby, there is no impact on the artery bed. It is to be borne in mind that the impact on the floor is believed to be a contributing factor to the graft failure, since Bates et al. [12] have shown evidence of the change in the flow character once it has impacted against the junction floor. Hence, having a smoothened flow and no impact on the floor of the coronary artery is a positive feature of the new SQA CABG design.

In the new SQA design, the stagnation point is vanished at either one or both of the ETS and STS anastomoses at different time intervals compared to the conventional ETS and parallel STS anastomoses. Stagnation point is always associated with a low WSS and high spatial WSSG region, contributing to IT and atherosclerosis development and increasing the risk of the aggregation of red blood cells. Hence, the absence of stagnation point is another positive feature of the coupled SQA design.

In the new SQA design, there is no vortex formed at the heel of the ETS anastomosis within the coronary artery, resulting in a relatively higher WSS along the artery walls and bed. The presence of a vortex increases the local particle residence time which is associated with sites of IH development [11, 161, 185] and may result in platelet activation [76] and fibrin

thrombus formation [53, 145]. The absence of vortex formation is also a positive feature of the coupled STS-ETS graft design.

In the planar new SQA design, the HPs are improved to some extent, especially at the heel and coronary artery bed of the ETS anastomosis, and at the toe and suture-line of the STS anastomosis of the new design, compared to the conventional ETS and parallel STS models, respectively, as shown in Table 3.2.

In the non-planar new SQA design, although the HP distribution is improved on the heel, bed, and suture-line of the ETS component compared to the conventional ETS model, the inferior distribution of HPs on the suture-line and in the graft (compared to isolated diamond STS model and the STS component of the corresponding planar SQA model, as shown in Table 3.2) makes the advantage of this new design debatable for a non-planar bypass grafting.

This new SQA design provides a spare route for the blood flow to the coronary artery in order to avoid re-operation in case of re-stenosis in either of the anastomoses. In case that re-stenosis happens first in the STS anastomosis of the (planar) new design, it is predicted that occlusion would occur within the coronary artery rather than in the graft, based on the low-WSS and high-OSI on the coronary artery wall and bed opposite to the heel of the STS anastomosis, as shown in Figures 3.29 and 3.31. Furthermore, it is demonstrated by Bonert et al. [17] that the parallel configuration is preferred for the graft patency. Therefore, in case of re-stenosis at the STS anastomosis of the (planar) new SQA design, the graft would be

still patent and the blood can still flow to the ETS anastomosis, eliminating the need for re-operation.

At the ETS anastomosis of the new SQA model, the flow field and distributions of HPs are generally improved at the heel region, the bed and wall of the coronary artery opposite to the heel (but not at the toe), as shown in Table 3.2. However, there is (i) a vortex formation along the graft inner wall at some time intervals, as illustrated in Figure 3.26, and (ii) a stagnation point at the heel, during the reversed flow, as shown in Figure 3.28. Hence, in case that re-stenosis happens first in the ETS anastomosis of the new SQA design, it is deemed that the occlusion would happen within the graft above the heel region stretched on the suture-line towards the toe of the ETS anastomosis (rather than in the coronary artery). Therefore, the passage for the blood flow would be still open through the STS anastomosis and the coronary artery, without the need for re-operation.

3.8 Conclusion

A novel CABG coupled-sequential anastomoses configuration is designed, and its flow fields and distributions of various WSS parameters are studied, and compared to those of the conventional distal anastomosis.

Although this design does involve one additional anastomosis (and prolonged operation time), some distinct advantages are observed in the flow field and distribution of HPs in this new coupled SQA design. Simulation results demonstrate that the new sequential anastomoses model provides: (i) a more uniform and smooth flow at the ETS anastomosis,

without any stagnation point on the artery bed and vortex formation in the heel region of the ETS anastomosis within the coronary artery; (ii) a spare route for the blood flow to the coronary artery, to avoid re-operation in case of re-stenosis in either of the anastomoses; and (iii) improved distribution of hemodynamic parameters at the coronary artery bed and in the heel region of the ETS anastomosis, with more moderate shear stress indices.

By investigating the effect of the partial flow through the proximal host artery in the case of partially stenosed coronary arteries, the results further confirm the existence of a critical value for stenosis severity, below which the distributions of HPs might be undesirably affected by the competitive flow problems.

Upon varying the new design parameters of the anastomotic angle and distance between the STS and ETS components, and comparing the out-of-plane design version with the in-plane design version, the superior design is found to be the planar SQA model with the anastomotic angle of 30° and distance of 30mm.

So now while an innovative CABG design is provided, its beneficial flow-simulation results would need to be validated by in vitro measurements, experimentally.

Chapter 4

4 In vitro measurements of velocity and WSS in the base models

In order to validate the beneficial flow-simulation results of the novel coupled SQA graft design, experimental measurements are conducted in vitro, using PIV technique. For this purpose, the flow fields inside the fabricated Polydimethylsiloxane (PDMS) replicas of the three base models, introduced earlier in the computational simulation study of Chapter 3, are measured and the resulting WSS is calculated accordingly, to be compared in different models, as well as with the computational simulation results.

4.1 Particle image velocimetry system

PIV is an optical measurement technique, allowing instantaneous acquisitions of an entire planar section of a flow field [143]. The PIV system used in this study, consists of a 15Hz Q-switched, double cavity pulsed Nd:YAG laser (Minilase-III, New Wave Research, USA) with an energy of 150mJ at a wavelength of 1064nm, producing a light sheet which is adjusted to illuminate the tracer particles in the symmetry plane of the models, as shown schematically in Figure 4.1.

Figure 4.1: Schematic view of the test rig and the flow circuit.

The particles' motion is recorded by means of a synchronized charge coupled device (CCD) Camera (FlowSense, Dantec Dynamics, Denmark), with a spatial resolution of 1600×1200 pixels, and a Nikon lens (AF Micro Nikkor, 60/2.8) positioned normal to the laser sheet.

4.2 Experimental setup

A schematic of the flow circuit is shown in Figure 4.1. In order to generate the physiological inlet flow waveform (shown earlier in Figure 3.4), a computer-controlled gear pump system (Micropump Inc., Vancouver WA USA) is used, including one varying-flow pump (Model HG0024-N23 PF1SGB1) and one steady-flow pump (Model HG0024-G050). Since each pump can only generate a unidirectional flow, the steady-flow pump is incorporated into the flow circuit in the opposite direction, in order to obtain the required bidirectional flow. A conical calming chamber is utilized to reduce the flow disturbances and obtain a uniform resultant flow from the two pumps. The flow rate is measured and monitored by means of an

electromagnetic flowmeter (Promag 53, Endress+Hauser, Germany) immediately upstream of the test section.

4.3 Model fabrication

The silicone rubber models of the three base anastomotic configurations are produced, using the method introduced by Chong et al. [29]. Briefly, an acrylic mould of the designed flow passage is fabricated by a computer numerical control (CNC) milling machine, and is used to make a low-melting point alloy cast (the alloy is made of Tin (13.3%), Lead (26.7%), Bismuth (50%), and Cadmium (10%)). The cast is then suspended in a rectangular acrylic container, using stainless steel connectors, and is immersed with a degassed mixture of silicone (Sylgard 184, Dow Corning) and curing agent. The mixture is left at $60\pm5^{\circ}\text{C}$ for 12 hours to cure. A replica of the flow passage in clear silicone (shown in Figure 4.2) is then obtained, after melting and removing the alloy cast by increasing the temperature to 105°C .

The physical models are bilateral symmetric with respect to the XZ plane, and the POS of the coronary artery is fully occluded during the experiment. In the parallel STS model, 15% of the blood flow is set to pass through the STS anastomosis into the coronary artery, and the remaining 85% is allowed to pass through the graft (on an average within each cardiac cycle), by adjusting the resistance at the outlets of the graft and coronary artery of this model. This flow division is adjusted to make the experimental flow condition consistent with that of the computational simulation.

Figure 4.2: Silicone rubber models of (a) the new coupled SQA graft design, (b) parallel STS, and (c) conventional ETS anastomosis, fabricated for this in vitro study.

4.4 Working fluid

A mixture of 30% glycerin and 70% sodium chloride (NaCl) solution by volume is used as the working fluid (blood analogue) in this study (the NaCl solution is made up of 1 part NaCl and 3 parts water by weight). The mixture's density is 1156kg/m^3 and its dynamic viscosity at the working temperature of 25°C is quantified by a controlled shear rate rheometer (Contraves low rate 40) to be $0.0054\text{Pa}\cdot\text{s}$ (5.4cP). The refractive index of the mixture is measured by a commercial refractometer (Atago 3T; High-Precision Model) to be 1.409, which matches that of the silicon elastomer models. This prevents any laser light refraction at the lumen walls of the models.

4.5 Tracer particles

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 [118]. Figure 4.3 demonstrates measurement uncertainty in digital cross-correlation PIV evaluation with respect to varying particle image diameter for single exposure/double frame PIV imaging. It reveals the existence of an optimum particle image diameter for digital PIV evaluation. This diameter is slightly more than 2 pixels (2.3 pixels for an interrogation area of 32×32 pixel) for the cross-correlation between two images [143].

Figure 4.3: Measurement uncertainty (RMS random error) in digital cross-correlation PIV evaluation with respect to varying particle image diameter for single exposure/double frame PIV imaging (taken from [143]).

The size of a particle image is determined by the particle diameter (d_p), the magnification coefficient (M), and the point response function of the lens. If the lens is diffraction limited, the point response function is an Airy function of diameter [2]:

$$d_s = 2.44(M+1)F\lambda \quad (4.1)$$

where F is the f-number of the camera lens, defined as the ratio between the focal length (f) and the aperture diameter (D_a), and λ is the wavelength of the laser sheet. Practically, this minimum image diameter (d_s) is only obtained when recording small particles (of the order of a few microns) at small magnifications. For larger particles and/or larger magnifications, the influence of geometric imaging becomes more dominant [143]. The image of a finite-diameter particle is given by the convolution of the point spread (Airy) function with the geometric image of the particle. Consequently, the particle image diameter (d_{image}) can be estimated by [3]:

$$d_{image} = \sqrt{(Md_p)^2 + d_s^2} \quad (4.2)$$

Magnification factor represents the ratio of the active area of the CCD camera to the physical linear size of the measurement area. The investigated area in the studied models is about $12 \times 9 \text{ mm}^2$, which is very close to the active area of the camera ($11.84 \times 8.88 \text{ mm}^2$). Consequently, M is about 1 ($0.95 < M < 1.05$) for different models in this study.

Therefore, in the present investigation, with $F=2.8$, $\lambda=1064 \text{ nm}$, $M=1$, and selecting $d_p=10 \mu\text{m}$, the particle image diameter is obtained as $d_{image}=17.65 \mu\text{m}$, which is equivalent to 2.38 pixels (as the pixel pitch is $d_{pitch} = \frac{11.84 \text{ mm}}{1600(\text{pixels})} = 7.4 \mu\text{m}$). This diameter is very near to the optimum particle image size of 2.3 pixels, shown in Figure 4.3. Hence, in this experiment, hollow glass spheres with mean diameter of $10 \mu\text{m}$, density of 1.1 g/cm^3 , and refractive index of 1.52 (HGS-10, Dantec Dynamics, Denmark) are used as tracer particles and seeded into the working fluid.

4.6 Statistical convergence and cyclic variation

The image acquisition in this phase-resolved PIV measurement is triggered by a Transistor-Transistor-Logic (TTL) signal (5V), generated by the gear pump interface unit, in order to phase-lock the measurements. The flow data are acquired at six different phase points in the flow cycle. For statistical convergence, 100 measurements are found to be sufficient for each time instant, in order to generate a stable velocity vector map.

There are no systematic tests to decide whether statistical convergence has been reached. In this study, however, the relative difference between two means with respect to the data set number of measurements, $\delta_{(n)}$, is calculated according to Equation (4.3), in order to determine the sample size N , necessary to achieve statistical convergence.

$$\delta_{(n)} = \left| \frac{\bar{\varphi}^{(n+1)} - \bar{\varphi}^{(n)}}{\bar{\varphi}^{(N)}} \right| \quad (4.3)$$

where $\bar{\varphi}^{(n)}$ is the computed average of the measured parameter φ , using n recordings of the data set ($\bar{\varphi}^{(n)} = \frac{1}{n} \sum_{i=1}^n \varphi_i$). The graphs for the measured parameters of velocity components, U_x and U_z , and velocity magnitude, $|U|$, are plotted in Figure 4.4. They suggest that convergence is ensured for these parameters with more than 80 recordings ($n \geq 80$), where the change in variables is less than 0.3% ($\delta \leq 0.003$) with more PIV measurements added.

As a measure of cyclic variation, the coefficient of variation (COV), defined as the ratio between the standard deviation and the mean, is calculated for the measured parameters U_x and U_z to be 0.14 and 0.2, respectively.

Figure 4.4: Convergence test of velocity components (a) U_x , (b) U_z , and (c) velocity magnitude $|U|$, passing from n samples to $n+1$ in the data set.

4.7 Pulse separation time

For an interrogation window side of length l_{int} , an adequate limit of $l_{int}/3$ have been found for recoverability of the displacement vector in digital cross-correlation PIV [189]. Consequently, the maximum particle image displacement on the CCD chip is recommended to be less than a quarter of the interrogation size, in order to ensure a reasonable SNR. This results in an upper limit threshold for the time interval between the two successive illumination pulses ($t_{separation}$) for each image pair:

$$t_{separation} < \frac{l_{int}}{4MV_p} = \frac{N_{int}d_{pitch}}{4MV_p} \quad (4.4)$$

where V_p is the particle velocity and N_{int} is the number of pixels on each interrogation window side ($N_{int}=32$ in this study). For the high and low velocity ranges of 0.5m/s and 0.05m/s in the present study, the corresponding threshold values are calculated to be 118 μ s and 1184 μ s, respectively. Hence, the pulse separation time for different phase points is set to values in the range of 100–500 μ s depending on the flow phase and the instantaneous velocity magnitude. Albeit, by using the adaptive correlation, the bond of $l_{int}/4$ for the particle displacement does no longer apply, and the pulse separation time can practically be somewhat longer than what corresponds to the 25% displacement of the final interrogation area (32 $\times$ 32 pixels in this study), but somewhat smaller than what corresponds to the 25% displacement of the initial interrogation (128 $\times$ 128 pixels in the present study) [152].

4.8 Processing of the data

4.8.1 Image processing

The recorded image pairs are pre-processed to remove background intensities and image noise (a masking of non-fluid regions with zero pixel value intensity is also performed to reduce the bias error originating from wall reflections) and are subsequently analyzed by a two-frame adaptive multi-grid cross-correlation algorithm with the final interrogation areas of 32 $\times$ 32 pixels, overlapped by 50% on each side, to yield the local displacement vector for each interrogation area, using DynamicStudio software (Version 2.20.18, Dantec Dynamics, Denmark). This method provides a total of 7326 velocity vectors for an area of 12 $\times$ 9mm².

4.8.2 Data post-processing (derivation of WSS)

The velocity field obtained by PIV is used to estimate the rate-of-shear ($\dot{\gamma}$) along the wall from the near-wall velocity gradient, and thereby the WSS, using Equation (4.5):

$$WSS = \mu \dot{\gamma} = \mu \frac{du_{\xi}}{d\eta} \quad (4.5)$$

where μ is the dynamic viscosity of the working fluid, u_{ξ} is the component of the velocity vector tangential to the wall, and η is the direction normal to the wall. The ξ - η wall-oriented coordinate system is utilized for the ease of calculation and presentation of the results. As shown in Figure 4.5, the origins of coordinates ξ_1 to ξ_3 are chosen on the heel, toe, and artery bed of the anastomosis, respectively.

Figure 4.5: The origin and direction of ξ - η coordinate system at (1) heel, (2) toe, and (3) artery bed of STS (left) and ETS (right) anastomoses.

The velocity gradient is estimated as the slope of a quadratic curve fit of the two near-wall velocity values [88, 116, 117]. For this purpose, a computer code is developed based on the finite element shape functions (see Appendix B), and is used to detect the near-wall velocities within the viscous boundary layer [45]. Briefly, the discrete pixel wall location for each data set is extracted (no wall movement is detected in this study); by marching on these wall points, the slope of each wall section, located between two neighboring wall points, is

calculated. Then, on the perpendicular bisector of each wall section, two points with an increment of 0.11mm (16 pixels) between the subsequent points are located within the flow boundary layer, and the tangential components of the velocity vectors (with respect to the corresponding wall section) are interpolated at these points based on the three nearest adjacent velocity vectors, using finite element shape functions. Subsequently, a quadratic curve is fitted to these data, assuming the no-slip condition at the wall. The obtained near-wall velocity profile function is then differentiated analytically, whose slope at the wall is determined as a measurement of the tangential shear rate component [88, 116, 117, 155].

The abovementioned WSS derivation method is first tested and compared for linear and quadratic curve fittings of the data with different numbers of near-wall points. Better results are obtained with a quadratic curve fitting (as compared with linear estimation), using two near-wall points, with errors of up to 32% as compared with the corresponding analytical results obtained for a fully-developed pulsatile flow in a straight tube. This is in agreement with Lou et al. [116] who indicated that the benefit of the extra point is doubtful as it forces the velocity profile to comply more with the data in the region farther away from the wall rather than with the data closer to the wall. Higher order polynomials are not tested since they have been reported to be generally less robust; because as the order of the curve fitting increases, the results become more sensitive to small amplitude errors, distributed in the data [116]. Hence, a quadratic curve fit of the two near-wall velocity values are used for wall shear rate calculation in this study.

4.9 Pre-validation of PIV measurements

In order to validate the accuracy and precision of the PIV measurements, a comparison is conducted between the PIV results for a fully developed sinusoidal flow ($Q = 140(1 + \sin(4.2t))$ ml/min) in a straight tube (with an inner diameter of 3mm) and the corresponding Womersley solution [190].

As shown in Figure 4.6, a good qualitative match is observed between the experimentally obtained and analytical velocity profiles at different phases of the flow cycle. The quantitative comparison of the results reveals an average relative difference of 8.6% in the velocity magnitude between the two sets of data. This reasonable discrepancy confirms that the accuracy of the PIV results is acceptable.

Figure 4.6: Comparison of the PIV measurement results with the analytical Womersley solution for a sinusoidal flow in a straight tube (a) for different phases of the flow cycle (b) up-scaled graph at $t/T=0.75$ for a better illustration of the velocity profile.

4.10 Results

4.10.1 Velocity profiles in the anastomotic region of the models

The velocity field in the symmetry plane is measured at the anastomotic region of the models, as shown in Figures 4.7 to 4.12, correspondingly, for the six instants of time, t_2 , t_3 , t_5 , t_6 , t_{11} , and t_{12} , wherein, the STS and ETS components of the new SQA design, parallel STS, and conventional ETS models are labeled as (a), (b), (c), and (d), respectively.

For the purpose of visualization, the velocity vectors obtained by a lower resolution (64×64 pixels) analysis are shown in these figures. However, for WSS calculation, the velocity fields of a higher resolution (32×32 pixels) are used, in order to attain a higher accuracy.

4.10.1.1 Acceleration phase

During the systolic mid-acceleration (t_2) and at the peak flow rate (t_3) in the conventional ETS anastomosis model, a vortex is formed at the heel region within the coronary artery, with a stagnation point on the artery floor at $\zeta_3=0.5\text{mm}$ and $\zeta_3=1.5\text{mm}$, respectively, due to the graft flow impinging on the artery bed, as shown in Figures 4.7(d) and 4.8(d), correspondingly. However, in the new SQA graft design model, the flow at the distal ETS anastomosis (Figures 4.7(b) and 4.8(b)) is very smooth without any vortex formation. There is no impingement on the artery floor, because the partial flow from the STS anastomosis along the coronary artery changes the velocity components of the ETS anastomosis flow toward the axis of the coronary artery rather than to the artery floor, as explained earlier in Chapter 3 for the corresponding simulation results.

At the STS anastomosis of the new SQA model (Figures 4.7(a) and 4.8(a)), a vortex is formed at the heel region along with a stagnation point on the artery bed. This is consistent with the flow field in the parallel STS anastomosis model (Figures 4.7(c) and 4.8(c)), and also with those of the earlier simulation results.

Figure 4.7: Measured flow field and velocity vectors in the anastomotic region of the models at systolic mid-acceleration (time t_2). (a) STS component of the SQA model, (b) ETS component of the SQA model, (c) parallel STS model, and (d) conventional ETS model. There is a vortex in the heel region of the conventional ETS model. However, in the ETS component of the SQA model, the flow is smooth without any vortex.

Figure 4.8: Measured flow field and velocity vectors in the anastomotic region of the models at the peak flow rate (time t_3). (a) STS component of the SQA model, (b) ETS component of the SQA model, (c) parallel STS model, and (d) conventional ETS model. Again, a vortex is present in the heel region of the conventional ETS model with the blood flow impacting the artery bed, whereas the flow at the ETS component of the SQA model is smooth and devoid of any vortex or impingement on the artery floor.

4.10.1.2 Deceleration and reversed flow phases

During the mid-deceleration phase of systole (t_5), the vortex at the heel region of the parallel STS model is increased in size (relative to that at the peak flow rate) and is stretched towards the center of the anastomosis, as demonstrated in Figure 4.9(c); however, there is a mild vortex on the artery floor at the STS component of the SQA model, as shown in Figure

4.9(a). At this time, the general flow field in the ETS anastomoses (Figure 4.9(b) and (d)) does not change remarkably, from that at the time of the peak flow.

Figure 4.9: Measured flow field and velocity vectors in the anastomotic region of the models at systolic mid-deceleration (time t_5). (a) STS component of the SQA model, (b) ETS component of the SQA model, (c) parallel STS model, and (d) conventional ETS model. Note the weak vortex in the STS component of the SQA design model versus the large vortex in the parallel STS model.

At time t_6 , the end of systole, partial backflow appears above the heel of the ETS anastomoses, at the inner wall of the graft curvature where the blood has lower inertia, and exhibits oscillatory flow characteristics due to the pulsatile nature of the graft waveform, as shown in Figure 4.10(b) and (d). At this time (t_6), the blood at the ETS anastomosis of the

new SQA model bifurcates into the distal part and into the proximal segment of the coronary artery toward the STS component. As described earlier for the simulation results, this backflow (from the ETS component through the coronary artery) prevents any flow from the graft into the coronary artery at the STS anastomosis of SQA model and causes some blood flowing from the coronary artery back into the graft toward the downstream ETS anastomosis, as demonstrated in Figure 4.10(a). At the heel of the conventional ETS anastomosis model, the fluid is flowing back into the proximal segment of the host artery (Figure 4.10(d)); this is different from the simulation results where two vortices are formed at the heel at this time instant. This can be attributable to the longer proximal section of the host artery (45mm) as compared to that of the computational model (10mm).

In the parallel STS model, illustrated in Figure 4.10(c), the vortex at the heel of the anastomosis further increases in size and covers about 70% of the anastomosis as the blood flows from the graft into the coronary artery. No backflow is observed in the graft above the parallel STS anastomosis, which is different from that of the computational results at this phase point. Comparison of the STS anastomosis of the new design (Figure 4.10(a)) with the parallel STS anastomosis (Figure 4.10(c)) demonstrates that in the new design the backflow from the ETS component into the coronary artery wipes out the vortex at the STS anastomosis, and thereby eliminates the stagnation point on the artery bed.

Figure 4.10: Measured flow field and velocity vectors in the anastomotic region of the models at time t_6 , the end of systole. (a) STS component of the SQA model, (b) ETS component of the SQA model, (c) parallel STS model, and (d) conventional ETS model. There is a large vortex in the parallel STS model. However, in the new SQA design model, the backflow into the coronary artery from the ETS component emerges into the STS component and eliminates the possibility of vortex formation within the coronary artery.

As the net flow rate just becomes negative (t_{11}), large vortices and recirculation areas appear in all the models. At the ETS anastomosis of the SQA model, two vortices form above the heel and toe, upstream of the distal anastomosis, and one within the coronary artery just distal to the anastomosis, as shown in Figure 4.11(b). However, in the conventional ETS anastomosis (Figure 4.11(d)), the two vortices are much larger in size, occupying most of the anastomotic region and the graft upstream of the anastomosis; however, the vortex in the coronary artery is smaller in size and located further downstream as compared to that in the

SQA model. At this time (t_{11}), the blood flows back towards the aorta through the graft at near-wall regions upstream of the anastomoses (except for the parallel STS model), while it still flows forward at the central regions near the graft axis.

In the parallel STS anastomosis model (Figure 4.11(c)), a large vortex occupies the entire anastomosis region. On the other hand, in the STS anastomosis of the SQA model, the vortex is almost negligent and is shifted over the toe of the anastomosis, as illustrated in Figure 4.11(a).

Figure 4.11: Measured flow field and velocity vectors in the anastomotic region of the models at time t_{11} , when the graft average velocity has just become negative. (a) STS component of the SQA model, (b) ETS component of the SQA model, (c) parallel STS model, and (d) conventional ETS model. Note the remarkably larger vortices in the conventional ETS and parallel STS models, compared to those in the corresponding ETS and STS components of the SQA design model.

At the peak reversed flow (t_{12}), although there is no particle residence at the ETS anastomosis of the new design, a stagnation point forms at the heel region ($\xi_1=0\text{mm}$) where the backward flow bifurcates into the graft and the coronary artery, as shown in Figure 4.12(b). At the STS anastomoses, the flow fields are almost the same in both the SQA design and parallel STS models, as demonstrated in Figure 4.12(a) and (c), respectively.

Figure 4.12: Measured flow field and velocity vectors in the anastomotic region of the models at the peak reversed flow (time t_{12}). (a) STS component of the SQA model, (b) ETS component of the SQA model, (c) parallel STS model, and (d) conventional ETS model. Note the presence of the stagnation point at the heel of the ETS anastomosis of the SQA model where the backward flow bifurcates between the graft and the coronary artery.

4.10.2 Local WSS in the models

The local WSS is evaluated at the heel, toe, and coronary artery bed of the anastomosis in all the models at the six time instants, and compared with that from the computational study, as shown in Figure 4.13 to Figure 4.16, wherein the WSS distributions at the heel, toe, and artery bed of the anastomosis are shown, respectively, in panels (a), (b), and (c). These graphs are also presented in Appendix C with a larger scale and less data in each figure for better readability.

4.10.2.1 Comparison of the WSS distribution in the anastomotic region of the 3 models

WSS distribution in the heel region of the ETS anastomoses: Upon comparing the WSS distribution in the heel region of the ETS component of the new design with that of the conventional ETS model (Figure 4.14(a) and Figure 4.16(a)), it is observed that the peak value of WSS is reduced on the graft inner wall of the new design as compared to the conventional ETS model (for instance from 1.3Pa to 0.8Pa at t_3). This is due to the lower flow rate passing through the graft toward ETS anastomosis in the SQA design compared to the conventional ETS model, since part of the flow is diverted into the coronary artery at the STS anastomosis of the new design. However, the WSS at the heel of the ETS anastomosis of the new SQA model within the coronary artery is considerably increased in magnitude compared to the conventional ETS model. This is because in the conventional ETS model, the blood is almost stagnant in the proximal segment of the coronary artery, while in the new design model the partial flow from the STS component through the coronary artery increases the absolute value of WSS at this location (note that the change in the sign of the WSS is due to the definition of the coordinate system at the heel region of the models). It is to be

borne in mind that the localized distribution of low WSS contributes to IT development. Hence, the WSS distribution is improved at the heel of the ETS component of the SQA model within the coronary artery.

WSS distribution in the toe region of the ETS anastomoses: At the toe of the ETS anastomosis of the SQA model and the conventional ETS model, the qualitative distribution of WSS is the same, as shown in Figure 4.14(b) and Figure 4.16(b). There is a sharp increase in the WSS magnitude to its peak at the toe, and then a rapid drop to form an apex, continued by a slow increase to an asymptotic value further downstream along the toe within the coronary artery during the high forward flow phases. With the increase of the graft Reynolds number (from t_2 to t_3), the peak value of the WSS at the toe is increasing from 10Pa and 9Pa to 20Pa and 16Pa, respectively, in the conventional ETS model and the ETS component of the new SQA model. This represents a more moderate distribution of WSS at the toe of the ETS component of the SQA model which can reduce the probability of atherosclerotic lesion development, since the main progress of atherosclerotic lesions and growth of plaque formation occurs in regions of extreme (either maxima or minima) WSS [91, 157]. While the experimental results do show a lower magnitude of peak WSS in the new design model, the simulation results for the two models match both qualitatively and quantitatively at this region.

WSS distribution on the coronary artery bed of the ETS anastomoses: On the coronary artery bed opposite to the heel of the ETS anastomosis ($-2\text{mm} \leq \xi_3 \leq 3\text{mm}$), the WSS is slightly higher in magnitude in the SQA model than that in the conventional ETS model, as

shown in Figure 4.14(c) and Figure 4.16(c), due to the blood flowing through the coronary artery segment between the two anastomoses of the novel SQA model, albeit the WSS magnitude is generally low in this region. This increase in the WSS magnitude, conjugated by the absence of the stagnation point on the artery bed in the ETS anastomosis of the SQA model (as mentioned earlier) can reduce the risk of IT and atherosclerosis development at this critical location. On moving downstream along the artery bed, the WSS magnitude increases, reaching its peak value opposite to the toe of the ETS anastomosis, as shown in Figure 4.14(c) and Figure 4.16(c), and then, reducing to an asymptotic value in both models (not shown here). These values of WSS at the downstream of the artery bed in the ETS anastomosis of both (the SQA and conventional ETS) models are higher than those along the toe of the anastomosis within the coronary artery, indicating that the flow is skewed toward the artery floor, inducing larger velocity gradients on the floor side.

WSS distribution in the heel region of the STS anastomoses: Upon comparing the distribution of WSS in the STS anastomosis of the new SQA model and the parallel STS model, shown respectively in Figure 4.13(a) and Figure 4.15(a), it is observed that at the heel region of the STS anastomosis of the two models, the qualitative distribution of the WSS is similar. However, at time t_{11} the WSS is positive (with respect to ξ_1 coordinate at the heel, shown in Figure 4.5) based on the experimental results obtained for the parallel STS model, which differs from the simulation results and that of the STS component of the new SQA model with negative WSS values. This is because there is no backflow present at the near-wall regions of the graft upstream of the STS anastomosis of the parallel STS model, as mentioned earlier.

WSS distribution in the toe region of the STS anastomoses: At the toe of the STS anastomosis of the two models, the distribution of WSS is about the same (for the experimental results). However, at time t_{11} , the magnitude of WSS on the graft and the coronary artery walls has different distributions in the two models, as demonstrated in Figure 4.13(b) and Figure 4.15(b). In the STS component of the new SQA model, due to the strong backflow through the coronary artery at this instant of time, the WSS magnitude is higher on the coronary artery wall at the toe of the anastomosis ($\xi_2 > 0\text{mm}$) than on the graft wall at the toe ($\xi_2 < 0\text{mm}$), where a small recirculation zone results in a low WSS magnitude (as shown earlier in Figure 4.11). However, in the parallel STS model, owing to the large vortices within the coronary artery, the WSS magnitude is lower on the artery wall at the toe than on the graft wall on account of the higher flow rate in the graft (than in the coronary artery). Consequently, in the toe region of the SQA model, the WSS on the coronary artery wall and on the graft wall is, respectively, higher and lower than that of the parallel STS model at this time instant (t_{11}).

WSS distribution on the coronary artery bed of the STS anastomoses: On the coronary artery bed, during the acceleration phase and the peak flow rate, the magnitude of WSS is much higher in the parallel STS model than that in the STS anastomosis of the new SQA model (2.7Pa versus 0.75Pa at $\xi_3=8.3\text{mm}$ at time t_3 for instance), as shown in Figure 4.13(c) and Figure 4.15(c), respectively. During the deceleration phase (t_5), in the parallel STS model, the WSS magnitude is generally low, with a region of negative values at the middle of the bed opposite to the anastomosis junction ($1\text{mm} \leq \xi_3 \leq 6.7\text{mm}$), indicating that the shear is directed proximally. This is due to the large vortex, formed in the coronary artery at

this time instant, as shown earlier in Figure 4.9(c). The zero value of WSS at point $\xi_3=6.7\text{mm}$ corresponds to the stagnation point, created just distal to the vortex. However, in the STS anastomosis of the new SQA model, at this time (t_5), the experimental results show fluctuations in the WSS values on the artery bed. This is mainly because of the inaccuracy inducted into the PIV results, caused by scattering of the laser light sheet due to the unevenness of the inner surfaces of the fabricated model at this region. These oscillations have also resulted in fluctuations in the sign of WSS, due to the very small (nearly zero) velocity magnitude at this time (t_5). Some fluctuations in the magnitude of WSS can also be observed in this model at other time instants. At time t_{11} , the WSS magnitude on the artery bed of the parallel STS model is much lower than that in the STS anastomosis of the new SQA model, due to the recirculation zones and low velocity regions created within the coronary artery in the parallel STS model. However, during the backflow phase (t_{12}), both models show similar WSS distributions.

Figure 4.13: WSS distribution in the STS component of the SQA model, along the (a) heel, (b) toe, and (c) artery bed.

Figure 4.14: WSS distribution in the ETS component of the SQA model, along the (a) heel, (b) toe, and (c) artery bed.

Figure 4.15: WSS distribution in the parallel STS model, along the (a) heel, (b) toe, and (c) artery bed.

Figure 4.16: WSS distribution in the conventional ETS model, along the (a) heel, (b) toe, and (c) artery bed.

4.10.2.2 Qualitative comparison between the experimental and computational results

Upon comparing the flow field and velocity vectors obtained from the experimental results with those from the simulation results, a fairly good agreement is observed between the two sets of data. For instance, comparison of the flow streamlines at time t_{11} in Figure 3.26, obtained from the computational simulation, with the corresponding measured velocity field, shown in Figure 4.11, demonstrates a fair match between the two flow fields, as follows. In the blood flow from the coronary artery into the graft, a tiny vortex is located over the toe of the STS component of the SQA model, along with a vortex formation above the heel of the ETS component of the SQA model; there is also a huge vortex occupying two-thirds of the anastomosis and the graft in the conventional ETS model, and a large vortex taking up the entire anastomosis region of the parallel STS model. It is noted in the simulation results in Figure 3.26, that the blood flows back towards the aorta through the graft in the near wall regions upstream of the anastomoses in all the models; however, this does not quite match the experimental results in the case of the parallel STS model, shown in Figure 4.11(c).

More discrepancies are noticed between the experimental and computational results in the parallel STS model than in the other models investigated. For instance, as explained earlier, at time t_{11} , the parallel STS model has a positive WSS in the heel region based on the experimental results, while negative WSS values are obtained from the corresponding simulation results (Figure 4.15(a)). This is a direct result of the forward flow obtained in the near wall regions of the graft upstream of the anastomosis in the parallel STS model at this time (t_{11}), while backward flows are observed in the corresponding regions of the simulation results. These incongruities can be attributed to the disparity of the boundary conditions, set

in the experiment, compared with those adjusted in the numerical simulation. In the computationally simulated model, 15% of the outflow is set to exit through the coronary artery, and the remaining 85% through the graft of the parallel STS model at all times. However, in the experimental in vitro model, this percentage allocation can be set only for the average outflow over each cycle. Therefore, at some particular instants of time in the cycle, there are different flow rates in the experimental model and the numerical one, which result in different velocity field and WSS distribution in the parallel STS model. Another causative reason is the imperfect repeatability (cycle-to-cycle variation) of the generated flow waveform which results in an imprecise adjustment of the image capturing (trigger) phase angle during the experiment. This factor can have a substantial influence at this particular instant of time (t_{11}), due to the very small average velocity magnitude at this time; this can even result in a change in the direction (or in the sign of the average velocity) of the flow, if the images are taken slightly ahead (leading) or behind (lagging) of the correct phase angle at which they are supposed to be taken.

Qualitative comparison of the WSS distribution obtained from the PIV results with that of the simulation results indicates that the experimental results are generally in a good match with the numerical results. However, some fluctuations and oscillations are observed in the experimental WSS distribution, which are not present in the numerical results, as for instance, at all times on the artery bed of the STS component of the SQA model and at times t_3 , t_5 , and t_6 on the artery bed of the conventional ETS model, as shown in Figure 4.13(c) and Figure 4.16(c), respectively. These errors can be attributed to the scratches caused on the inner wall surface of the models during the removal of the alloy cast remainders from the

lumen walls of the models. This has, in turn, resulted in unevenness of the models' inner surface which has caused refraction of the laser sheet, resulting in inaccurate measurement of velocity, and consequently the WSS calculation. Also, the surface unevenness results in particle deposition, especially at low-velocity regions, which introduces errors into the velocity measurements.

Generally, a better qualitative agreement between the WSS distribution obtained from the experimental and numerical results is observed at locations where a higher number of boundary points exists in order to capture the variation of WSS (such as at the toe of the ETS anastomosis and on the artery bed; very similar trends in experimental and simulation results are noted in Figure 4.14(b) and (c) and Figure 4.16(b) and (c) for instance), compared to those locations with only a few boundary points (such as at the heel and toe of the STS anastomoses; for instance, note the difference between the experimental and simulation results in Figure 4.13(a) and Figure 4.15(b)).

Overall, the WSS distribution patterns derived from PIV experiments are observed to share similar trends with those of numerical simulations.

4.11 Discussion and conclusion

PIV measurements are used in this in vitro investigation to complement and validate the earlier computational modeling, from which more complex HPs have been derived to quantify hemodynamics in the novel CABG coupled SQA design model.

The experimental results demonstrate that the new SQA model provides (i) a more uniform and smooth flow at the ETS anastomosis, without any stagnation point on the artery bed and vortex formation in the heel region of the ETS anastomosis within the coronary artery; (ii) less flow recirculation and stagnation on the artery bed at the STS component of the SQA model as compared to the parallel STS model; and (iii) a higher magnitude of WSS on the artery floor at both the STS and ETS components of the SQA model, compared to the parallel STS and conventional ETS anastomosis models, respectively. These can reduce the probability of IT and atherosclerotic lesion development at these critical anastomotic sites.

Generally, the flow fields are qualitatively matched between the simulation and PIV measurement results (except for the STS component of the SQA model at times t_5 and t_6 where the vortex formations are not consistent between the two data sets, and for the parallel STS model at times t_6 and t_{11} , where no backflow is observed within the graft in the experimental results). Also, the trend of WSS distributions of the experimental results and the computational simulation results are qualitatively similar within the investigated regions of this in vitro study.

However, a quantitative comparison between the two data sets is not meaningful, and hence, is not made. This is because the fluid properties and boundary conditions of the experiment are not exactly the same as those of the computational simulation. The dynamic and kinematic viscosities of the fluid, used in the experiment, are higher than those of the blood, employed in the simulation, by 32% and 20%, respectively; this is due to the need for matching the refractive index of the working fluid with that of the silicon models. In

addition, the silicon models, used in the experiment, are not absolutely rigid (although no wall movement is observed in the symmetry plane); while a rigid wall assumption has been made in the computational simulations. Moreover, the applied boundary condition in the computationally simulated parallel STS model forces 15% of the outflow to exit through the coronary artery, and the remaining 85% through the graft of the parallel STS model at all times; while in the experiment, this percentage allocation can be set only for the average outflow over each cycle, as mentioned earlier. Thus, at some particular instants of time in the cycle, flow rates in the experimental model are different from those in the numerical one, which results in different velocity field and WSS distribution in the parallel STS model between the two data sets. These result in having different conditions between the experiment and simulation, which does not allow a quantitative comparison between the two studies. Moreover, it has been shown that the estimated WSS distributions from the experimental results are highly dependent on the curve-fitting method used to calculate the wall shear rate, and it has been suggested that numerical models should be validated using velocity measurement data and not estimated WSS values [181], albeit some robust methods have recently been suggested for improving the estimation of near-wall velocity gradients to optimize fitting parameters [87].

Overall, the flow fields and WSS distributions obtained from the experimental results are in a good qualitative match with those from the computational simulations, which can further confirm the advantages of the novel SQA design over the conventional ETS anastomosis. This in vitro investigation can be employed as a validation for the earlier computational study.

Chapter 5

5 Effects of vessel wall compliance and non-Newtonian rheology [85]

5.1 Introduction

So far, a novel design for coronary arterial bypass surgical grafting has been developed, its beneficial blood flow patterns and WSS distributions have been shown by means of CFD simulations, and the simulation results have been validated in vitro, using PIV technique.

In the preliminary computational simulation of blood flow of this coupled SQA design, the graft and the artery are adopted to be rigid vessels and the blood is assumed to be a Newtonian fluid. These assumptions are made in the vast majority of the computational studies of blood flow in arteries, which might be due to difficulties of solving the coupled fluid flow–structural deformation problem. However, the arterial wall is a viscoelastic deformable tissue, and its deformation interacts with the pulsatile blood flow. As a result of this interaction, hemodynamic factors of the blood flow are influenced by the mechanical behavior of the wall, and the dynamic properties of the wall are affected by the transient behavior of the blood flow.

In recent years, due to advances in computational methods, performing fluid–structure interaction (FSI) simulations has been facilitated, and more coupled FSI computational studies have been conducted. Perktold and Rappitsch [138, 139] simulated the blood flow in compliant models of carotid artery bifurcations and showed a quantitative influence of the wall compliance on the flow patterns and WSS magnitude. Tang et al. [172] conducted FSI simulations of a non-linear thick-wall model of carotid arteries with an asymmetric stenosis to quantify the effects of stenosis severity, eccentricity, and pressure conditions on blood flow and wall behaviors to determine conditions under which artery compression and plaque rupture might occur. By numerical modeling of blood flow and low-density lipoprotein (LDL) transport in a porohyperelastic arterial wall model, Koshiba et al. [92] have demonstrated that the blood flow, arterial wall deformation, and filtration flow all affect the LDL concentration, and that LDL accumulation is due to stagnation and the presence of filtration flow. Hence, they concluded that FSI analysis is indispensable for realistic simulation of a flow field and the LDL concentration patterns in both the lumen and wall.

Although FSI is found to be important in coronary arterial flow simulations by some investigations (including the above reviewed studies), there are also studies indicating that the effect of arterial wall deformation on arterial flow can be insignificant. Leuprecht et al. [105] investigated pulsatile flow patterns and vessel wall mechanics in conventional and Miller-cuff types of distal ETS anastomoses of bypass grafts. Their results of the flow studies in distensible vessel wall models showed a rather small influence on the flow field relative to the rigid wall models, despite rather large side wall deformations in the anastomotic region.

Therefore, in this chapter, further simulations are carried out primarily in the light of estimating the significance of vessel wall compliance effect on HPs distribution in the proposed CABG coupled SQA design. The objective of this chapter is, hence, to (i) investigate the effects of wall compliance and non-Newtonian rheology of blood on the local flow field and HPs distribution, and (ii) verify the previously observed advantages of the novel CABG coupled SQA design over the conventional ETS configuration in a more realistic bio-mechanical condition.

The effects of wall elasticity and non-Newtonian rheology are investigated in the superior SQA model (with the anastomotic angle of 30° and 30mm distance between the STS and ETS anastomoses) and its corresponding conventional ETS model. For this purpose, a two-way FSI analysis is carried out, and the transient wall equations and the flow equations are solved in an implicitly coupled approach, using an iterative procedure.

5.2 Computational models and boundary conditions

A two-way (bidirectional) FSI simulation of blood flow in compliant-wall CABG models is conducted using the commercial computational software ANSYS Workbench (ANSYS Inc.) for the coupling of the finite-element-based software, ANSYS, with the finite-volume-based software, ANSYS CFX. Therein, the calculated displacements of the solid (vessel) structure are transferred to the boundary walls of the fluid domain and the computed forces in CFX are sent back to the solid domain during each stagger (coupling) iteration.

5.2.1 Vessel wall model

Blood vessels experience large strain in vivo, particularly near branches and graft artery junctions [8]. However, as the focus of this investigation is on the flow fields and HPs distribution rather than the intramural stress distributions, a small strain (large deformation) approximation of blood vessel mechanics is utilized, as commonly used in other earlier studies [5, 149, 178]. The transient structural equilibrium equation is

$$\{\mathbf{F}_{(t)}\} = [\mathbf{M}]\{\ddot{\mathbf{u}}_{(t)}\} + [\mathbf{K}]\{\mathbf{u}_{(t)}\} \quad (5.1)$$

Where $\{\mathbf{F}\}$ is the load vector, $[\mathbf{M}]$ is the structural mass matrix, $[\mathbf{K}]$ is the structural stiffness matrix, $\{\mathbf{u}\}$ is the nodal displacement vector, and $\{\ddot{\mathbf{u}}\}$ is the nodal acceleration vector.

The equilibrium equations for the vessel wall structure are solved with stress boundary conditions (the calculated pressure and WSS values from the fluid domain) at the fluid–structure interface and constraint conditions (at the graft inlet and the coronary artery outlet to prevent rigid body motion), in order to estimate the vessel wall displacements.

The vessel walls are assumed to be isotropic, incompressible, and homogeneous with a density of 1060kg/m³ [125], and modeled as a linearly elastic, geometrically non-linear shell structure [71, 139]. Poisson’s ratio is regarded as $\nu \approx 0.5$ to express the incompressibility of the isotropic vessel wall material.

The stiffness of venous walls is highly nonlinear, exhibiting an increasing elastic modulus for higher strains. At low (venous) pressures, veins have a lower stiffness than arteries;

however, at arterial pressures, stiffness of arterialized vein grafts increases to a level even higher than that of arteries. Wesly et al. [184] have measured the incremental elastic moduli (Young's modulus) of human saphenous vein in both longitudinal and circumferential directions at different transmural pressures. As the vessels are strongly restricted in the axial direction and their elongation is negligible under in vivo conditions [41, 67], the value of circumferential elastic modulus is used as the Young's modulus for the isotropic graft wall material in this study. This value is interpolated to be $E_{\theta}=2.2\text{MPa}$ at a mean physiologic transmural arterial wall pressure of 100mmHg. Also, as the arterial wall stiffness is increased in atherosclerotic arteries and in this study we are not investigating the effects of compliance mismatch, the same value of elastic modulus is employed for the arterial wall too.

The wall thickness of human LAD coronary artery has been measured in atherosclerotic patients both by high-frequency, two-dimensional transthoracic echocardiography (to be $1.9\pm0.3\text{mm}$) and by high-frequency epicardial echocardiography (to be $1.8\pm0.2\text{mm}$) [62]. Further, it has been demonstrated that autogenous veins undergo medial thickening when used as arterial bypass grafts [42]. Accordingly, the wall thickness of both the graft and artery is taken to be 2mm in this investigation.

5.2.2 Blood flow model

Blood flow through the CABG is assumed to be a three-dimensional, time-dependent, incompressible, isothermal, and laminar flow. In distensible models, the modified equations of motion for fluid mechanics computations (with corrected convective velocity due to

moving boundaries [78]), which are obtained by applying the Leibnitz Rule on the integral conservation equations, are as follows.

$$\frac{d}{dt} \int_{V(t)} \rho dV + \int_S \rho (\mathbf{U}_j - \mathbf{W}_j) dn_j = 0 \quad (5.2)$$

$$\frac{d}{dt} \int_{V(t)} \rho \mathbf{U}_i dV + \int_S \rho (\mathbf{U}_j - \mathbf{W}_j) \mathbf{U}_i dn_j = - \int_S P dn_i + \int_S \eta \left(\frac{\partial \mathbf{U}_i}{\partial \mathbf{x}_j} + \frac{\partial \mathbf{U}_j}{\partial \mathbf{x}_i} \right) dn_j \quad (5.3)$$

where $\mathbf{U}_j$ and $\mathbf{W}_j$ are, respectively, the components of the flow velocity and the velocity of the control volume boundary (mesh velocity). V and S denote volume and surface regions of integration, respectively, and dn_j are the differential Cartesian components of the outward normal surface vector.

The mesh velocity at an inner point of the flow domain is calculated from the wall movement by a “Displacement Diffusion” mesh motion model, in which the displacements applied on the boundaries are diffused to other mesh points in a way that the relative mesh distribution of the initial mesh is preserved. For instance, as the initial mesh is relatively fine in boundary layers, it remains comparatively fine after the mesh motion model is applied.

To model the shear thinning behavior of blood, the Carreau-Yasuda model [16] is employed

$$\eta = \eta_\infty + (\eta_0 - \eta_\infty) \left[1 + (\lambda \dot{\gamma})^a \right]^{\frac{(n-1)}{a}} \quad (5.4)$$

where $\dot{\gamma}$ represents a scalar measure of the rate of deformation tensor ($\mathbf{D} = [\nabla \mathbf{U} + (\nabla \mathbf{U})^T]/2$), defined as

$$\dot{\gamma} = \sqrt{2tr(\mathbf{D}^2)} \quad (5.5)$$

and the other parameters are obtained from the experimental data of a blood analog by Gijsen et al. [60] to be: $\eta_0=22 \times 10^{-3} \text{Pa}\cdot\text{s}$, $\eta_\infty=2.2 \times 10^{-3} \text{Pa}\cdot\text{s}$, $\lambda=0.11 \text{s}$, $\alpha=0.644$, and $n=0.392$.

A fully developed pulsatile flow is applied at the graft inlet with the same velocity waveform as demonstrated earlier in Figure 3.4, and the Womersley solution [190] is implemented as the inlet boundary condition. The traction-free outflow boundary condition is applied at the coronary artery outlet, and the no-slip boundary condition is specified on all walls.

The governing equations are solved numerically by a finite volume method and the CFD software, ANSYS CFX, using a fully implicit second-order backward Euler differencing scheme. The convergence criterion (a normalized residual, obtained based on the imbalance in the linearized system of discrete equations) is set to 10^{-5} in this study. The time-step size is taken to be 0.01s.

5.3 Validation of FSI Methodology

In order to validate the FSI simulations and the method used, a simple sinusoidal flow in a straight compliant tube is modeled and the numerical results are compared with the corresponding analytical solution due to Zamir [193].

The length and radius of the tube, and the thickness and elastic modulus of the wall are, respectively, 0.42m, 0.005m, 0.0005m, and 20MPa. The fluid has the same properties as the Newtonian blood in the present study, and the frequency of oscillation is set to be 1Hz.

The applied boundary pressure waveforms are

$$P_{inlet} = 30 + 1000 \sin(2\pi t) \quad \text{Pa} \quad (5.6)$$

$$P_{outlet} = 1000 \sin(2\pi t - 0.0139456) \quad \text{Pa} \quad (5.7)$$

Figure 5.1 demonstrates the comparison of the calculated non-dimensional velocity profiles at a cross-section located at the distance of 0.4m from the entrance of the tube. The velocity is normalized using $R^* \omega$ as the characteristic scale, where R^* is the radius of the tube plus half the thickness of the tube wall and ω is the angular frequency of oscillation. There is a very good agreement between the analytical solution and the obtained numerical solution with an average relative error of 5.1%.

Figure 5.1: Comparison of analytical solution due to Zamir [193] and the current numerical solution at $t=6.26s$, $6.45s$, $6.75s$, and $7.00s$. The symbols are due to the current numerical solution and the solid lines are due to the analytical solution.

Based on these validation results, hence, it is concluded that the fluid-structure interaction method used in the present study is accurate in predicting the fluid dynamics of the coronary arterial bypass graft models investigated.

5.4 Results

Flow field, WSS, and wall deformations are studied at several points and cross-sections of the models as shown in Figure 5.2.

Figure 5.2: The superior SQA model with the ETS anastomotic angle of 30° and 30mm distance between the two anastomoses. S_1 to S_{10} and P_1 to P_8 indicate, respectively, the cross-sections and the points at which velocity profiles and WSS variations are discussed.

5.4.1 Wall deformation

The mesh displacement contour in the SQA model at the peak internal pressure during diastole ($t/T=0.43$) is shown in Figure 5.3. The wall deformation pattern remains

qualitatively unchanged during the cardiac cycle. The maximum mesh displacement is about 0.5mm, occurring at the side walls of the STS anastomosis of the SQA model in the middle of the suture-line, where the normal pressure causes the maximum moment (about axes X and Z) on the artery and the graft wall structure, due to the high pressure and long scissor ($L_{STS}=9\text{mm}$) on the blood vessels at this location. Likewise, at the ETS component of the SQA model and in the conventional ETS model, the maximum displacement occurs on the side walls of the anastomosis, nearer to the heel rather than to the toe.

At the peak internal pressure, the increase in the diameter of the graft and of the coronary artery at locations immediately proximal and distal to the anastomosis of the conventional ETS model is about 0.16, 0.06, and 0.04mm (equivalent to 4%, 3%, and 2% diameter variation (DV) ratio) respectively. This value increases up to 5% in the coronary artery of the SQA model proximal to the STS anastomosis. Schaar et al. [153] reported up to 2% circumferential strain (equivalent to 2% DV) in human coronary arteries using three-dimensional ultrasound-based intravascular palpography. Zeng et al. [194] measured 15% of maximum temporal cross-sectional area variation averaged along the RCA (which corresponds to about 8% DV) using multi-slice CT. Also, canine elastic arteries have been reported to experience 6–10% DV over a cardiac cycle driven by the pressure pulse [6, 135]. Hence, the calculated diameter variations in the present FSI simulation are comparable to experimental findings.

Figure 5.3: Mesh displacement contour in the superior SQA model at the peak pressure ($t/T=0.43$), with the maximum value occurring at the side walls of the STS anastomosis. The wall deformation pattern remains qualitatively unchanged during the cardiac cycle.

5.4.2 Flow patterns

The general structure of the flow patterns in the compliant model is about the same as that in the rigid-wall model (which have been discussed in detail in Chapter 3), as shown in Figure 5.4 for time $t_6=0.32s$, for instance. The very advantages which had been observed in the flow fields of the SQA configuration in comparison with that of the conventional ETS anastomosis in the case of rigid-wall model with Newtonian fluid are present in the compliant model as well.

Figure 5.4: Flow streamlines in the symmetry plane of the SQA model at time $t_6=0.32s$; (a) compliant model, (b) rigid-wall model; similar qualitative flow characteristics are present in the two models.

In order to investigate the effect of non-Newtonian rheology of blood on the flow field, the axial velocity profiles at various sections in the symmetry plane of the SQA model at the end of systole ($t_6=0.32s$) are demonstrated in Figure 5.5 for both the Newtonian and non-Newtonian fluid models. The axial velocity profile of the non-Newtonian fluid is somewhat

flattened due to its shear thinning behavior, and is less skewed towards the outer wall of the graft curvature, as compared to that of the Newtonian fluid, especially at sections S_3 , S_4 , and S_5 at the STS component (Figure 5.5(a)) and at section S_6 at the ETS component (Figure 5.5(b)) of the SQA model.

Figure 5.5: Axial velocity profiles at various sections in the symmetry plane of the SQA model at the end of systole ($t_6=0.32s$) for the non-Newtonian (continuous line) and Newtonian (dashed line) fluid models. (a) STS anastomosis of the SQA model, (b) ETS anastomosis of the SQA model.

To exemplify the effect of wall compliance and non-Newtonian rheology of blood on the reversed flow, the axial velocity profile at section S_{10} , located distal to the ETS anastomosis of the SQA model, at time $t_{11}=0.84s$, when the graft net flow rate just becomes negative, is

shown in Figure 5.6. Comparison between the Newtonian and non-Newtonian fluid models (in both the rigid and compliant models) demonstrates that the velocity profile of the non-Newtonian fluid is somewhat flattened, due to its shear-thinning behavior. Comparison between the rigid and compliant models (for both the Newtonian and non-Newtonian fluid models) illustrates a considerable reduction of reversed flow in the distensible model. This is because when the graft flow rate decreases during the deceleration phase, in order to satisfy the fluid's mass conservation in the rigid-wall model, this decrease can be compensated for, only by means of reducing the flow velocity. However, in the compliant model, the vessel's contraction partially compensates the flow rate drop by reducing the cross sectional area; consequently, less would be left to be compensated for, by reducing the velocity. As a result, less reversed flow is present in the distensible-wall models. These results are consistent with those of earlier studies [27, 71].

Figure 5.6: Axial velocity profiles in different models at section S_{10} , at time $t_{11}=0.84s$, when the graft net flow rate has just become negative. A considerable decrease of the reversed flow is obvious in the distensible model, compared to that in the rigid-wall model.

Figure 5.7 shows the secondary flows at two cross sections (S_3 and S_9) in the SQA model for both the Newtonian and non-Newtonian fluid models at the peak flow rate ($t_3=0.13s$). At both sections, counter-rotating vortices (Dean vortices) are evident, with nearly symmetric streamlines due to the planarity of the models (little asymmetry observed is due to the small buckling of the structural model as a result of the constraints applied). At section S_3 , the secondary flows are weakened in the case of non-Newtonian fluid as compared to those of Newtonian fluid, which is consistent with the results of earlier studies [27]. However, as the cross sectional area is reduced at section S_9 , the velocity, and consequently, the near-wall shear rates are increased at this section where the flows from the coronary artery and the graft are merged. Hence, the shear-thinning property of the non-Newtonian fluid reveals an opposing effect on the secondary flows at different locations of this section: the secondary velocity is increased at locations near to the wall; but, it is slightly decreased in the central region as compared to the case of Newtonian fluid model. This is because in the near-wall region of this section at this time instant, the fluid shear rate is higher than the threshold value (calculated to be $\approx 382s^{-1}$ in this study), above which the viscosity of the non-Newtonian fluid falls below the constant viscosity of the Newtonian fluid; however, in the central region, the shear rate is below the threshold.

In all cases, the secondary flows are weakened along the coronary artery (distal to the ETS anastomosis) owing to the effect of the fluid viscosity (not shown here).

Figure 5.7: Secondary flows at two cross sections in the SQA model (S_3 at the middle of the STS anastomosis (upper panel) and S_9 located distal to the ETS anastomosis (lower panel)) for the Newtonian (left) and non-Newtonian (right) fluid models at the peak flow rate ($t_3=0.13s$). The shape of the rigid wall model is shown by dashed lines to illustrate the deformation of the vessel walls. The contours demonstrate the magnitude of the secondary flow, and they have the same scale for both the sections to facilitate the comparison (but, this is not the case for the vectors).

5.4.3 Temporal and spatial variations of WSS

The temporal variations of WSS are investigated at some particular points on the vessel wall (P_1 to P_8 whose locations are shown in Figure 5.2) throughout the cardiac cycle, and are compared for the non-Newtonian fluid between the rigid and compliant models, as demonstrated in Figure 5.8. Among the points studied (including those whose graphs are not

shown in Figure 5.8), P_7 , located at the toe of the ETS anastomosis, shows the minimum disparity between the WSS time-history of the rigid and compliant models where the two graphs are almost identical (Figure 5.8(a)). On the other hand, P_6 , located on the graft outer wall proximal to the ETS anastomosis, demonstrates the most discrepancy with up to 21% increase in the WSS magnitude in the rigid model compared to that of the distensible model (Figure 5.8(b)), which can be attributable to the higher DV in the graft than in the coronary artery. The WSS time-history graphs of the points P_3 , P_4 , and P_5 (not shown here) look similar to those of P_7 and P_6 , with their magnitude disparity between the rigid and compliant models varying between those of the two points P_7 and P_6 ($<21\%$). The profile of the WSS curves at proximal locations such as P_1 is more analogous to the calculated pressure waveform (see Figure 5.8(c)), than those at distal locations. The overall shape of the WSS time-history curves is similar between the rigid and distensible models, with the WSS magnitude being generally higher in the rigid-wall model due to its smaller vessel diameter and the consequent higher velocity. However, at point P_8 , located on the ceiling wall of the coronary artery just distal to the toe of the ETS anastomosis, the magnitude of the WSS in the compliant model is higher than that in the rigid model (Figure 5.8(d)), unlike the other points. This is due to the higher flow separation at this point in the rigid-wall model than in the distensible model, which results in a significant reduction of WSS magnitude.

Figure 5.8: Temporal variations of WSS throughout the cardiac cycle at various points on the wall. (a) at P₇, located at the toe of the ETS anastomosis, (b) at P₆, located on the graft outer wall proximal to the ETS anastomosis (c) at P₁, located on the artery bed in the middle of the STS anastomosis (d) P₈, located on the ceiling wall of the coronary artery just distal to the toe of the ETS anastomosis. The calculated pressure waveform is shown by dashed line in panel (c).

Figure 5.9 demonstrates instantaneous WSS distributions along the coronary artery bed of the SQA model for the four cases of the rigid and compliant wall with the Newtonian and non-Newtonian fluid models at four different time points. During the systolic acceleration phase ($t_2=0.06s$) as shown in Figure 5.9(a), on the artery bed before the middle of the ETS anastomosis ($x \leq 0.0941m$), the WSS is higher for the non-Newtonian fluid due to its shear thinning behavior and the low shear rate in this region (in both the rigid and compliant models). However, on the artery bed opposite to the ETS anastomosis and further distal, the

shear thinning behavior causes the WSS for the non-Newtonian fluid to become smaller than that for the Newtonian fluid, owing to the high shear rate in this region caused by the flow from the graft merging with that from the coronary artery at the ETS anastomosis. The WSS is somewhat higher in the rigid-wall model than that in the distensible model for both the Newtonian and non-Newtonian fluid models. At this time instant, the shear rate in the segment of the coronary artery located between the two anastomoses, and at the location distal to the ETS anastomosis is, respectively, lower and higher than the aforementioned threshold (above which the viscosity of non-Newtonian fluid becomes lower than that of the Newtonian fluid). Therefore, as the flow rate increases to its peak value ($t_3=0.13s$), the difference between the WSS magnitudes (for the Newtonian and non-Newtonian fluids) decreases in the former region, while it increases in the latter one, as shown in Figure 5.9(b). Nevertheless, the qualitative distribution of WSS on the artery bed at the peak flow rate is similar to that during the acceleration phase, with the peak value occurring opposite to the toe of the ETS anastomosis.

Figure 5.9(c) demonstrates the WSS distribution on the artery bed at the end of systole ($t_6=0.32s$). The magnitude of the WSS for the non-Newtonian fluid is generally higher than that for the Newtonian fluid in both the compliant and rigid-wall models, as a result of the low shear rate at this time instant (negative values of WSS indicate reversed flow). At locations distal to the ETS anastomosis, the WSS magnitude in the rigid-wall model is higher than that in the compliant model for both Newtonian and non-Newtonian fluids. However, in the coronary artery segment located between the two anastomoses, the WSS magnitude in the distensible model is higher than that in the rigid model. This is because at

this moment (late systolic deceleration), the low pressure results in the coronary artery contraction and reduction of the vessel diameter, and consequently, an increase in the WSS magnitude. The same phenomenon occurs in late diastole too (not shown here). This is in agreement with the results of earlier FSI simulation studies of the blood flow in the right coronary artery reported by Zeng et al. [194] and Torii et al. [174]. Also, similar result can be observed in an ETS anastomosis FSI study by Hofer et al. [71], albeit this aspect (the opposing effect of wall distensibility on WSS distribution) has not been pointed out.

Figure 5.9: Instantaneous WSS distributions along the coronary artery bed of the SQA model at different time points. (a) during systolic acceleration phase ($t_2=0.06s$), (b) at systolic peak flow ($t_3=0.13s$), (c) end of systole ($t_6=0.32s$), (d) at peak reversed flow ($t_{12}=0.87s$). The shape of the vessel walls is shown by dashed line in panel (a).

At the peak reversed flow ($t_{12}=0.87s$), the WSS magnitude for the non-Newtonian fluid is considerably higher than that for the Newtonian fluid along the artery bed in both the rigid and distensible models, due to the low shear rate at this time instant, as shown in Figure 5.9(d). Also, the WSS magnitude is slightly higher in the rigid-wall model than in the compliant model.

5.4.4 Hemodynamic parameters distribution

In order to investigate the effect of wall distensibility and non-Newtonian rheology on the distribution of HPs at the critical sites of the anastomosis namely the toe, heel, bed, and suture-line (as shown earlier in Figure 3.32), the segmental averages of the HPs, including TAWSS, non-dimensional TAWSSG, and OSI, are calculated and presented in Table 5.1. The following can be inferred from the tabulated results.

TAWSS: Comparison of the TAWSS between the rigid and compliant models (both for the Newtonian and non-Newtonian fluid models) demonstrates a decrease in the TAWSS at all critical locations in the compliant model, which ranges between 3% (on the suture-line) and 32% (on the heel) in the conventional ETS model, and from 4% (at the toe of the STS anastomosis) to 27% (on the suture-line of the STS anastomosis) in the SQA model. This is consistent with the results of the earlier studies reporting that wall motion reduces the mean WSS in a straight elastic tube model [183], and in an elastic abdominal aortic bifurcation model [97].

Table 5.1: Comparison of the segmental averages of $\langle HP \rangle_s$.

Wall model:		Rigid						Distensible						
Fluid model:		Newtonian			Non-Newtonian			Newtonian			Non-Newtonian			
Anastomosis model	Location	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>	
Conventional ETS model	1- Suture line	0.04	2.12	15.09	0.04	2.06	14.94	0.05	2.05	13.30	0.04	1.99	13.66	
	2- Toe	0.01	6.69	34.02	0.01	5.65	28.47	0.01	6.14	31.00	0.02	5.23	26.34	
	3- Heel	0.09	0.56	8.29	0.07	0.71	9.57	0.11	0.38	6.10	0.09	0.52	7.97	
	4- Bed	0.09	1.67	5.46	0.08	1.55	4.64	0.11	1.47	5.01	0.09	1.40	4.29	
Coupled sequential anastomoses model	ETS component	1- Suture line	0.03	2.51	15.12	0.03	2.39	15.00	0.03	2.10	11.44	0.04	2.05	11.61
		2- Toe	0.01	6.33	36.95	0.02	5.36	31.23	0.01	5.85	29.71	0.02	5.01	25.24
		3- Heel	0.08	0.49	4.39	0.07	0.69	6.26	0.08	0.40	3.52	0.07	0.61	5.50
		4- Bed	0.05	1.86	4.93	0.05	1.76	4.05	0.06	1.76	5.02	0.06	1.59	3.88
	STS component	5- Suture line-STS	0.05	0.65	5.94	0.05	0.80	6.54	0.05	0.47	5.37	0.05	0.62	6.39
		6- Toe-STs	0.04	0.70	6.03	0.05	0.80	6.00	0.04	0.67	7.32	0.05	0.77	7.44
		7- Heel-STs	0.08	0.41	4.42	0.08	0.54	5.38	0.09	0.32	3.44	0.07	0.45	4.89
		8- Bed-STs	0.22	0.17	0.40	0.18	0.25	0.50	0.24	0.15	0.45	0.18	0.22	0.55

Upon comparing the TAWSS between the Newtonian and non-Newtonian fluid models (in both compliant and rigid-wall models), it is seen that at the ETS anastomosis (of both the conventional and SQA models) in the case of non-Newtonian fluid, the TAWSS is decreased at the toe, suture-line, and on the bed, while it is increased at the heel. On the other hand, at the STS anastomosis, the TAWSS is increased at all the critical locations. This reduction at the ETS anastomosis and increase at the STS anastomosis is due to the shear thinning behavior of the non-Newtonian fluid, as the shear rate is generally high at the ETS anastomosis while it is low at the STS anastomosis.

TAWSSG: Comparison of the TAWSSG between the rigid and compliant models (both for the Newtonian and non-Newtonian fluid models) indicates that the TAWSSG is generally decreased in compliant models at the ETS anastomosis of both the conventional and SQA models (except on the artery bed of the ETS anastomosis of the SQA model in the case of Newtonian fluid). At the STS anastomosis of the SQA model, the TAWSSG is decreased at the heel and on the suture-line, while it is increased at the toe and on the artery bed of the distensible models.

Comparison of the TAWSSG between the Newtonian and non-Newtonian fluid models (in both compliant and rigid-wall models), demonstrates that the TAWSSG at the ETS anastomosis (of both the conventional and SQA models) is reduced at the toe and on the artery bed, while it is increased at the heel, and is negligibly ($<3\%$) changed on the suture-line in the case of the non-Newtonian fluid model. At the STS anastomosis, the TAWSSG is increased on the artery bed, suture-line, and at the heel, while it has experienced less than 2% change at the toe in the case of non-Newtonian fluid.

OSI: As shown in Table 5.1, the wall compliance somewhat increases the OSI in all the models, albeit the OSI value is generally low due to the flow having mostly a forward direction during the cardiac cycle.

The non-Newtonian rheology has an opposing effect on the OSI, in accordance with the shear thinning behavior. At locations with high shear rate where the shear thinning effect reduces the fluid viscosity and facilitates the oscillation of the flow (such as at the toe of the anastomosis), the OSI is increased in the case of non-Newtonian fluid model. Conversely, at locations with low shear rate where the shear thinning effect increases the fluid viscosity and impedes the flow oscillation (for instance at the heel and on the artery bed), the non-Newtonian rheology reduces the OSI. This effect is mostly pronounced on the artery bed at the STS anastomosis of the SQA model, where the OSI is reduced from 0.24 to 0.18 in the distensible model and from 0.22 to 0.18 in the rigid-wall model.

The OSI is slightly lower at the heel and on the artery bed of the ETS anastomosis of the SQA model, than in the conventional ETS anastomosis. Moreover, the OSI on the artery bed at the STS anastomosis of the SQA configuration is lower in the case of compliant model with non-Newtonian fluid, than in the case of the rigid-wall model with Newtonian fluid.

5.5 Discussion

In this chapter, a two-way coupled FSI analysis of the CABG SQA design is performed. The effects of vessel wall compliance and shear thinning property of blood are investigated on the flow field and HP distributions and the performance of this coupled

SQA configuration in comparison with the conventional ETS anastomosis is evaluated in a more realistic bio-mechanical condition.

5.5.1 Model Assumptions and Limitations

As the focus of this investigation is on the flow fields and HPs distribution rather than the intramural stress distributions, a small strain (large deformation) approximation of blood vessel mechanics is utilized. The vessel walls are assumed to be isotropic and homogeneous, and modeled as a linearly elastic, geometrically non-linear shell structure [71, 139], and the same value of elastic modulus is employed for both the graft and the arterial wall.

5.5.2 Evaluation of Results

As described in the Results, the velocity profiles of non-Newtonian flow are flattened (as illustrated in Figures 5.5 and 5.6) and the TAWSS is reduced at high shear rates due to shear thinning behavior of the blood (as shown in Table 5.1). In simple language, the blood has the property of losing its viscosity at high variations of velocity, which makes it less sticky and more fluent, and let the fluid layers flow more easily over each other. Since the change in the velocity is higher in the near wall region and lower in the core region, this characteristic facilitates the flow in the former region and impedes it in the latter one. Hence, the velocity profile is flattened as compared to the parabolic velocity profile of a Newtonian fluid.

When a non-Newtonian fluid is approximated by a Newtonian model, the constant viscosity of the Newtonian model represents the average viscosity of the non-Newtonian fluid within its working range of shear rates. Thus, comparison of the two fluids results

in lower viscosity (and WSS values) at high shear rates (higher than the aforementioned threshold) and higher viscosity (and WSS values) at low shear rates (below the aforementioned threshold) for the non-Newtonian fluid as compared to the equivalent Newtonian fluid.

As observed in the Results, at some locations, the effects of wall compliance and non-Newtonian rheology on the HPs distribution are in line, while at some other locations these effects are opposing. For instance, the wall compliance and non-Newtonian rheology both decrease the TAWSSG at the toe of the ETS anastomosis (from 36.95 to 29.71 and from 36.95 to 31.23, respectively, in the SQA model), which result in a further reduction (to 25.24) when comparing the “compliant-wall with non-Newtonian fluid” model with the “rigid-wall with Newtonian fluid” model, due to the accumulation of these effects. However, at the heel of the ETS anastomosis, for example, the non-Newtonian rheology increases the TAWSS (from 0.56Pa to 0.71Pa in the rigid model), while the wall compliance decreases this parameter (from 0.56Pa to 0.38Pa in the case of Newtonian fluid); and the accumulation of these opposing effects results in a negligible overall change (from 0.56Pa to 0.52Pa) when a comparison between the two above mentioned models is made.

Nevertheless, the interesting point is the fact that at some particular locations, the accumulation of the two effects does not result in an expected outcome as above. For instance, at the toe of the STS anastomosis of the SQA model, the non-Newtonian rheology slightly decreases the TAWSSG in the rigid model from 6.03 to 6, while the wall compliance increases this HP from 6.03 to 7.32. Nonetheless, the accumulation of the two effects does not result in a value between 6 and 7.32, but in a higher value of

7.44. This fact demonstrates that the effect of one parameter (either non-Newtonian rheology or wall compliance) is not independent from the other one. As in this example, the non-Newtonian rheology has slightly decreased the TAWSSG in the rigid-wall model (from 6.03 to 6), while it has increased this HP in the compliant model (from 7.32 to 7.44). Likewise, on the artery bed of the ETS anastomosis of the SQA model for instance, the wall compliance has slightly increased the TAWSSG (from 4.93 to 5.02) in the case of the Newtonian fluid model, while it has decreased this HP (from 4.05 to 3.88) in the case of the non-Newtonian fluid model.

This phenomenon might be attributable to the interaction of the shear thinning property of the blood with the sudden, local variations of shear rate due to expansions and contractions of the compliant vessel wall during the cardiac cycle. As the vessel wall moves, the shear rate may increase or decrease at different points, depending on the relative movement of the wall and the fluid. This results in some instantaneous local variations of WSS which consequences in some extreme (high or low) spatial WSSG that unexpectedly affects the value of TAWSSG over the cardiac cycle. This phenomenon suggests that it is essential to study and incorporate the effects of these parameters (wall compliance and non-Newtonian rheology) simultaneously, rather than discretely and individually, as they are not independent and cannot be superimposed.

The HPs distribution illustrates that the advantages of the SQA model over the conventional ETS anastomosis, which had been observed in the rigid-wall model with the Newtonian fluid previously in Chapter 3, are present in the compliant model with the non-Newtonian fluid too. For instance, the TAWSS is increased on the artery bed of the

ETS anastomosis of the SQA model to 1.59Pa, from 1.40Pa in the conventional ETS model.

In addition, the TAWSS at the heel of the ETS anastomosis is slightly reduced in the conventional ETS anastomosis (from 0.56Pa to 0.52Pa), while it is increased in the SQA configuration (from 0.49Pa to 0.61Pa) in the compliant model with non-Newtonian fluid, as compared to those in the rigid-wall model with Newtonian fluid. This results in having the TAWSS at the heel of the ETS anastomosis in the SQA model to be higher than that in the conventional ETS model, while the opposite is observed in the rigid-wall model with Newtonian fluid. This reveals another advantage of the SQA configuration over the conventional ETS anastomosis which had not been disclosed in the preliminary study of this design, using rigid-wall and Newtonian fluid models.

As shown in Table 5.1, the TAWSSG is decreased at all the critical locations of the ETS anastomosis in the SQA configuration as compared to the conventional ETS anastomosis in the case of compliant model with non-Newtonian fluid, while this advantage can be observed only at the heel and on the artery bed in the case of the rigid-wall model with Newtonian fluid. This manifests a more uniform distribution of WSS at the ETS anastomosis of the SQA configuration, which can lessen the vessel wall permeability and atherosclerotic lesion development, and further unveils the advantages of the SQA design over the conventional ETS anastomosis.

5.6 Conclusion

A two-way coupled FSI analysis of the novel CABG SQA is carried out in conjunction with the shear thinning property of blood to investigate the performance of this coupled

SQA configuration in comparison with the conventional ETS anastomosis in a more realistic bio-mechanical condition, with an emphasis on the effects of wall compliance and non-Newtonian rheology on the HPs distribution.

The simulation results indicate that the velocity patterns and qualitative distribution of WSS parameters do not change significantly in the compliant model despite quite large side-wall deformations in the anastomotic regions. The WSS magnitude is generally reduced in the distensible model, as compared to that in the rigid-wall model, resulting in a lower TAWSS in the compliant model. The wall compliance has generally decreased the TAWSSG, while it has somewhat increased the oscillatory nature of the flow.

The effect of non-Newtonian rheology on the HPs is heterogeneous. The ETS anastomoses (of both the conventional and SQA models) experience mostly a decrease in the TAWSS (except at the heel), while the STS anastomosis of the SQA model undergoes an increase in this HP. The flow oscillation is increased at the toe of the anastomosis, whereas it is decreased at the heel and on the artery bed, due to the shear thinning behavior of the blood.

It is observed that the effects of wall compliance and non-Newtonian rheology are not independent, and that they influence each other. Hence, it is essential to investigate the effects of these parameters simultaneously (and not individually) in each particular model.

Although vessel wall compliance and non-Newtonian rheology have shown modest influence on the HPs in each model, they have unveiled further advantages of the

coupled SQA model over the conventional ETS anastomosis which had not been revealed in the study with the rigid-wall and Newtonian fluid models in Chapter 3. Therefore, it can be concluded that the inclusion of wall compliance and non-Newtonian rheology in flow simulation of blood vessels can be essential in quantitative and comparative analyses. This investigation further verifies the hemodynamic benefits of the blood flow in the coupled SQA configuration in a more realistic bio-mechanical condition.

Chapter 6

6 Conclusions and future works

In the present study, a novel coupled SQA configuration for the distal CABG anastomoses is proposed based on the advantageous flow characteristics observed within the STS anastomosis in sequential bypass grafts. The flow fields and HPs are studied within the model, and compared to those of the conventional ETS distal anastomosis and parallel STS anastomosis by means of CFD simulation. Also, sensitivity analysis for the suggested SQA design is conducted by computational simulations and comparison of several models within the physiological range of the parameters involved.

Subsequently, to complement and validate the flow-simulation results, experimental measurements are conducted in vitro, using PIV technique. The measured velocity fields and the calculated WSS are studied and compared with those obtained from the preliminary computational simulations, in which the graft and the artery are adopted to be rigid vessels and the blood is assumed to be a Newtonian fluid.

Finally, a two-way coupled FSI analysis is carried out in conjunction with the shear thinning property of blood to investigate the performance of the coupled SQA configuration in a more realistic bio-mechanical condition, in the presence of wall compliance and non-Newtonian blood rheology.

6.1 Key findings and conclusions

The preliminary simulation results demonstrate that in the novel SQA design, during the acceleration and early deceleration phases, part of the graft flow is diverted into the coronary artery at the STS anastomosis. This flow in the coronary artery lifts up the flow coming from the graft at the ETS anastomosis and helps to direct the graft flow smoothly into the coronary artery. Thereby, there is no flow impingement on the artery bed, reducing the probability of the graft failure [12]. Also, the stagnation point is vanished in the SQA design at either one or both of the ETS and STS anastomoses at different time intervals compared to the conventional ETS and parallel STS anastomoses, mitigating the possibility of IT and atherosclerosis development and the risk of the aggregation of red blood cells. Besides, there is no vortex formed at the heel of the ETS anastomosis of the SQA model within the coronary artery, which results in a relatively higher WSS along the artery walls and bed, and reduces the local particle residence time and consequently the chance of IH development [11, 161, 185] and platelet activation [76].

It is observed that in the planar SQA design, the HPs are improved to some extent, especially at the heel and coronary artery bed of the ETS anastomosis, and at the toe and suture-line of the STS anastomosis of the new design, compared to the conventional ETS and parallel STS models, respectively. However, the advantage of the SQA design is debatable for a non-planar bypass grafting.

Moreover, it is important to note that this SQA design provides a spare route for the blood flow to the coronary artery in order to avoid re-operation in case of re-stenosis in either of the anastomoses.

By investigating the effect of the partial flow through the proximal host artery in the case of partially stenosed coronary arteries, the results further confirm the existence of a critical value for stenosis severity, below which the distributions of HPs might be undesirably affected by the competitive flows problem.

Upon varying the design parameters of the anastomotic angle and distance between the STS and ETS components, and comparing the out-of-plane design version with the in-plane design version, the superior design is found to be the planar SQA model with the anastomotic angle of 30° and distance of 30mm.

The acquired experimental results are generally in a fairly good qualitative match with those from the computational simulations. The overall flow fields are qualitatively matched between the simulation and PIV measurement results and the WSS distribution patterns derived from the PIV experiments share similar trends with those of computational simulations. Hence, the in vitro investigation can be considered as a validation for the computational study which can further confirm the beneficial flow-simulation results and the advantages of the novel SQA design over the conventional ETS anastomosis.

The bidirectional coupled FSI simulation results indicate that the velocity patterns and qualitative distribution of WSS parameters do not change significantly in the compliant model despite quite large side-wall deformations in the anastomotic regions. The WSS magnitude is generally reduced in the distensible model, as compared to that in the rigid-wall model, resulting in a lower TAWSS in the compliant model. The wall compliance

has generally decreased the TAWSSG, while it has somewhat increased the oscillatory nature of the flow.

The effect of non-Newtonian rheology on the HPs is found to be heterogeneous. The ETS anastomoses (of both the conventional and SQA models) experience mostly a decrease in the TAWSS (except at the heel), while the STS anastomosis of the SQA model undergoes an increase in this HP. The flow oscillation is decreased at the heel and on the artery bed, whereas it is increased at the toe of the anastomosis, due to the shear thinning behavior of the blood.

It is observed that the effects of wall compliance and non-Newtonian rheology are not independent, and that they influence each other. Hence, it is necessary to investigate the effects of these parameters simultaneously (and not individually) in each particular model.

Although vessel wall compliance and non-Newtonian rheology show modest influence on the HPs in each model, they have unveiled further advantages of the coupled SQA model over the conventional ETS anastomosis, which had not been revealed in the study with the rigid-wall and Newtonian fluid models (for instance, the fact that the TAWSS at the heel of the ETS anastomosis in the SQA model is higher than that in the conventional ETS model). Therefore, it can be concluded that the inclusion of wall compliance and non-Newtonian rheology in flow simulation of blood vessels can be essential in quantitative and comparative analyses. The FSI analysis has further verified the hemodynamic benefits of the blood flow in the coupled SQA configuration in a more realistic bio-mechanical condition.

In conclusion, although the coupled SQA design does involve one additional anastomosis (and prolonged operation time), it brings about some positive features and provides distinct advantages in the flow field and distribution of HPs, including: (i) a more uniform and smooth flow at the ETS anastomosis, without any stagnation point on the artery bed and vortex formation in the heel region of the ETS anastomosis within the coronary artery; (ii) a spare route for the blood flow to the coronary artery, to avoid re-operation in case of re-stenosis in either of the anastomoses; and (iii) improved distribution of hemodynamic parameters at the coronary artery bed and in the heel region of the ETS anastomosis, with more moderate shear stress indices. These may motivate the use of this design over the conventional ETS anastomosis. However, prior to clinical adoption of this novel SQA design, it is necessary to conduct animal studies, in order to find out the biological response and consequences of the employment of this suggested design in vivo.

This investigation has successfully met the original targets and specific aims, defined earlier in Chapter 1, by designing an advantageous configuration for CABG and optimizing its performance by modification of the geometrical parameters involved, validating the CFD simulation results experimentally, and incorporating the effects of vessel wall elasticity and non-Newtonian blood rheology into the simulations.

As mentioned earlier in Chapter 2, optimal anastomosis design must take into account practical issues such as surgical construction, and as reviewed, the available designs of anastomotic configurations which are feasible to be constructed during operation using autogenous materials (including Miller cuff, Taylor patch, and Tyrrell collar) have not shown a remarkable enhancement in patency of bypass grafts. Besides, the available

configurations which have shown considerable improvement in HPs distribution (such as the designs by O'Brien [127] and Walsh [182]) cannot be constructed during operation using autogenous grafts and need to be made of synthetic materials due to their complex geometry (which results in high compliance mismatch at the synthetic graft-blood vessel interface leading to IT formation [11]). Hence, the present study has improved and advanced the current status of this research field by offering a novel design of anastomotic configuration which can be constructed during operation using autogenous materials and at the same time provides distinct advantages in the flow field and distribution of HPs.

6.2 Future works

There are some limitations and a few simplifying assumptions made in the present study. For instance, the cardiac motion is ignored [151, 195]; the geometry of the coronary artery is simplified as a straight tube, and the effects of unevenness of the lumens' inner walls are neglected [84]; the wall mechanics and intramural stresses are not studied, and the focus is only on the blood flow and HPs distribution. Besides, only the distal anastomosis of CABG is taken into consideration.

Hence, a possible direction for future works is to conduct more comprehensive computational simulations, by utilizing complete CABG models with a more realistic geometry of the coronary arteries and grafts, and taking into consideration the study of the wall mechanics and intramural stresses, as well as the effects of compliance mismatch.

However, computational simulations and in vitro measurements can only provide mechanical and not biological responses of the investigated CABG models under various flow conditions. Therefore, in order to move this concept to clinical practice, it is required to perform in vivo animal studies of the suggested SQA design, which can demonstrate the actual outcome of the proposed CABG anastomotic configuration, a resultant of all the mechanical and biological factors involved. For this purpose, animals (such as sheep or pig) with the heart size close to that of human can be utilized and both the conventional ETS and the coupled SQA configurations should be performed on two separate groups. Histological and morphometric analyses can be implemented [22] in both early (eight weeks or less post-implantation [7]) and mid-term (less than one year) stages by sacrificing the animals, followed by measurements and comparison of the intimal thickness at anastomotic sections [96] of the two groups.

References

- [1] Abbott, W. M., Megerman, J., Hasson, J. E., Litalien, G., and Warnock, D. F., 1987, "Effect of compliance mismatch on vascular graft patency," *Journal of Vascular Surgery*, 5(2), pp. 376–382.
- [2] Adrian, R. J., 1991, "Particle-imaging techniques for experimental fluid mechanics," *Annual Review of Fluid Mechanics*, 23(1), pp. 261–304.
- [3] Adrian, R. J., and Yao, C. S., 1985, "Pulsed laser technique application to liquid and gaseous flows and the scattering power of seed materials," *Applied Optics*, 24(1), pp. 44–52.
- [4] Allaire, E., and Clowes, A. W., 1997, "Endothelial cell injury in cardiovascular surgery: The intimal hyperplastic response," *Annals of Thoracic Surgery*, 63(2), pp. 582–591.
- [5] Aoki, T., and Ku, D. N., 1993, "Collapse of diseased arteries with eccentric cross section," *Journal of Biomechanics*, 26(2), pp. 133–142.
- [6] Atabek, H. B., Ling, S. C., and Patel, D. J., 1975, "Analysis of coronary flow fields in thoracotomized dogs," *Circulation Research*, 37(6), pp. 752–761.
- [7] Ballyk, P. D., Walsh, C., Butany, J., and Ojha, M., 1997, "Compliance mismatch may promote graft-artery intimal hyperplasia by altering suture-line stresses," *Journal of Biomechanics*, 31(3), pp. 229–237.
- [8] Ballyk, P. D., Walsh, C., and Ojha, M., 1995, "Effect of intimal thickening on the stress distribution at an end-to-side graft-artery junction," in: Hull, ed. *Advances in Bioengineering*, ASME, San Francisco, CA.
- [9] Bandyk, D. F., Seabrook, G. R., Moldenhauer, P., Lavin, J., Edwards, J., Cato, R., and Towne, J. B., 1988, "Hemodynamics of vein graft stenosis," *Journal of Vascular Surgery*, 8(6), pp. 688–695.
- [10] Bartley, T. D., Bigelow, J. C., and Page, U. S., 1972, "Aortocoronary bypass grafting with multiple sequential anastomoses to a single vein," *Archives of Surgery*, 105(6), pp. 915–917.
- [11] Bassiouny, H. S., White, S., Glagov, S., Choi, E., Giddens, D. P., and Zarins, C. K., 1992, "Anastomotic intimal hyperplasia: Mechanical injury or flow induced," *Journal of Vascular Surgery*, 15(4), pp. 708–717.
- [12] Bates, C. J., O'Doherty, D. M., and Williams, D., 2001, "Flow instabilities in a graft anastomosis: A study of the instantaneous velocity fields," *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, 215(6), pp. 579–587.
- [13] Berne, R. M., and Levy, M. N., 2001, *Cardiovascular Physiology*, Mosby, St. Louis, MO.

- [14] Bertolotti, C., and Deplano, V., 2000, "Three-dimensional numerical simulations of flow through a stenosed coronary bypass," *Journal of Biomechanics*, 33(8), pp. 1011–1022.
- [15] Bertolotti, C., Deplano, V., Fuseri, J., and Dupouy, P., 2001, "Numerical and experimental models of post-operative realistic flows in stenosed coronary bypasses," *Journal of Biomechanics*, 34(8), pp. 1049–1064.
- [16] Bird, R. B., Armstrong, R. C., and Hassager, O., 1987, *Dynamics of polymer liquids*, Wiley, New York.
- [17] Bonert, M., Myers, J. G., Fremes, S., Williams, J., and Ethier, C. R., 2002, "A numerical study of blood flow in coronary artery bypass graft side-to-side anastomoses," *Annals of Biomedical Engineering*, 30(5), pp. 599–611.
- [18] Bourassa, M. G., 1991, "Fate of venous grafts: The past, the present and the future," *Journal of the American College of Cardiology*, 17(5), pp. 1081–1083.
- [19] Brien, T. O., Walsh, M., and McGloughlin, T., 2005, "On reducing abnormal hemodynamics in the femoral end-to-side anastomosis: The influence of mechanical factors," *Annals of Biomedical Engineering*, 33(3), pp. 310–322.
- [20] Brumby, S. A., Petrucco, M. F., Walsh, J. A., and Bond, M. J., 1992, "A retrospective analysis of infra-inguinal arterial reconstruction: Three year patency rates," *Australian and New Zealand Journal of Surgery*, 62(4), pp. 256–260.
- [21] Buchanan, J. R., Kleinstreuer, C., Hyun, S., and Truskey, G. A., 2003, "Hemodynamics simulation and identification of susceptible sites of atherosclerotic lesion formation in a model abdominal aorta," *Journal of Biomechanics*, 36(8), pp. 1185–1196.
- [22] Butany, J. W., David, T. E., and Ojha, M., 1998, "Histological and morphometric analyses of early and late aortocoronary vein grafts and distal anastomoses," *Canadian Journal of Cardiology*, 14(5), pp. 671–677.
- [23] Campeau, L., Enjalbert, M., and Lesperance, J., 1984, "The relation of risk factors to the development of atherosclerosis in saphenous-vein bypass grafts and the progression of disease in the native circulation. A study 10 years after aortocoronary bypass surgery," *New England Journal of Medicine*, 311(21), pp. 1329–1332.
- [24] Caro, C. G., Fitz-Gerald, J. M., and Schroter, R. C., 1971, "Atheroma and arterial wall shear. Observation, correlation and proposal of a shear dependent mass transfer mechanism for atherogenesis," *Proceedings of the Royal Society of London. Series B. Biological sciences*, 177(46), pp. 109–159.
- [25] Carrel, A., and Guthrie, C. C., 1906, "Anastomosis of blood vessels by the patching method and transplantation of the kidney," *Journal of the American Medical Association*, 47, pp. 1648–1651.
- [26] Chang, C. C., and Atabek, H. B., 1961, "The inlet length for oscillatory flow and its effects on the determination of the rate of flow in arteries," *Physics in Medicine and Biology*, 6(2), pp. 303–317.
- [27] Chen, J., Lu, X. Y., and Wang, W., 2006, "Non-Newtonian effects of blood flow on hemodynamics in distal vascular graft anastomoses," *Journal of Biomechanics*, 39(11), pp. 1983–1995.

- [28] Chervu, A., and Moore, W. S., 1990, "An overview of intimal hyperplasia," *Surgery Gynecology & Obstetrics*, 171(5), pp. 433–447.
- [29] Chong, C. K., Rowc, C. S., Sivancsan, S., Rattray, A., Black, R. A., Shortland, A. P., and How, T. V., 1999, "Computer aided design and fabrication of models for in vitro studies of vascular fluid dynamics," *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, 213(1), pp. 1–4.
- [30] Clowes, A. W., and Clowes, M. M., 1980, "The influence of hypertension on injury-induced myointimal thickening," *Surgery*, 88(2), pp. 254–259.
- [31] Clowes, A. W., Kirkman, T. R., and Clowes, M. M., 1986, "Mechanisms of arterial graft failure. II. Chronic endothelial and smooth muscle cell proliferation in healing polytetrafluoroethylene prostheses," *Journal of Vascular Surgery*, 3(6), pp. 877–884.
- [32] Clowes, A. W., Reidy, M. A., and Clowes, M. M., 1983, "Kinetics of cellular proliferation after arterial injury. I. Smooth muscle growth in the absence of endothelium," *Laboratory Investigation*, 49(3), pp. 327–333.
- [33] Cole, J. S., Watterson, J. K., and O'Reilly, M. J. G., 2002, "Numerical investigation of the haemodynamics at a patched arterial bypass anastomosis," *Medical Engineering and Physics*, 24(6), pp. 393–401.
- [34] Cole, J. S., Wijesinghe, L. D., Watterson, J. K., and Scott, D. J. A., 2002, "Computational and experimental simulations of the haemodynamics at cuffed arterial bypass graft anastomoses," *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, 216(2), pp. 135–143.
- [35] Cox, J. L., Chiasson, D. A., and Gotlieb, A. I., 1991, "Stranger in a strange land: The pathogenesis of saphenous vein graft stenosis with emphasis on structural and functional differences between veins and arteries," *Progress in Cardiovascular Diseases*, 34(1), pp. 45–68.
- [36] Davies, M. G., and Hagen, P. O., 1994, "Pathobiology of intimal hyperplasia," *British Journal of Surgery*, 81(9), pp. 1254–1269.
- [37] Davies, P. F., 1995, "Flow-mediated endothelial mechanotransduction," *Physiological Reviews*, 75(3), pp. 519–560.
- [38] DePaola, N., Gimbrone Jr, M. A., Davies, P. F., and Dewey Jr, C. F., 1992, "Vascular endothelium responds to fluid shear stress gradients," *Arteriosclerosis and Thrombosis*, 12(11), pp. 1254–1257.
- [39] Deplano, V., Bertolotti, C., and Boiron, O., 2001, "Numerical simulations of unsteady flows in a stenosed coronary bypass graft," *Medical and Biological Engineering and Computing*, 39(4), pp. 488–499.
- [40] Dilley, R. J., McGeachie, J. K., and Prendergast, F. J., 1988, "A review of the histologic changes in vein-to-artery grafts, with particular reference to intimal hyperplasia," *Archives of Surgery*, 123(6), pp. 691–696.
- [41] Dobrin, P., 1983, "Vascular mechanics," in: J. T. Shepherd, and F. M. Abboud, eds. *Handbook of Physiology, Section 2: The Cardiovascular System, Volume III, Peripheral Circulation and Organ Blood Flow*. M. d. Bethesda: American Physiological Society, pp. 80–83.

- [42] Dobrin, P. B., Littooy, F. N., and Endean, E. D., 1989, "Mechanical factors predisposing to intimal hyperplasia and medial thickening in autogenous vein grafts," *Surgery*, 105(3), pp. 393–400.
- [43] Edwards, G. A., and Roberts, G., 1992, "Development of an ovine collagen-based composite biosynthetic vascular prosthesis," *Clinical Materials*, 9(3-4), pp. 211–223.
- [44] Einav, S., Avidor, J., and Vidne, B., 1985, "Haemodynamics of coronary artery - saphenous vein bypass," *Journal of Biomedical Engineering*, 7(4), pp. 305–309.
- [45] Ethier, C. R., Steinman, D. A., Zhang, X., Karpik, S. R., and Ojha, M., 1998, "Flow waveform effects on end-to-side anastomotic flow patterns," *Journal of Biomechanics*, 31(7), pp. 609–617.
- [46] Fei, D. Y., Thomas, J. D., and Rittgers, S. E., 1994, "The effect of angle and flow rate upon hemodynamics in distal vascular graft anastomoses: A numerical model study," *Journal of Biomechanical Engineering*, 116(3), pp. 331–336.
- [47] Fillinger, M. F., Reinitz, E. R., Schwartz, R. A., Resetarits, D. E., Paskanik, A. M., Bruch, D., and Bredenberg, C. E., 1990, "Graft geometry and venous intimal-medial hyperplasia in arteriovenous loop grafts," *Journal of Vascular Surgery*, 11(4), pp. 556–566.
- [48] FitzGibbon, G. M., Kafka, H. P., Leach, A. J., Keon, W. J., Hooper, G. D., and Burton, J. R., 1996, "Coronary bypass graft fate and patient outcome: Angiographic follow-up of 5,065 grafts related to survival and reoperation in 1,388 patients during 25 years," *Journal of the American College of Cardiology*, 28(3), pp. 616–626.
- [49] Flemma, R. J., Johnson, W. D., and Lepley, D., 1971, "Triple aorto-coronary vein bypass as treatment for coronary insufficiency," *Archives of Surgery*, 103(1), pp. 82–83.
- [50] Frauenfelder, T., Boutsianis, E., Schertler, T., Husmann, L., Leschka, S., Poulikakos, D., Marincek, B., and Alkadhi, H., 2007, "Flow and wall shear stress in end-to-side and side-to-side anastomosis of venous coronary artery bypass grafts," *BioMedical Engineering Online*, 6.
- [51] Frayne, R., Steinman, D. A., Ethier, C. R., and Rutt, B. K., 1995, "Accuracy of MR phase contrast velocity measurements for unsteady flow," *Journal of Magnetic Resonance Imaging*, 5(4), pp. 428–431.
- [52] Friedman, M. H., Bargerion, C. B., Duncan, D. D., Hutchins, G. M., and Mark, F. F., 1992, "Effects of arterial compliance and non-Newtonian rheology on correlations between intimal thickness and wall shear," *Journal of Biomechanical Engineering*, 114(3), pp. 317–320.
- [53] Friedrich, P., and Reininger, A. J., 1995, "Occlusive thrombus formation on indwelling catheters: In vitro investigation and computational analysis," *Thrombosis and Haemostasis*, 73(1), pp. 66–72.
- [54] Fry, D. L., 1968, "Acute vascular endothelial changes associated with increased blood velocity gradients," *Circulation Research*, 22(2), pp. 165–197.
- [55] Furuse, A., Klopp, E. H., Brawley, R. K., and Gott, V. L., 1972, "Hemodynamics of Aorta-to-Coronary Artery Bypass: Experimental and Analytical Studies," *The Annals of Thoracic Surgery*, 14(3), pp. 282–293.
- [56] Gagne, P. J., Martinez, J., DeMassi, R., Gregory, R., Parent, F. N., Gayle, R., Meier Iii, G. H., and Philput, C., 2000, "The effect of a venous anastomosis Tyrell vein collar

on the primary patency of arteriovenous grafts in patients undergoing hemodialysis," *Journal of Vascular Surgery*, 32(6), pp. 1149–1154.

[57] Galjee, M. A., Van Rossum, A. C., Doesburg, T., Hofman, M. B. M., Falke, T. H. M., and Visser, C. A., 1996, "Quantification of coronary artery bypass graft flow by magnetic resonance phase velocity mapping," *Magnetic Resonance Imaging*, 14(5), pp. 485–493.

[58] Galjee, M. A., vanRossum, A. C., Doesburg, T., vanEenige, M. J., and Visser, C. A., 1996, "Value of magnetic resonance imaging in assessing patency and function of coronary artery bypass grafts - An angiographically controlled study," *Circulation*, 93(4), pp. 660–666.

[59] Gentile, A. T., Mills, J. L., Gooden, M. A., Hagerty, R. D., Berman, S. S., Hughes, J. D., Kleinert, L. B., and Williams, S. K., 1998, "Vein patching reduces neointimal thickening associated with prosthetic graft implantation," *American Journal of Surgery*, 176(6), pp. 601–607.

[60] Gijssen, F. J. H., Van De Vosse, F. N., and Janssen, J. D., 1999, "The influence of the non-Newtonian properties of blood on the flow in large arteries: Steady flow in a carotid bifurcation model," *Journal of Biomechanics*, 32(6), pp. 601–608.

[61] Giordana, S., Sherwin, S. J., Peiro, J., Doorly, D. J., Crane, J. S., Lee, K. E., Cheshire, N. J. W., and Caro, C. G., 2005, "Local and global geometric influence on steady flow in distal anastomoses of peripheral bypass grafts," *Journal of Biomechanical Engineering*, 127(7), pp. 1087–1098.

[62] Gradus-Pizlo, I., Bigelow, B., Mahomed, Y., Sawada, S. G., Rieger, K., and Feigenbaum, H., 2003, "Left anterior descending coronary artery wall thickness measured by high-frequency transthoracic and epicardial echocardiography includes adventitia," *American Journal of Cardiology*, 91(1), pp. 27–32.

[63] Greenwald, S. E., and Berry, C. L., 2000, "Improving vascular grafts: The importance of mechanical and haemodynamic properties," *Journal of Pathology*, 190(3), pp. 292–299.

[64] Grondin, C. M., and Limet, R., 1977, "Sequential Anastomoses in Coronary Artery Grafting: Technical Aspects and Early and Late Angiographic Results," *The Annals of Thoracic Surgery*, 23(1), pp. 1–8.

[65] Hakaim, A. G., Nalbandian, M. N., Heller, J. K., Chowla, A. C., and Oldenburg, W. A., 2003, "Improved patency of prosthetic arteriovenous grafts with an acute anastomotic angle and flow diffuser," *Journal of Vascular Surgery*, 37(5), pp. 1032–1035.

[66] Haruguchi, H., and Teraoka, S., 2003, "Intimal hyperplasia and hemodynamic factors in arterial bypass and arteriovenous grafts: A review," *Journal of Artificial Organs*, 6(4), pp. 227–235.

[67] Hasegawa, H., and Kanai, H., 2004, "Measurement of elastic moduli of the arterial wall at multiple frequencies by remote actuation for assessment of viscoelasticity," *Japanese Journal of Applied Physics, Part 1: Regular Papers and Short Notes and Review Papers*, 43(5 B), pp. 3197–3203.

[68] He, X., and Ku, D. N., 1996, "Pulsatile flow in the human left coronary artery bifurcation: Average conditions," *Journal of Biomechanical Engineering*, 118(1), pp. 74–82.

- [69] Henry, F. S., Küpper, C., and Lewington, N. P., 2002, "Simulation of flow through a Miller cuff bypass graft," *Computer methods in biomechanics and biomedical engineering*, 5(3), pp. 207–217.
- [70] Hida, S., Chikamori, T., Hirayama, T., Usui, Y., Yanagisawa, H., Morishima, T., Ishimaru, S., and Yamashina, A., 2003, "Beneficial effect of coronary artery bypass grafting as assessed by quantitative gated single-photon emission computed tomography," *Circulation Journal*, 67(6), pp. 499–504.
- [71] Hofer, M., Rappitsch, G., Perktold, K., Trubel, W., and Schima, H., 1996, "Numerical study of wall mechanics and fluid dynamics in end-to-side anastomoses and correlation to intimal hyperplasia," *Journal of Biomechanics*, 29(10), pp. 1297–1308.
- [72] How, T. V., Rowe, C. S., Gilling-Smith, G. L., and Harris, P. L., 2000, "Interposition vein cuff anastomosis alters wall shear stress distribution in the recipient artery," *Journal of Vascular Surgery*, 31(5), pp. 1008–1017.
- [73] <http://herkules.oulu.fi/isbn951426973X/html/x840.html>.
- [74] http://www.medicinenet.com/coronary_artery_bypass_graft/article.htm.
- [75] http://www.medicinenet.com/coronary_artery_bypass_graft/page4.htm.
- [76] Hughes, P. E., and How, T. V., 1995, "Flow structures at the proximal side-to-end anastomosis. Influence of geometry and flow division," *Journal of Biomechanical Engineering*, 117(2), pp. 224–236.
- [77] Hughes, P. E., and How, T. V., 1996, "Effects of geometry and flow division on flow structures in models of the distal end-to-side anastomosis," *Journal of Biomechanics*, 29(7), pp. 855–872.
- [78] Hughes, T. J. R., Liu, W. K., and Zimmermann, T. K., 1981, "Lagrangian-Eulerian finite element formulation for incompressible viscous flows," *Computer Methods in Applied Mechanics and Engineering*, 29(3), pp. 329–349.
- [79] Hyun, S., Kleinstreuer, C., and Archie Jr, J. P., 2000, "Hemodynamics analyses of arterial expansions with implications to thrombosis and restenosis," *Medical Engineering and Physics*, 22(1), pp. 13–27.
- [80] Ip, J. H., Fuster, V., Badimon, L., Badimon, J., Taubman, M. B., and Chesebro, J. H., 1990, "Syndromes of accelerated atherosclerosis: Role of vascular injury and smooth muscle cell proliferation," *Journal of the American College of Cardiology*, 15(7), pp. 1667–1687.
- [81] Ishibashi, H., Sunamura, M., and Karino, T., 1995, "Flow patterns and preferred sites of intimal thickening in end-to-end anastomosed vessels," *Surgery*, 117(4), pp. 409–420.
- [82] Jackson, Z. S., Ishibashi, H., Gotlieb, A. I., and Lowell Langille, B., 2001, "Effects of anastomotic angle on vascular tissue responses at end-to-side arterial grafts," *Journal of Vascular Surgery*, 34(2), pp. 300–307.
- [83] Kabinejadian, F., Chua, L. P., Ghista, D. N., Sankaranarayanan, M., and Tan, Y. S., 2010, "A novel coronary artery bypass graft design of sequential anastomoses," *Annals of Biomedical Engineering*, 38(10), pp. 3135–3150.
- [84] Kabinejadian, F., Chua, L. P., Ghista, D. N., and Tan, Y. S., 2010, "CABG models flow simulation study on the effects of valve remnants in the venous graft," *Journal of Mechanics in Medicine and Biology*, 10(4), pp. 593–609.

- [85] Kabinejadian, F. and Ghista, D. N., 2011, "Compliant model of a coupled sequential coronary arterial bypass graft: Effects of vessel wall elasticity and non-Newtonian rheology on blood flow regime and hemodynamic parameters distribution," *Medical Engineering and Physics*, in press.
- [86] Kakos, G. S., Sabiston, D. C., Hagen, P. O., Davis, R. W., Dixon, S. H., and Oldham, H. N., 1972, "Coronary artery hemodynamics after aorto-coronary artery vein bypass. An experimental evaluation," *Journal of Thoracic and Cardiovascular Surgery*, 63(6), pp. 849–853.
- [87] Karri, S., Charonko, J., and Vlachos, P. P., 2009, "Robust wall gradient estimation using radial basis functions and proper orthogonal decomposition (POD) for particle image velocimetry (PIV) measured fields," *Measurement Science and Technology*, 20(4).
- [88] Katritsis, D., Kaiktsis, L., Chaniotis, A., Pantos, J., Efstathopoulos, E. P., and Marmarelis, V., 2007, "Wall Shear Stress: Theoretical Considerations and Methods of Measurement," *Progress in Cardiovascular Diseases*, 49(5), pp. 307–329.
- [89] Keynton, R. S., Evancho, M. M., Sims, R. L., Rodway, N. V., Gobin, A., and Rittgers, S. E., 2001, "Intimal hyperplasia and wall shear in arterial bypass graft distal anastomoses: An in vivo model study," *Journal of Biomechanical Engineering*, 123(5), pp. 464–473.
- [90] Kissin, M., Kansal, N., Pappas, P. J., DeFouw, D. O., Durán, W. N., and Hobson II, R. W., 2000, "Vein interposition cuffs decrease the intimal hyperplastic response of polytetrafluoroethylene bypass grafts," *Journal of Vascular Surgery*, 31(1 I), pp. 69–83.
- [91] Kleinstreuer, C., Nazemi, M., and Archie, J. P., 1991, "Hemodynamics analysis of a stenosed carotid bifurcation and its plaque-mitigating design," *Journal of Biomechanical Engineering*, 113(Compendex), pp. 330–335.
- [92] Koshiba, N., Ando, J., Chen, X., and Hisada, T., 2007, "Multiphysics simulation of blood flow and LDL transport in a porohyperelastic arterial wall model," *Journal of Biomechanical Engineering*, 129(3), pp. 374–385.
- [93] Kraiss, L. W., Geary, R. L., Mattsson, E. J. R., Vergel, S., Au, Y. P. T., and Clowes, A. W., 1996, "Acute reductions in blood flow and shear stress induce platelet-derived growth factor- α expression in baboon prosthetic grafts," *Circulation Research*, 79(1), pp. 45–53.
- [94] Ku, D. N., Giddens, D. P., Zarins, C. K., and Glagov, S., 1985, "Pulsatile flow and atherosclerosis in the human carotid bifurcation. Positive correlation between plaque location and low and oscillating shear stress," *Arteriosclerosis*, 5(3), pp. 293–302.
- [95] Kute, S. M., and Vorp, D. A., 2001, "The effect of proximal artery flow on the hemodynamics at the distal anastomosis of a vascular bypass graft: Computational study," *Journal of Biomechanical Engineering*, 123(3), pp. 277–283.
- [96] Leask, R. L., Butany, J., Johnston, K. W., Ethier, C. R., and Ojha, M., 2005, "Human saphenous vein coronary artery bypass graft morphology, geometry and hemodynamics," *Annals of Biomedical Engineering*, 33(3), pp. 301–309.
- [97] Lee, C. S., and Tarbell, J. M., 1997, "Wall shear rate distribution in an abdominal aortic bifurcation model: Effects of vessel compliance and phase angle between pressure and flow waveforms," *Journal of Biomechanical Engineering*, 119(3), pp. 333–342.

- [98] Lei, M., Archie, J. P., and Kleinstreuer, C., 1997, "Computational design of a bypass graft that minimizes wall shear stress gradients in the region of the distal anastomosis," *Journal of Vascular Surgery*, 25(4), pp. 637–646.
- [99] Lei, M., Giddens, D. P., Jones, S. A., Loth, F., and Bassiouny, H., 2001, "Pulsatile flow in an end-to-side vascular graft model: Comparison of computations with experimental data," *Journal of Biomechanical Engineering*, 123(1), pp. 80–87.
- [100] Lei, M., Kleinstreuer, C., and Archie, J. P., 1997, "Hemodynamic simulations and computer-aided design of graft-artery junctions," *Journal of Biomechanical Engineering*, 119(3), pp. 343–348.
- [101] Lei, M., Kleinstreuer, C., and Archie Jr, J. P., 1996, "Geometric design improvements for femoral graft-artery junctions mitigating restenosis," *Journal of Biomechanics*, 29(12), pp. 1605–1614.
- [102] Lei, M., Kleinstreuer, C., and Truskey, G. A., 1995, "Numerical investigation and prediction of atherogenic sites in branching arteries," *Journal of Biomechanical Engineering*, 117(3), pp. 350–357.
- [103] Lei, M., Kleinstreuer, C., and Truskey, G. A., 1996, "A focal stress gradient-dependent mass transfer mechanism for atherogenesis in branching arteries," *Medical Engineering and Physics*, 18(4), pp. 326–332.
- [104] Lemson, M. S., Tordoir, J. H. M., Van Det, R. J., Welten, R. J. T. J., Burger, H., Estourgie, R. J. A., Stroecken, H. J. G., and Leunissen, K. M. L., 2000, "Effects of a venous cuff at the venous anastomosis of polytetrafluoroethylene grafts for hemodialysis vascular access," *Journal of Vascular Surgery*, 32(6), pp. 1155–1163.
- [105] Leuprecht, A., Perktold, K., Prosi, M., Berk, T., Trubel, W., and Schima, H., 2002, "Numerical study of hemodynamics and wall mechanics in distal end-to-side anastomoses of bypass grafts," *Journal of Biomechanics*, 35(2), pp. 225–236.
- [106] Li, X. M., and Rittgers, S. E., 1999, "Hemodynamic factors at the distal end-to-side anastomosis of a bypass graft with different POS:DOS ratios," *American Society of Mechanical Engineers, Bioengineering Division (Publication) BED*, 42, pp. 225–226.
- [107] Li, X. M., and Rittgers, S. E., 2001, "Hemodynamic factors at the distal end-to-side anastomosis of a bypass graft with different POS:DOS flow ratios," *Journal of Biomechanical Engineering*, 123(3), pp. 270–276.
- [108] Liu, M. W., Roubin, G. S., and King III, S. B., 1989, "Restenosis after coronary angioplasty: Potential biologic determinants and role of intimal hyperplasia," *Circulation*, 79(6), pp. 1374–1387.
- [109] Lloyd-Jones, D., Adams, R. J., Brown, T. M., Carnethon, M., Dai, S., De Simone, G., Ferguson, T. B., Ford, E., Furie, K., Gillespie, C., Go, A., Greenlund, K., Haase, N., Hailpern, S., Ho, P. M., Howard, V., Kissela, B., Kittner, S., Lackland, D., Lisabeth, L., Marelli, A., McDermott, M. M., Meigs, J., Mozaffarian, D., Mussolino, M., Nichol, G., Roger, V. L., Rosamond, W., Sacco, R., Sorlie, P., Stafford, R., Thom, T., Wasserthiel-Smoller, S., Wong, N. D., and Wylie-Rosett, J., 2010, "Executive summary: Heart disease and stroke statistics-2010 update: A report from the american heart association," *Circulation*, 121(7), pp. e46–e215.
- [110] LoGerfo, F. W., Quist, W. C., and Nowak, M. D., 1983, "Downstream anastomotic hyperplasia. A mechanism of failure in Dacron® arterial grafts," *Annals of Surgery*, 197(4), pp. 479–483.

- [111] Longest, P. W., and Kleinstreuer, C., 2000, "Computational haemodynamics analysis and comparison study of arterio-venous grafts," *Journal of Medical Engineering and Technology*, 24(3), pp. 102–110.
- [112] Longest, P. W., Kleinstreuer, C., and Archie Jr, J. P., 2003, "Particle hemodynamics analysis of Miller cuff arterial anastomosis," *Journal of Vascular Surgery*, 38(6), pp. 1353–1362.
- [113] Longest, P. W., Kleinstreuer, C., and Deanda, A., 2005, "Numerical simulation of wall shear stress and particle-based hemodynamic parameters in pre-cuffed and streamlined end-to-side anastomoses," *Annals of Biomedical Engineering*, 33(12 SPEC. ISS.), pp. 1752–1766.
- [114] Loth, F., Fischer, P. F., and Bassiouny, H. S., 2008, "Blood flow in end-to-side anastomoses," *Annual Review of Fluid Mechanics*, 40, pp. 367–393.
- [115] Loth, F., Jones, S. A., Zarins, C. K., Giddens, D. P., Nassar, R. F., Glagov, S., and Bassiouny, H. S., 2002, "Relative contribution of wall shear stress and injury in experimental intimal thickening at PTFE end-to-side arterial anastomoses," *Journal of Biomechanical Engineering*, 124(1), pp. 44–51.
- [116] Lou, Z., Yand, W. J., and Stein, P. D., 1993, "Errors in the estimation of arterial wall shear rates that result from curve fitting of velocity profiles," *Journal of Biomechanics*, 26(4-5), pp. 383–390.
- [117] Masaryk, A. M., Frayne, R., Unal, O., Krupinski, E., and Strother, C. M., 1999, "In vitro and in vivo comparison of three MR measurement methods for calculating vascular shear stress in the internal carotid artery," *American Journal of Neuroradiology*, 20(2), pp. 237–245.
- [118] Melling, A., 1997, "Tracer particles and seeding for particle image velocimetry," *Measurement Science and Technology*, 8(12), pp. 1406–1416.
- [119] Miller, J. H., Foreman, R. K., Ferguson, L., and Faris, I., 1984, "Interposition vein cuff for anastomosis of prosthesis to small artery," *Australian and New Zealand Journal of Surgery*, 54(3), pp. 283–285.
- [120] Moore, S., Friedman, R. J., and Singal, D. P., 1976, "Inhibition of injury induced thromboatherosclerotic lesions by anti platelet serum in rabbits," *THROMB.DIATHES.HAEMORRH.*, 35(1), pp. 70–81.
- [121] Morinaga, K., Okadome, K., and Kuroki, M., 1985, "Effect of wall shear stress on intimal thickening of arterially transplanted autogenous veins in dogs," *Journal of Vascular Surgery*, 2(3), pp. 430–433.
- [122] Nazemi, M., Kleinstreuer, C., Archie, J. P., and Sorrell, F. Y., 1989, "Fluid flow and plaque formation in an aortic bifurcation," *Journal of Biomechanical Engineering-Transactions of the Asme*, 111(4), pp. 316–324.
- [123] Nazemi, M., Kleinstreuer, C., and Archie Jr, J. P., 1990, "Pulsatile two-dimensional flow and plaque formation in a carotid artery bifurcation," *Journal of Biomechanics*, 23(10), pp. 1031–1037.
- [124] Nerem, R. M., 1992, "Vascular fluid mechanics, the arterial wall, and atherosclerosis," *Journal of Biomechanical Engineering*, 114(3), pp. 274–282.
- [125] Nichols, W. W., and O'Rourke, M. F., 1990, *McDonald's Blood Flow in Arteries. Theoretical, Experimental and Clinical Principles*, Edward Arnold, London

- [126] Norberto, J. J., Sidawy, A. N., Trad, K. S., Jones, B. A., Neville, R. F., Najjar, S. F., Sidawy, M. K., and DePalma, R. G., 1995, "The protective effect of vein cuffed anastomoses is not mechanical in origin," *Journal of Vascular Surgery*, 21(4), pp. 558–566.
- [127] O'Brien, T. P., Grace, P., Walsh, M., Burke, P., and McGloughlin, T., 2005, "Computational investigations of a new prosthetic femoral-popliteal bypass graft design," *Journal of Vascular Surgery*, 42(6), pp. 1169–1175.
- [128] Ojha, M., 1993, "Spatial and temporal variations of wall shear stress within an end-to-side arterial anastomosis model," *Journal of Biomechanics*, 26(12), pp. 1377–1388.
- [129] Ojha, M., 1994, "Wall shear stress temporal gradient and anastomotic intimal hyperplasia," *Circulation Research*, 74(6), pp. 1227–1231.
- [130] Ojha, M., Cobbold, R. S. C., and Johnston, K. W., 1994, "Influence of angle on wall shear stress distribution for an end-to-side anastomosis," *Journal of Vascular Surgery*, 19(6), pp. 1067–1073.
- [131] Oneill, M. J., Wolf, P. D., Oneill, T. K., Montesano, R. M., and Waldhausen, J. A., 1981, "A rationale for the use of sequential coronary artery bypass grafts," *Journal of Thoracic and Cardiovascular Surgery*, 81(5), pp. 686–690.
- [132] Ouriel, K., Donayre, C., Shortell, C. K., Cimino, C., Donnelly, J., Oxley, D., and Green, R. M., 1991, "The hemodynamics of thrombus formation in arteries," *Journal of Vascular Surgery*, 14(6), pp. 757–763.
- [133] Papaharilaou, Y., Doorly, D. J., and Sherwin, S. J., 2002, "The influence of out-of-plane geometry on pulsatile flow within a distal end-to-side anastomosis," *Journal of Biomechanics*, 35(9), pp. 1225–1239.
- [134] Passerini, A. G., Milsted, A., and Rittgers, S. E., 2003, "Shear stress magnitude and directionality modulate growth factor gene expression in preconditioned vascular endothelial cells," *Journal of Vascular Surgery*, 37(1), pp. 182–190.
- [135] Patel, D. J., and Fry, D. L., 1964, "In situ pressure-radius-length measurements in ascending aorta of anesthetized dogs," *Journal of Applied Physiology* 19(3), pp. 413–416.
- [136] Peacock, J., Jones, T., Tock, C., and Lutz, R., 1998, "The onset of turbulence in physiological pulsatile flow in a straight tube," *Experiments in Fluids*, 24(1), pp. 1–9.
- [137] Perktold, K., Leuprecht, A., Prosi, M., Berk, T., Czerny, M., Trubel, W., and Schima, H., 2002, "Fluid dynamics, wall mechanics, and oxygen transfer in peripheral bypass anastomoses," *Annals of Biomedical Engineering*, 30(4), pp. 447–460.
- [138] Perktold, K., and Rappitsch, G., 1993, "Numerical analysis of arterial wall mechanics and local blood flow phenomena," in: J. M. E. Tarbell, ed. *Advances in Bioengineering*, ASME, New York, pp. 127–130.
- [139] Perktold, K., and Rappitsch, G., 1995, "Computer simulation of local blood flow and vessel mechanics in a compliant carotid artery bifurcation model," *Journal of Biomechanics*, 28(7), pp. 845–856.
- [140] Pietrabissa, R., Inzoli, F., and Fumero, R., 1990, "Simulation study of the fluid dynamics of aorto-coronary bypass," *Journal of Biomedical Engineering*, 12(5), pp. 419–424.

- [141] Politis, A. K., Stavropoulos, G. P., Christolis, M. N., Panagopoulos, P. G., Vlachos, N. S., and Markatos, N. C., 2008, "Numerical modelling of simulated blood flow in idealized composite arterial coronary grafts: Transient flow," *Journal of Biomechanics*, 41(1), pp. 25–39.
- [142] Qiao, A., and Liu, Y., 2006, "Influence of graft-host diameter ratio on the hemodynamics of CABG," *Bio-Medical Materials and Engineering*, 16(3), pp. 189–201.
- [143] Raffel, M., Willert, C. E., Wereley, S. T., and Kompenhans, J., 2007, *Particle Image Velocimetry*, Springer-Verlag, Berlin.
- [144] Raptis, S., and Miller, J. H., 1995, "Influence of a vein cuff on polytetrafluoroethylene grafts for primary femoropopliteal bypass," *British Journal of Surgery*, 82(4), pp. 487–491.
- [145] Reininger, A. J., Heinzmann, U., Reininger, C. B., Friedrich, P., and Wurzing, L. J., 1994, "Flow mediated fibrin thrombus formation in an endothelium-lined model of arterial branching," *Thrombosis Research*, 74(6), pp. 629–641.
- [146] Rihal, C. S., Raco, D. L., Gersh, B. J., and Yusuf, S., 2003, "Indications for Coronary Artery Bypass Surgery and Percutaneous Coronary Intervention in Chronic Stable Angina: Review of the Evidence and Methodological Considerations," *Circulation*, 108(20), pp. 2439–2445.
- [147] Rittgers, S. E., Karayannacos, P. E., and Guy, J. F., 1978, "Velocity distribution and intimal proliferation in autologous vein grafts in dogs," *Circulation Research*, 42(6), pp. 792–801.
- [148] Ross, R., 1993, "The pathogenesis of atherosclerosis: A perspective for the 1990s," *Nature*, 362(6423), pp. 801–809.
- [149] Salzar, R. S., Thubrikar, M. J., and Eppink, R. T., 1995, "Pressure-induced mechanical stress in the carotid artery bifurcation: A possible correlation to atherosclerosis," *Journal of Biomechanics*, 28(11), pp. 1333–1340.
- [150] Sankaranarayanan, M., Ghista, D. N., Chua, L. P., Tan, Y. S., Sundaravadivelu, K., and Kassab, G. S., in press, "Blood Flow in an Out-of-Plane Aorto-left Coronary Sequential Bypass Graft," in: J. M. Guccione, G. S. Kassab, and M. Ratcliffe, eds. *Computational Cardiovascular Mechanics: Modeling and Applications in Heart Failure*, Springer-Verlag, New York.
- [151] Santamarina, A., Weydahl, E., Siegel Jr, J. M., and Moore Jr, J. E., 1998, "Computational analysis of flow in a curved tube model of the coronary arteries: Effects of time-varying curvature," *Annals of Biomedical Engineering*, 26(6), pp. 944–954.
- [152] Scarano, F., and Riethmuller, M. L., 1999, "Iterative multigrid approach in PIV image processing with discrete window offset," *Experiments in Fluids*, 26(6), pp. 513–523.
- [153] Schaar, J. A., Regar, E., Mastik, F., McFadden, E. P., Saia, F., Disco, C., De Korte, C. L., De Feyter, P. J., Van Der Steen, A. F. W., and Serruys, P. W., 2004, "Incidence of high-strain patterns in human coronary arteries: Assessment with three-dimensional intravascular palpography and correlation with clinical presentation," *Circulation*, 109(22), pp. 2716–2719.
- [154] Schlichting, H., 1979, *Boundary-Layer Theory*, McGraw-Hill, New York.

- [155] Shaaban, A. M., and Duerinckx, A. J., 2000, "Wall shear stress and early atherosclerosis: A review," *American Journal of Roentgenology*, 174(6), pp. 1657–1665.
- [156] Shah, P. J., Gordon, I., Fuller, J., Seevanayagam, S., Rosalion, A., Tatoulis, J., Raman, J. S., and Buxton, B. F., 2003, "Factors affecting saphenous vein graft patency: Clinical and angiographic study in 1402 symptomatic patients operated on between 1977 and 1999," *Journal of Thoracic and Cardiovascular Surgery*, 126(6), pp. 1972–1977.
- [157] Shahcheraghi, N., Dwyer, H. A., Cheer, A. Y., Barakat, A. I., and Rutaganira, T., 2002, "Unsteady and three-dimensional simulation of blood flow in the human aortic arch," *Journal of Biomechanical Engineering-Transactions of the Asme*, 124(4), pp. 378–387.
- [158] Sherwin, S. J., Shah, O., Doorly, D. J., Peiró, J., Papaharilaou, Y., Watkins, N., Caro, C. G., and Dumoulin, C. L., 2000, "The influence of out-of-plane geometry on the flow within a distal end- to-side anastomosis," *Journal of Biomechanical Engineering*, 122(1), pp. 86–95.
- [159] Siouffi, M., Deplano, V., and Pélissier, R., 1998, "Experimental analysis of unsteady flows through a stenosis," *Journal of Biomechanics*, 31(1), pp. 11–19.
- [160] Smith S.C, Jr., Dove, J. T., Jacobs, A. K., Kennedy, J. W., Kereiakes, D., Kern, M. J., Kuntz, R. E., Popma, J. J., Schaff, H. V., Williams, D. O., Gibbons, R. J., Alpert, J. P., Eagle, K. A., Faxon, D. P., Fuster, V., Gardner, T. J., Gregoratos, G., and Russell, R. O., 2001, "ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines) - Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1993 Guidelines for Percutaneous Transluminal Coronary angioplasty) Endorsed by the society for Cardiac Angiography and Interventions," *Circulation*, 103(24), pp. 3019–3041.
- [161] Sottiurai, V. S., 1999, "Distal anastomotic intimal hyperplasia: Histocytomorphology, pathophysiology, etiology, and prevention," *International Journal of Angiology*, 8(1), pp. 1–10.
- [162] Sottiurai, V. S., Lim Sue, S., Feinberg Ii, E. L., Bringaze, W. L., Tran, A. T., and Batson, R. C., 1988, "Distal anastomotic intimal hyperplasia: Biogenesis and etiology," *European Journal of Vascular Surgery*, 2(4), pp. 245–256.
- [163] Sottiurai, V. S., Yao, J. S. T., Batson, R. C., Sue, S. L., Jones, R., and Nakamura, Y. A., 1989, "Distal anastomotic intimal hyperplasia: Histopathologic character and biogenesis," *Annals of Vascular Surgery*, 3(1), pp. 26–33.
- [164] Speziale, G., 2001, "Competitive Flow and Steal Phenomenon in Coronary Surgery," in: *Intraoperative Graft Patency Verification in Cardiac and Vascular Surgery*, Futura Publishing, New York.
- [165] Staalsen, N. H., 1995, "The anastomosis angle does change the flow fields at vascular end-to-side anastomoses in vivo," *Journal of Vascular Surgery*, 21(3), pp. 460–471.
- [166] Staalsen, N. H., Ulrich, M., Kim, W. Y., Pedersen, E. M., How, T. V., and Hasenkam, J. M., 1995, "In vivo analysis and three-dimensional visualisation of blood flow patterns at vascular end-to-side anastomoses," *European Journal of Vascular and Endovascular Surgery*, 10(2), pp. 168–181.

- [167] Steinman, D. A., and Ethier, C. R., 1994, "The effect of wall distensibility on flow in a two-dimensional end-to-side anastomosis," *Journal of Biomechanical Engineering*, 116(3), pp. 294–301.
- [168] Stonebridge, P. A., Prescott, R. J., and Ruckley, C. V., 1997, "Randomized trial comparing infrainguinal polytetrafluoroethylene bypass grafting with and without vein interposition cuff at the distal anastomosis," *Journal of Vascular Surgery*, 26(4), pp. 543–550.
- [169] Suggs, W. D., Hendriques, H. F., and DePalma, R. G., 1988, "Vein cuff interposition prevents juxta-anastomotic neointimal hyperplasia," *Annals of Surgery*, 207(6), pp. 717–723.
- [170] Sunamura, M., Ishibashi, H., and Karino, T., 2007, "Flow patterns and preferred sites of intimal thickening in diameter-mismatched vein graft interpositions," *Surgery*, 141(6), pp. 764–776.
- [171] Szilagyi, D. E., Elliott, J. P., and Hageman, J. H., 1973, "Biologic fate of autogenous vein implants as arterial substitutes: Clinical, angiographic and histopathologic observations in femoro popliteal operations for atherosclerosis," *Annals of Surgery*, 178(3), pp. 232–246.
- [172] Tang, D., Yang, C., Kobayashi, S., Zheng, J., and Vito, R. P., 2003, "Effect of stenosis asymmetry on blood flow and artery compression: A three-dimensional fluid-structure interaction model," *Annals of Biomedical Engineering*, 31(10), pp. 1182–1193.
- [173] Taylor, R. S., Loh, A., McFarland, R. J., Cox, M., and Chester, J. F., 1992, "Improved technique for polytetrafluoroethylene bypass grafting: Long-term results using anastomotic vein patches," *British Journal of Surgery*, 79(4), pp. 348–354.
- [174] Torii, R., Wood, N. B., Hadjiloizou, N., Dowsey, A. W., Wright, A. R., Hughes, A. D., Davies, J., Francis, D. P., Mayet, J., Yang, G. Z., Thom, S. A. M., and Xu, X. Y., 2009, "Fluid-structure interaction analysis of a patient-specific right coronary artery with physiological velocity and pressure waveforms," *Communications in Numerical Methods in Engineering*, 25(5), pp. 565–580.
- [175] Trubel, W., Moritz, A., Schima, H., Raderer, F., Scherer, R., Ullrich, R., Losert, U., and Polterauer, P., 1994, "Compliance and formation of distal anastomotic intimal hyperplasia in Dacron mesh tube constricted veins used as arterial bypass grafts," *ASAIO Journal*, 40(3), pp. M273–M278.
- [176] Tyrrell, M. R., and Wolfe, J. H. N., 1991, "New prosthetic venous collar anastomotic technique: Combining the best of other procedures," *British Journal of Surgery*, 78(8), pp. 1016–1017.
- [177] Virmani, R., Kolodgie, F. D., Burke, A. P., Farb, A., and Schwartz, S. M., 2000, "Lessons from sudden coronary death - A comprehensive morphological classification scheme for atherosclerotic lesions," *Arteriosclerosis Thrombosis and Vascular Biology*, 20(5), pp. 1262–1275.
- [178] Vorp, D. A., Raghavan, M. L., Borovetz, H. S., Greisler, H. P., and Webster, M. W., 1995, "Modeling the transmural stress distribution during healing of bioresorbable vascular prostheses," *Annals of Biomedical Engineering*, 23(2), pp. 178–188.
- [179] Vural, K. M., Sener, E., and Tasdemir, O., 2001, "Long-term patency of sequential and individual saphenous vein coronary bypass grafts," *European Journal of Cardio-Thoracic Surgery*, 19(2), pp. 140–144.

- [180] Waller, B., and Schlant, R., 1986, "Anatomy of the Heart," in: Hurst's the Heart, McGraw-Hill, London.
- [181] Walsh, M., McGloughlin, T., Liepsch, D. W., O'Brien, T., Morris, L., and Ansari, A. R., 2003, "On using experimentally estimated wall shear stresses to validate numerically predicted results," *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, 217(2), pp. 77–90.
- [182] Walsh, M. T., McGloughlin, T. M., and Grace, P., "A Vascular Graft ", U. S. Patent US7651526B2, 2010.
- [183] Wang, D. M., and Tarbell, J. M., 1995, "Nonlinear analysis of oscillatory flow, with a nonzero mean, in an elastic tube (artery)," *Journal of Biomechanical Engineering*, 117(1), pp. 127–135.
- [184] Wesly, R. L. R., Vaishnav, R. N., Fuchs, J. C. A., and et al., 1975, "Static linear and nonlinear elastic properties of normal and arterialized venous tissue in dog and man," *Circulation Research*, 37(4), pp. 509–520.
- [185] White, S. S., Zarins, C. K., Giddens, D. P., Bassiouny, H., Loth, F., Jones, S. A., and Glagov, S., 1993, "Hemodynamic patterns in two models of end-to-side vascular graft anastomoses: Effects of pulsatility, flow division, Reynolds number, and hood length," *Journal of Biomechanical Engineering*, 115(1), pp. 104–111.
- [186] Whittemore, A. D., Clowes, A. W., COUCH, N. P., and MANNICK, J. A., 1981, "Secondary femoro-popliteal reconstruction," *Annals of Surgery*, 193, pp. 35–42.
- [187] Wiesner, T. F., Levesque, M. J., Rooz, E., and Nerem, R. M., 1988, "Epicardial coronary blood flow including the presence of stenoses and aorto-coronary bypasses II: Experimental comparison and parametric investigations," *Journal of Biomechanical Engineering*, 110(2), pp. 144–149.
- [188] Wijesinghe, L. D., Mahmood, T., and Scott, D. J. A., 1999, "Axial flow fields in cuffed end-to-side anastomoses: Effect of angle and disease progression," *European Journal of Vascular and Endovascular Surgery*, 18(3), pp. 240–244.
- [189] Willert, C. E., and Gharib, M., 1991, "Digital particle image velocimetry," *Experiments in Fluids*, 10(4), pp. 181–193.
- [190] Womersley, J. R., 1955, "Method for the calculation of velocity, rate of flow and viscous drag in arteries when the pressure gradient is known," *The Journal of physiology*, 127(3), pp. 553–563.
- [191] Yasuura, K., Takagi, Y., Ohara, Y., Takami, Y., Matsuura, A., and Okamoto, H., 2000, "Theoretical analysis of right gastroepiploic artery grafting to right coronary artery," *The Annals of Thoracic Surgery*, 69(3), pp. 728–731.
- [192] Zahab, Z. E., Divo, E., and Kassab, A., 2010, "Minimisation of the wall shear stress gradients in bypass grafts anastomoses using meshless CFD and genetic algorithms optimisation," *Computer methods in biomechanics and biomedical engineering*, 13(1), pp. 35–47.
- [193] Zamir, M., 2000, *The Physics of Pulsatile Flow*, Springer-Verlag, New York.
- [194] Zeng, D., Boutsianis, E., Ammann, M., Boomsma, K., Wildermuth, S., and Poulikakos, D., 2008, "A study on the compliance of a right coronary artery and its impact on wall shear stress," *Journal of Biomechanical Engineering*, 130(4), pp. 1–11.

[195] Zeng, D., Ding, Z., Friedman, M. H., and Ross Ethier, C., 2003, "Effects of cardiac motion on right coronary artery hemodynamics," *Annals of Biomedical Engineering*, 31(4), pp. 420–429.

Appendix A – User Defined Function

The user defined function (UDF) provided to implement the time-varying velocity profile (Womersley solution) at the inlet of the models within FLUENT is enclosed in this appendix.

```
#include "udf.h"
#define ww 6.98131700797732          /* ww is the angular frequency */
#define R 0.002                     /* R is the graft radius */
#define mu 0.00408                  /* mu is the dynamic viscosity */
#define ss 1.796662e+006
DEFINE_PROFILE(x_unsteady_velocity, thread, position)

{
    face_t f;
    int m,n,k;
    real x[ND_ND];
    real F;
    real
    z,y,ratio,u,sum,KK,sum1real,sum1img,sum2real,sum2img,sub2,sub1,sub3,sum3real,sum
    3img,tt,ttt,
        sss,RR;
    real upreal,upimg,downreal,downimg,aareal,aaimg,bbimg,bbreal,rreal,last,an,coos,siin;
    real bb[100][2];
    real t=CURRENT_TIME;
    tt=ww*t;                          /* tt is the current phase */

    /* the following are the Fourier coefficients */
    bb[0][0]=5.85645;
    bb[1][0]=-0.9246;  bb[1][1]=-0.00645;
    bb[2][0]=-0.73508;  bb[2][1]=-1.06853;
    bb[3][0]=-1.11255;  bb[3][1]=-0.14543;
    bb[4][0]=-0.03458;  bb[4][1]=-0.09495;
    bb[5][0]=-0.27608;  bb[5][1]=-0.40193;
    bb[6][0]=-0.06248;  bb[6][1]=0.06435;
```

```

bb[7][0]=.158475; bb[7][1]=-0.16463;
bb[8][0]=-0.07928; bb[8][1]=-0.08903;
bb[9][0]=-0.0051; bb[9][1]=0.031425;
bb[10][0]=-0.01163; bb[10][1]=-0.01973;
bb[11][0]=-0.03053; bb[11][1]=-0.00585;
bb[12][0]=-0.0327; bb[12][1]=0.011625;
bb[13][0]=0.0174; bb[13][1]=0.025575;
bb[14][0]=0.00435; bb[14][1]=-0.02213;
bb[15][0]=-0.02648; bb[15][1]=0.0261;
bb[16][0]=0.00675; bb[16][1]=0.01515;
bb[17][0]=-0.021; bb[17][1]=-0.00263;
bb[18][0]=-0.0195; bb[18][1]=0;
bb[19][0]=-0.01688; bb[19][1]=0.001875;
bb[20][0]=0.0045; bb[20][1]=-0.00975;
bb[21][0]=-0.01433; bb[21][1]=-0.0132;
bb[22][0]=0.00165; bb[22][1]=0.00885;
bb[23][0]=0.005025; bb[23][1]=-0.00818;
bb[24][0]=-0.0069; bb[24][1]=-0.00255;
bb[25][0]=-0.00585; bb[25][1]=0.000525;
bb[26][0]=-0.0015; bb[26][1]=0.00225;
bb[27][0]=-0.00143; bb[27][1]=-0.00315;
bb[28][0]=-0.00645; bb[28][1]=0.007875;
bb[29][0]=0.0078; bb[29][1]=0.00975;
bb[30][0]=-0.00173; bb[30][1]=-0.00255;
bb[31][0]=-0.0069; bb[31][1]=0.010425;
bb[32][0]=0.000225; bb[32][1]=0.0009;

```

```

begin_f_loop(f, thread)
{
  F_CENTROID(x,f,thread);
  sum=0;
  z=x[2];
  y=x[1];
  RR=sqrt(z*z+y*y)/R; /* RR is the normalized radius */

  if(RR>1.0)
  {
    ratio=1;
  }
  if(RR<=1.0)
  {
    ratio=RR;
  }
}

```



```
F=2*bb[0][0]*(1-ratio*ratio)*0.01;      /* F is the first term of Equation (3.7) */
```

```
/* the following section calculates the second term of Equation (3.7) */
```

```
for(n=1;n<=32;n++)
{
    ttt=n*tt;
    coos=cos(ttt);
    siin=sin(ttt);
    sss=n*ss;
    an=R*sqrt(sss);
    sum1real=1;
    sum1img=0;
    sum2real=1;
    sum2img=0;
    sum3real=1;
    sum3img=0;

    for(m=1;m<=10;m++)
    {
        KK=1;
        for(k=1;k<=m;k++)
        {
            KK=KK*k;
        }
        sub1=pow(-0.25,m)/(KK*KK)*pow((an*ratio),(2*m));
        sub2=pow(-0.25,m)/(KK*KK)*pow(an,(2*m));
        sub3=sub2/(m+1);

        if(m%4==0)
        {
            sum1real=sum1real+sub1;
            sum2real=sum2real+sub2;
            sum3real=sum3real+sub3;
        }

        if(m%4==2)
        {
            sum1real=sum1real-sub1;
            sum2real=sum2real-sub2;
            sum3real=sum3real-sub3;
        }

        if(m%4==1)
        {
```

```

sum1img=sum1img-sub1;
sum2img=sum2img-sub2;
sum3img=sum3img-sub3;
}

if(m%4==3)
{
sum1img=sum1img+sub1;
sum2img=sum2img+sub2;
sum3img=sum3img+sub3;
}

}
upreal=sum2real-sum1real;
upimg=sum2img-sum1img;
downreal=sum2real-sum3real;
downimg=sum2img-sum3img;

aareal=(upreal*downreal+upimg*downimg)/(downreal*downreal+downimg*downimg);
aaimg=(upimg*downreal-
upreal*downimg)/(downreal*downreal+downimg*downimg);

bbreal=aareal*coos-aaimg*siin;
bbimg=aareal*siin+aaimg*coos;
rreal=bb[n][0]*bbreal-bb[n][1]*bbimg;
sum=sum+2*rreal*0.01;
}
last=F+sum; /* last is the axial velocity of Equation (3.7)
*/

F_PROFILE(f,thread,position)=last;
}
end_f_loop(f,thread)
}

DEFINE_EXECUTE_AT_END(execute_at_end)
{

Domain *d;

face_t f;
real wall_shear_force, area, WSS;
real A[ND_ND],W_SHEAR[ND_ND];
int Zone_ID=3;

```

```

Thread *t;
d = Get_Domain(1);
t=Lookup_Thread(d,Zone_ID);

begin_f_loop(f, t)

{

    F_AREA(A,f,t);
    area = NV_MAG(A);
    wall_shear_force = NV_MAG(F_STORAGE_R_N3V(f,t, SV_WALL_SHEAR));
    F_UDMI(f,t,0)= wall_shear_force/area;

    C_UDMI(F_C0(f,t),THREAD_T0(t),1)=C_UDMI(F_C0(f,t),THREAD_T0(t),1)+F_UDMI(f,t,0);

    /* the following section stores the wall shear stress values in cells */

    C_UDMI(F_C0(f,t),THREAD_T0(t),2)=C_UDMI(F_C0(f,t),THREAD_T0(t),2)+F_STORAGE_R_N3V(f,t, SV_WALL_SHEAR)[0]/area;

    C_UDMI(F_C0(f,t),THREAD_T0(t),3)=C_UDMI(F_C0(f,t),THREAD_T0(t),3)+F_STORAGE_R_N3V(f,t, SV_WALL_SHEAR)[1]/area;

    C_UDMI(F_C0(f,t),THREAD_T0(t),4)=C_UDMI(F_C0(f,t),THREAD_T0(t),4)+F_STORAGE_R_N3V(f,t, SV_WALL_SHEAR)[2]/area;
    /* the following section calculates the components of wall shear force */
    W_SHEAR[0]=C_UDMI(F_C0(f,t),THREAD_T0(t),2);
    W_SHEAR[1]=C_UDMI(F_C0(f,t),THREAD_T0(t),3);
    W_SHEAR[2]=C_UDMI(F_C0(f,t),THREAD_T0(t),4);

    /* the following section calculates the OSI */
    C_UDMI(F_C0(f,t),THREAD_T0(t),5)= 0.5*(1-
    NV_MAG(W_SHEAR)/C_UDMI(F_C0(f,t),THREAD_T0(t),1));

    }
end_f_loop(f, t)
}

/* the following section calculates the Berne and Levy waveform */
DEFINE_PROFILE(z_unsteady_velocity, thread, position)

{

```

```

face_t f;
int timestep;
real x[ND_ND];
real last;
real V[200];
int t=N_TIME;

V[0]=0.275;  V[1]=0.286;
V[2]=0.305;  V[3]=0.346;
V[4]=0.392;  V[5]=0.431;
V[6]=0.475;  V[7]=0.508;
V[8]=0.545;  V[9]=0.576;
V[10]=0.607; V[11]=0.638;
V[12]=0.659; V[13]=0.673;
V[14]=0.684; V[15]=0.692;
V[16]=0.697; V[17]=0.701;
V[18]=0.702; V[19]=0.701;
V[20]=0.697; V[21]=0.688;
V[22]=0.681; V[23]=0.670;
V[24]=0.660; V[25]=0.642;
V[26]=0.623; V[27]=0.602;
V[28]=0.580; V[29]=0.551;
V[30]=0.506; V[31]=0.473;
V[32]=0.425; V[33]=0.449;
V[34]=0.524; V[35]=0.571;
V[36]=0.591; V[37]=0.593;
V[38]=0.590; V[39]=0.583;
V[40]=0.573; V[41]=0.564;
V[42]=0.554; V[43]=0.547;
V[44]=0.539; V[45]=0.532;
V[46]=0.524; V[47]=0.517;
V[48]=0.512; V[49]=0.506;
V[50]=0.501; V[51]=0.494;
V[52]=0.487; V[53]=0.480;
V[54]=0.474; V[55]=0.465;
V[56]=0.456; V[57]=0.449;
V[58]=0.444; V[59]=0.438;
V[60]=0.433; V[61]=0.426;
V[62]=0.418; V[63]=0.411;
V[64]=0.404; V[65]=0.398;
V[66]=0.392; V[67]=0.386;
V[68]=0.381; V[69]=0.377;
V[70]=0.372; V[71]=0.367;
V[72]=0.362; V[73]=0.359;

```

```
V[74]=0.353; V[75]=0.348;  
V[76]=0.345; V[77]=0.339;  
V[78]=0.333; V[79]=0.328;  
V[80]=0.325; V[81]=0.319;  
V[82]=0.314; V[83]=0.308;  
V[84]=0.303; V[85]=0.296;  
V[86]=0.289; V[87]=0.280;  
V[88]=0.274; V[89]=0.267;
```

```
begin_f_loop(f, thread)  
{  
    F_CENTROID(x,f,thread);  
    timestep=t%90;  
    last=V[timestep];  
    F_PROFILE(f,thread,position)=last*0.01;  
}  
end_f_loop(f,thread)  
}
```

Appendix B – Fortran code provided for calculation of WSS from the PIV results

```
PROGRAM MAIN3
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
COMMON XX(99,74,1),YY(99,74,1),UU(99,74,1),VV(99,74,1)
COMMON SS(99,74,1),BBX(100),BBY(100),BBD(100),TT(20)
COMMON BX1,BX2,BXC,BY1,BY2,BYC,ANGLE,DIS(20)
INTEGER I,J,T,L,NUMBER,N
INTEGER POINTX, POINTY
REAL X,Y,WSR(100,20),WSS(100,20),U(100),SUM
REAL SUM1,SUM2
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
CALL INITIATION
U(1)=0.0
DIS(1)=0.0
NUMBER=3
C "NUMBER" is the number of the near-wall points, including the point on the wall
C itself
T=1
C
DO 300 L=1,99
DO 200 N=2,NUMBER
CALL FINDPOINT(L,DIS(N),X,Y,POINTX,POINTY)
CALL TRIANGLE (X,Y,POINTX,POINTY,T,U(N))
200 CONTINUE
C
CALL POLYFIT(NUMBER,DIS,U,WSR(L,T))
WSS(L,T)=5.4*WSR(L,T)
WRITE(*,*)WSS(L,T),T
300 CONTINUE
C
C
```

```

OPEN (10, FILE='INNERWSS.TXT')
WRITE (10,*) 'TITLE = "WSS Plots"'
WRITE (10,*) 'VARIABLES = "DISTANCE", "WSS"'
WRITE (10,*) 'ZONE I=99, J=74'
DO 5000 I=1,99
WRITE (10,*) BBD(I), WSS(I,T)
5000 CONTINUE
CLOSE(10)
WRITE(*,*)WSS(1,1),WSS(1,2)
END

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
SUBROUTINE INITIATION
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C   This subroutine reads the velocity components of the whole vector field and the
C   location of the boundary points
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
COMMON XX(99,74,1),YY(99,74,1),UU(99,74,1),VV(99,74,1)
COMMON SS(99,74,1),BBX(100),BBY(100),BBD(100),TT(20)
COMMON BX1,BX2,BXC,BY1,BY2,BYC,ANGLE,DIS(20)
INTEGER I,J,L
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
DO 98 I=2,20
DIS(I)=REAL(I-1)*0.11
98 CONTINUE
DIS(1)=0.0
C
DO 99 I=1, 20
TT(I)=REAL(I-1)/100*5
WRITE (*,*) TT(I)
99 CONTINUE
L=1
OPEN (3,FILE='data.DAT')
DO 200 I=1,99
DO 100 J=1,74
READ (3,*) XX(I,J,L), YY(I,J,L), UU(I,J,L), VV(I,J,L), SS(I,J,L)
100 CONTINUE
200 CONTINUE
CLOSE (3)
C

```

```

        DO 250 I=1,99
            DO 260 J=1,74
                IF (SS(I,J,L).EQ.8) THEN
                    UU(I,J,L)=0.0
                    VV(I,J,L)=0.0
                ELSE
                    UU(I,J,L)=UU(I,J,L)
                    VV(I,J,L)=VV(I,J,L)
                END IF
260    CONTINUE
250    CONTINUE
C
    OPEN (4,FILE='BOUNDARY.txt')
    DO 300 I=1,99
        READ (4,*) BBX(I),BBY(I),BBD(I)
300    CONTINUE
    CLOSE(4)
    OPEN (5,FILE='CHECKBOUNDARY.txt',status='replace')
    DO 301 I=1,99
        WRITE (5,*) BBX(I),BBY(I),BBD(I)
301    CONTINUE
    CLOSE(5)
    OPEN (6,FILE='checkdata.txt',status='replace')
        DO 401 I=1,99
            DO 402 J=1,74
                WRITE (6,*) XX(I,J,L), YY(I,J,L), UU(I,J,L), VV(I,J,L), SS(I,J,L)
402    CONTINUE
401    CONTINUE
        CLOSE (6)
    END

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
    SUBROUTINE FINDPOINT(P,DISS,X,Y,POINTX,POINTY)
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C    This subroutine calculates the location (coordinates) of the points normal to the
C    boundary at which the velocity values are supposed to be interpolated
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
    COMMON XX(99,74,1),YY(99,74,1),UU(99,74,1),VV(99,74,1)
    COMMON SS(99,74,1),BBX(100),BBY(100),BBD(100),TT(20)
    COMMON BX1,BX2,BXC,BY1,BY2,BYC,ANGLE,DIS(20)

```



```

INTEGER P,I,J,POINTX,POINTY
REAL X,Y,DISS,PI,NN,KK
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
PI=3.1415926
BX1=BBX(P)
BY1=BBY(P)
BX2=BBX(P+1)
BY2=BBY(P+1)
BXC=0.5*(BX1+BX2)
BYC=0.5*(BY1+BY2)
C
IF (BX1.EQ.BX2) THEN
NN=0
X=BXC+DISS
Y=BYC
ANGLE=REAL(PI/2)
C WRITE(*,*) 'VERTICAL LINE'
ELSE IF (BY1.EQ.BY2) THEN
KK=0
X=BXC
Y=BYC-DISS
ANGLE=0.0
C WRITE (*,*) 'HORIZONTAL LINE'
ELSE
KK=(BY2-BY1)/(BX2-BX1)
NN=-1/KK
X=BXC+DISS*1/(SQRT(NN*NN+1))
Y=BYC+NN*DISS*1/(SQRT(NN*NN+1))
ANGLE=REAL(ATAN(KK))
END IF
C
I=2
100 IF (XX(I,1,1).LT.X.AND.I.LT.99) THEN
I=I+1
GO TO 100
END IF
POINTX=I-1
J=2
200 IF (YY(1,J,1).LT.Y.AND.J.LT.74) THEN
J=J+1

```

```

GO TO 200
END IF
POINTY=J-1
400  END

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
SUBROUTINE TRIANGLE (X,Y,I,J,T,TANU)
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C   This subroutine finds the three nearest velocity vectors to each of the abovementioned
C   points and interpolates the tangential components of the velocity vectors (with respect
C   to the corresponding wall section) at these points based on the three nearest adjacent
C   velocity vectors, using finite element shape functions
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
COMMON XX(99,74,1),YY(99,74,1),UU(99,74,1),VV(99,74,1)
COMMON SS(99,74,1),BBX(100),BBY(100),BBD(100),TT(20)
COMMON BX1,BX2,BXC,BY1,BY2,BYC,ANGLE,DIS(20)
REAL X,X1,X2,X3,Y,Y1,Y2,Y3,U,V,U1,U2,U3,TANU
REAL S,NE1,NE2,NE3,L1,L2,L3,L4,DIRECTION,LL
INTEGER I,J,T
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
L1=SQRT((X-XX(I,J,T))*(X-XX(I,J,T))+(Y-YY(I,J,T))*(Y-YY(I,J,T)))
L2=SQRT((X-XX(I+1,J,T))*(X-XX(I+1,J,T))+(Y-YY(I+1,J,T))*(Y-YY(I+1,J,T)))
L3=SQRT((X-XX(I,J+1,T))*(X-XX(I,J+1,T))+(Y-YY(I,J+1,T))*(Y-YY(I,J+1,T)))
L4=SQRT((X-XX(I+1,J+1,T))*(X-XX(I+1,J+1,T))+(Y-YY(I+1,J+1,T))*(Y-
C   YY(I+1,J+1,T)))

LL=MAX(L1,L2,L3,L4)
IF (L1.EQ.LL) THEN
X1=XX(I+1,J,T)
Y1=YY(I+1,J,T)
U1=UU(I+1,J,T)
V1=VV(I+1,J,T)
X2=XX(I,J+1,T)
Y2=YY(I,J+1,T)
U2=UU(I,J+1,T)
V2=VV(I,J+1,T)
X3=XX(I+1,J+1,T)
Y3=YY(I+1,J+1,T)
U3=UU(I+1,J+1,T)
V3=VV(I+1,J+1,T)

```

ELSE IF (L2.EQ.LL)**THEN**

X1=XX(I,J,T)

Y1=YY(I,J,T)

U1=UU(I,J,T)

V1=VV(I,J,T)

X2=XX(I,J+1,T)

Y2=YY(I,J+1,T)

U2=UU(I,J+1,T)

V2=VV(I,J+1,T)

X3=XX(I+1,J+1,T)

Y3=YY(I+1,J+1,T)

U3=UU(I+1,J+1,T)

V3=VV(I+1,J+1,T)

C

ELSE IF (L3.EQ.LL)**THEN**

X1=XX(I,J,T)

Y1=YY(I,J,T)

U1=UU(I,J,T)

V1=VV(I,J,T)

X2=XX(I+1,J,T)

Y2=YY(I+1,J,T)

U2=UU(I+1,J,T)

V2=VV(I+1,J,T)

X3=XX(I+1,J+1,T)

Y3=YY(I+1,J+1,T)

U3=UU(I+1,J+1,T)

V3=VV(I+1,J+1,T)

C

ELSE

X1=XX(I,J,T)

Y1=YY(I,J,T)

U1=UU(I,J,T)

V1=VV(I,J,T)

X2=XX(I+1,J,T)

Y2=YY(I+1,J,T)

U2=UU(I+1,J,T)

V2=VV(I+1,J,T)

X3=XX(I,J+1,T)

Y3=YY(I,J+1,T)

U3=UU(I,J+1,T)

```

V3=VV(I,J+1,T)
END IF
C
S=0.5*((X2*Y3-X3*Y2)-(X1*Y3-X3*Y1)+(X1*Y2-X2*Y1))
NE1=1/(2*S)*((X2*Y3-X3*Y2)+(Y2-Y3)*X+(X3-X2)*Y)
NE2=1/(2*S)*((X3*Y1-X1*Y3)+(Y3-Y1)*X+(X1-X3)*Y)
NE3=1/(2*S)*((X1*Y2-X2*Y1)+(Y1-Y2)*X+(X2-X1)*Y)
U=U1*NE1+U2*NE2+U3*NE3
V=V1*NE1+V2*NE2+V3*NE3
TANU=U*COS(ANGLE)+V*SIN(ANGLE)
DIRECTION=U*(BX2-BX1)+V*(BY2-BY1)
TANU=SIGN(TANU,DIRECTION)
C
END

CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
SUBROUTINE POLYFIT(M,X,Y,COEF)
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
C This subroutine fits a quadratic curve to the aforementioned interpolated tangential
C velocity component data at each wall point, assuming the no-slip condition at the wall,
C and calculates the tangential shear rate component as the slope of the obtained near-
C wall velocity profile function at the wall
CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
REAL X(M), Y(M)
REAL SUMXY, SMXXY, SQUX, CUBX, QUDX, COEF
INTEGER M
SMXXY=0.0
CUBX=0.0
SUMXY=0.0
SQUX=0.0
QUDX=0.0
DO 10 I=1, M
SMXXY=SMXXY+X(I)*X(I)*Y(I)
CUBX=CUBX+X(I)*X(I)*X(I)
SUMXY=SUMXY+X(I)*Y(I)
SQUX=SQUX+X(I)*X(I)
QUDX=QUDX+X(I)*X(I)*X(I)
10 CONTINUE
COEF=(SUMXY*QUDX-CUBX*SMXXY)/(SQUX*QUDX-CUBX*CUBX)
END

```

Appendix C – WSS distribution in the anastomotic region of the three base models

The graphs of WSS data presented in Chapter 4 (Figure 4.13 to Figure 4.16) are re-plotted in this appendix with a larger scale and less data in each figure for better readability, wherein “Exp” denotes the experimentally obtained WSS data and “Sim” denotes the WSS data from the CFD simulation results of Chapter 3.

Figure C.1: WSS distribution along the heel of the STS component of the SQA model at times t_2 , t_6 , and t_{11} .

Figure C.2: WSS distribution along the heel of the STS component of the SQA model at times t_3 , t_5 , and t_{12} .

Figure C.3: WSS distribution along the toe of the STS component of the SQA model at times t_2 , t_6 , and t_{11} .

Figure C.4: WSS distribution along the toe of the STS component of the SQA model at times t_3 , t_5 , and t_{12} .

Figure C.5: WSS distribution along the bed of the STS component of the SQA model at times t_2 , t_6 , and t_{11} .

Figure C.6: WSS distribution along the bed of the STS component of the SQA model at times t_3 , t_5 , and t_{12} .

Figure C.7: WSS distribution along the heel of the ETS component of the SQA model at times t_2 , t_6 , and t_{11} .

Figure C.8: WSS distribution along the heel of the ETS component of the SQA model at times t_3 , t_5 , and t_{12} .

Figure C.9: WSS distribution along the toe of the ETS component of the SQA model at times t_2 , t_6 , and t_{11} .

Figure C.10: WSS distribution along the toe of the ETS component of the SQA model at times t_3 , t_5 , and t_{12} .

Figure C.11: WSS distribution along the bed of the ETS component of the SQA model at times t_2 , t_6 , and t_{11} .

Figure C.12: WSS distribution along the bed of the ETS component of the SQA model at times t_3 , t_5 , and t_{12} .

Figure C.13: WSS distribution along the heel of the anastomosis in the parallel STS model at times t_2 , t_6 , and t_{11} .

Figure C.14: WSS distribution along the heel of the anastomosis in the parallel STS model at times t_3 , t_5 , and t_{12} .

Figure C.15: WSS distribution along the toe of the anastomosis in the parallel STS model at times t_2 , t_6 , and t_{11} .

Figure C.16: WSS distribution along the toe of the anastomosis in the parallel STS model at times t_3 , t_5 , and t_{12} .

Figure C.17: WSS distribution along the bed of the anastomosis in the parallel STS model at times t_2 , t_6 , and t_{11} .

Figure C.18: WSS distribution along the bed of the anastomosis in the parallel STS model at times t_3 , t_5 , and t_{12} .

Figure C.19: WSS distribution along the heel of the anastomosis in the conventional ETS model at times t_2 , t_6 , and t_{11} .

Figure C.20: WSS distribution along the heel of the anastomosis in the conventional ETS model at times t_3 , t_5 , and t_{12} .

Figure C.21: WSS distribution along the toe of the anastomosis in the conventional ETS model at times t_2 , t_6 , and t_{11} .

Figure C.22: WSS distribution along the toe of the anastomosis in the conventional ETS model at times t_3 , t_5 , and t_{12} .

Figure C.23: WSS distribution along the bed of the anastomosis in the conventional ETS model at times t_2 , t_6 , and t_{11} .

Figure C.24: WSS distribution along the bed of the anastomosis in the conventional ETS model at times t_3 , t_5 , and t_{12} .

Appendix D – Lead author published papers

During the course of this PhD study, some papers have been provided out of this investigation, three of which have already been published in peer reviewed journals. These three papers (References 83, 84, and 85) are enclosed in this appendix.

A Novel Coronary Artery Bypass Graft Design of Sequential Anastomoses

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Associate Editor Peter E. McHugh oversaw the review of this article.

Abstract—In this paper, the hemodynamics in a three-dimensional out-of-plane sequential bypass graft model is first investigated. Based on the advantageous flow characteristics observed within the side-to-side (STS) anastomosis in the sequential bypass graft simulation, a new CABG coupled-sequential anastomosis configuration is designed, entailing coupled STS and end-to-side (ETS) anastomotic components. In this new CABG design, the flow fields and distributions of various wall shear stress parameters within the STS and ETS anastomotic regions are studied, and compared to those of the conventional distal anastomosis, by means of computational fluid dynamics simulation of pulsatile Newtonian blood flow. Simulation results demonstrate that the new sequential anastomoses model provides: (i) a more uniform and smooth flow at the ETS anastomosis, without any stagnation point on the artery bed and vortex formation in the heel region of the ETS anastomosis within the coronary artery; (ii) a spare route for the blood flow to the coronary artery, to avoid re-operation in case of re-stenosis in either of the anastomoses; and (iii) improved distribution of hemodynamic parameters at the coronary artery bed and in the heel region of the ETS anastomosis, with more moderate shear stress indices. These advantages of the new design over the conventional ETS anastomosis are influenced by the occlusion ratio of the native coronary artery, and are most prominent when the proximal segment of the coronary artery is fully occluded. By varying the design parameters of the anastomotic angle and distance between the two anastomoses, the superior coupled STS–ETS anastomoses design is found to have the anastomotic angle of 30° and 30 mm distance between the two (STS and ETS) components.

Keywords—Stenosed coronary artery, Hemodynamic parameters, Side-to-side and end-to-side anastomoses, Anastomotic angle, CFD modeling.

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LIST OF ABBREVIATIONS

CABG	Coronary artery bypass graft
CFD	Computational fluid dynamic
ETS	End-to-side
HP	Hemodynamic parameter
IH	Intimal hyperplasia
IT	Intimal thickening
LAD	Left anterior descending artery
LCA	Left coronary artery
LCx	Left circumflex artery
LMCA	Left main coronary artery
OM	Obtuse marginal
OSI	Oscillatory shear index
RCA	Right coronary artery
SV	Saphenous vein
SQA	Sequential anastomosis/anastomoses
STS	Side-to-side
TAWSS	Time-averaged wall shear stress
TAWSSG	Time-averaged wall shear stress gradient
WSS	Wall shear stress
WSSG	Wall shear stress gradient

INTRODUCTION

Anastomotic intimal hyperplasia (IH) is the major cause of graft re-stenosis. It is well proven that hemodynamic factors are involved in the formation and development of IH. These hemodynamic factors include low and oscillating wall shear stress (WSS),^{15,16,33,40} large spatial wall shear stress gradient (WSSG),^{12,34,35} and long residence time of blood cells.^{31,40} Several studies have indicated the correlation between these hemodynamic factors and localized sites of intimal thickening (IT), namely the arterial floor,

heel, toe, and suture line of an anastomosis. Hence, in numerical studies, the improvement of these hemodynamic factors has been utilized as an indicator to achieve superior geometries and higher patency rates for bypass grafts.

Sequential Bypass Grafting

The sequential bypass grafting technique, first described by Flemma *et al.*¹⁸ and Bartley *et al.*,³ is a technique in which two or more coronary artery anastomoses are made with a single graft, usually the saphenous vein (SV). Intraoperative studies demonstrate a higher blood flow²⁴ and a higher velocity³⁹ in the proximal (preanastomotic) segment of a sequential graft than in a single coronary graft with an end-to-side (ETS) anastomosis. Higher patency rates have also been observed through postangiograms in the side-to-side (STS) anastomoses than in the ETS anastomoses.²⁹ Moreover, according to results obtained by our group,⁴³ the STS anastomosis has a smoother flow with smaller spatial gradients of WSS as compared to the ETS anastomosis, which may motivate the use of sequential bypass grafting over multiple bypass grafting.

New Coupled Anastomosis Design

It is well established that in the graft-occluded artery anastomotic region, impingement of blood flow on the artery floor and the flow recirculation at the heel play a critical role in the re-stenosis of the CABG distal anastomosis. Although many designs are suggested to improve the flow field at the distal anastomosis of the CABG, they do not exhibit large deviation from the general flow characteristics, such as the vortex formed at the heel or the impact of blood on the artery bed.

Our group has conducted numerous studies, both numerically and experimentally, in order to investigate the effects of geometrical parameters, including anastomotic angle,^{9,11} out-of-plane graft,⁴² shape of distal anastomosis by designing connecting sleeves,¹⁰ and complete CABG modeling.⁵⁶ Optimization of these parameters in a conventional ETS anastomosis can improve the flow field and distributions of hemodynamic parameters (HPs) to some extent. However, in order to further improve the hemodynamics and alleviate the drawbacks of the available CABG anastomosis designs, a new coupled-sequential anastomosis (SQA) configuration design is developed, based on the beneficial results of sequential bypass grafts. The flow field in this SQA design is studied by means of numerical simulation of pulsatile Newtonian blood flow, and compared with a conventional CABG ETS anastomosis.

In this paper, a typical SQA flow analysis is presented followed by the suggested new STS–ETS coupled SQA design. After showing the advantages of the new design, the effects of two design parameters, namely the anastomotic angle and distance between the two anastomoses, on the distribution of HPs is studied. Finally, the performance of the new coupled SQA design is examined for an out-of-plane CABG model and also for the case of a partial flow, present through the proximal host artery.

NEW COUPLED STS–ETS ANASTOMOSES BYPASS GRAFT DESIGN

The impetus for the new CABG coupled SQA design has been the results of our blood flow study in a typical SQA design configuration. We, hence, first present this study briefly, and then the coupled SQA design analysis and results.

Sequential Aorto-Left Coronary Bypass Graft Model Geometric Parameter Values

The sequential aorto-left coronary bypass graft model is depicted in Fig. 1. Since our primary interest is to understand the hemodynamic features in the anastomotic regions, only the proximal segment of the left anterior descending (LAD) artery is considered in the model. The 3D geometry of the aorto-coronary bypass graft model is constructed based on surgical observations, using the commercial software, GAMBIT.

The ascending aorta is considered to have a length of 80 mm with a diameter of 25 mm. The right coronary artery (RCA) has a circular cross section with 3.2 mm diameter at its junction to the aorta, and the SV graft is of 4 mm diameter. The diameters of the left main coronary artery (LMCA), LAD artery, left circumflex artery (LCx) along with the obtuse marginals OM1 and OM2 are 4.7, 4.5, 3.1, 1.25, and 1.26 mm with respective lengths of 13.5, 6.0, 100, 48.8, and 52.0 mm.¹³

As shown in Fig. 1, the SV graft originates from the aorta at point A, and it is anastomosed to the 90% proximally occluded OM1 branch (of stenotic length 4.3 mm) at point B with a STS anastomosis. It is then anastomosed in an ETS fashion to the 80% proximally occluded OM2 branch (of stenotic length 3.4 mm) at point C.

Computational Model and Flow Conditions

Blood flow through the CABG is assumed to have the characteristics of three-dimensional, time-dependent,

FIGURE 1. Sequential aorto-left coronary bypass graft model; the saphenous vein originating from the aorta at point A is anastomosed to the branches of the LCx artery namely the obtuse marginals OM1 and OM2 at points B and C in STS and ETS fashions, respectively.

incompressible, isothermal, Newtonian, and laminar flow, whose governing equations are:

Continuity equation,

$$\nabla \cdot \mathbf{u} = 0 \quad (1)$$

and Navier–Stokes equation,

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

where $\mathbf{u}$ is the velocity vector, t is the time, and p is the pressure. The density (ρ) and dynamic viscosity (μ) of blood are assumed to be 1050 kg/m^3 and 0.00408 Pa s , respectively.

The inlet Reynolds numbers, based on the mean velocities and the diameters of the respective vessels, are 421, 128, 40, and 106 for the aorta, the LCx, the branches OM1 and OM2, respectively. The input and output conditions are the measured time-varying flow rate waveforms at the aorta entrance,²² LAD exit (by phase contrast MRI scanning),⁴⁹ RCA entrance (by Doppler flowmeter catheter),³⁷ and the calculated time-varying flow rate waveforms at the exits of the aorta and LCx branches. The flow discharge values are set proportional to the third power of the branching vessel diameter according to Murray's law.³⁸ A detailed explanation of the procedure for obtaining the flow waveforms for the input and output conditions along with the relevant references is reported in our earlier work.⁴²

In this study, the vein and arteries are considered as rigid tubes (the effects of vessel wall elasticity and

fluid–structure interaction are not investigated), and the no-slip boundary condition is applied to all walls.

The governing equations are solved numerically by a finite volume method and the commercial computational fluid dynamic (CFD) package, FLUENT (Fluent User's Guide, Fluent, Lebanon, NH), using the segregated solver. The semi-implicit SIMPLEC algorithm is used as the pressure–velocity coupling scheme. Convergence is achieved when the scaled residual is decreased to 5×10^{-5} in this study. The scaled residual for the continuity equation is the total absolute rate of mass creation in all the computational cells divided by its maximum value obtained in the first five iterations. For the Navier–Stokes equation, the residual for the FLUENT's segregated solver is defined as the imbalance in the momentum conservation equation for each discretized cell, summed over all the computational cells.

The mesh sensitivity is tested on the velocity and WSS, by varying the number of grid cells. The computational domain is considered to be sufficient for this study, when further mesh refinement can only result in $<3\%$ change in velocity and 1% change in WSS at some examined sections.

Hemodynamic Parameters Characterizing the Flow Patterns

Based on clinical evidence, disturbed flow patterns play a key role in the onset and progression of atherosclerosis and IH. Therefore, HPs can be utilized as

indicators to show susceptible sites of IT and favorable conditions for thrombi formation.¹ In this paper, the relevant HPs of WSS and WSSG⁸ are calculated in the models, according to the following expressions:

$$WSS = \mu \left(\frac{\partial \mathbf{u}}{\partial \mathbf{n}} \right) \Big|_{\text{Wall}} \quad (3)$$

$$WSSG = \sqrt{\left(\frac{\partial \tau_x}{\partial x} \right)^2 + \left(\frac{\partial \tau_y}{\partial y} \right)^2 + \left(\frac{\partial \tau_z}{\partial z} \right)^2}, \quad (4)$$

where $\mathbf{n}$ is the inner unit vector normal to the wall and τ_x , τ_y , and τ_z are the WSS vector (traction) components.

Results

The flow characteristics were analyzed at four important instances of the cardiac cycle: (1) the start of ejection, (2) during mid-ejection, (3) during early diastole, and (4) during mid-diastole. The results indicate that the STS anastomosis region experiences a maximum WSS of approximately 0.5 Pa at minimum inflow to approximately 5 Pa at maximum inflow. Based on the comparison with the existing experimental investigations,³⁶ these ranges reveal that the STS anastomosis contributes to a safe hemodynamic pattern. On the other hand in the ETS anastomosis region, the maximum WSS during the cardiac cycle ranges from approximately 1.56 Pa at minimum inflow (at the start of ejection) to approximately 48 Pa at maximum inflow (at mid-diastole). For this region, the sites of high WSS are the toe and the artery (OM2) floor. There is a low WSSG in the STS anastomosis region, with a sharp gradient at the toe of the ETS anastomosis (about 4 vs. 26 N/m³ at mid-diastole for instance, as shown in Fig. 2), which spreads down (with a slight fall in the magnitude) to the floor of the ETS anastomosis with the distal regions of the OM2 branch experiencing negligible WSSG.

Our results show that there is a large variation in WSS in the distal anastomotic region, owing to the nonuniform flow patterns resulting from the impingement of blood flow from the graft into the artery. This flow behavior results in a nonuniform WSS distribution in the CABG, toward the possibility of IH formation. Upon comparing the hemodynamics in the sequential bypass graft model with a multiple bypass graft model, our studies have revealed that the WSSG in the multiple bypass graft anastomoses model is higher than that observed in the sequential bypass graft model (28 vs. 26 N/m³ at mid-diastole for example). Hence, the influence of the STS anastomosis B on the ETS anastomosis C (as indicated in Fig. 2) contributes to a better WSSG environment, which is in agreement with the results reported by Qiao *et al.*⁴¹

FIGURE 2. Wall shear stress gradient (WSSG) distribution around the anastomoses at mid-diastole. The peak value is seen at the toe of the ETS anastomosis, whereas in the STS anastomosis region, WSSG is low.

More detailed information on this study can be obtained from our book chapter.⁴³ This study has provided us the impetus and basis to develop a new coupled STS–ETS anastomosis bypass graft design.

New Coupled STS–ETS Anastomoses Bypass Graft Configuration (in Comparison With Isolated STS and ETS Anastomosed Grafts)

Based on the beneficial results of sequential bypass grafting in the above study, a new configuration for the CABG is designed, to improve the flow field and HP distributions of the conventional ETS anastomoses. In this distal SQA design, shown in Fig. 3a, there is initially a STS anastomosis distal to the stenosis, and then the graft end is anastomosed to the same coronary artery further downstream in an ETS fashion.

Three base models: In order to evaluate and compare the advantages and disadvantages of our suggested SQA design over a conventional ETS anastomosis configuration, three base CFD models are designed and evaluated: (i) the new coupled anastomoses configuration, shown in Fig. 3a, (ii) a parallel STS anastomosis (Fig. 3b), and (iii) a conventional ETS anastomosis (Fig. 3c). The latter two are the reference models to be compared, respectively, with the STS component of the new design (in order to study the possible effects of the ETS anastomosis of the new design on its STS component) and with its ETS component.

Models' dimensions: The dimensions of the three base models are listed in Table 1, where D_G , D_A , L_P , L_{STS} , L_{ETS} , L_D , and d stand, respectively, for the graft

FIGURE 3. Various anastomotic models, (a) the new proposed coupled STS–ETS model design (b) parallel STS anastomosis (c) conventional ETS anastomosis model with an anastomotic angle of 45° . A fully developed pulsatile flow is applied at the grafts inlet and outlets; in case of the parallel STS model (b), 85% of the blood flow is set to exit through the graft outlet.

TABLE 1. Dimensions of the base models' geometry^a.

Model	D_G	D_A	L_P	L_{STS}	L_{ETS}	L_D	D
New design	4	2	6.5	8	7	48	30
Conventional ETS	4	2	10	NA	7	48	NA
Parallel STS	4	2	6.5	8	NA	48	NA

^aAll dimensions are given in mm.

diameter, coronary artery diameter, length of the proximal section of the host artery, length of the STS anastomosis, length of the ETS anastomosis, length of the distal section of the host artery, and distance between the two anastomoses in the new SQA model, as shown in Fig. 3.

The base models are considered to have an ETS anastomotic angle of 45° with the fully occluded proximal segment of the coronary artery. The models are designed to be planar, based on the study of Galjee *et al.*²¹ who demonstrated that the typical location and

course of SV in RCA bypass graft can be assumed to be approximately planar.

Computational Modeling and Flow Conditions

The proximal anastomosis of the graft to the aorta is not analyzed in this study, and the focus is only on the distal anastomosis. Hence, a fully developed pulsatile flow is applied at the graft inlet; its flow waveform and the velocity profile are based on measurements by magnetic resonance phase velocity mapping within a CABG.²⁰ However, some modifications are made to smoothen the waveform. This waveform (with the time period of 0.9 s adapted for this study) is demonstrated in Fig. 4. The Womersley solution⁵³ is assumed for the inlet axial velocity profile, which is derived as a fully developed pulsatile flow and implemented as the inlet boundary condition¹⁶ to calculate the velocity for the pulsatile flow. The exit flow is assumed to be in a fully developed condition, due to

the 48-mm-long distal segment of the coronary artery models. Thereby, the FLUENT's outflow boundary condition is set to assume a zero normal gradient for all flow variables except pressure.

In the parallel STS model, 15% of the blood flow is set to pass through the STS anastomosis into the coronary artery, and the remaining 85% is assumed

to pass through the graft to the (distally located) ETS anastomotic junction. The above percentage is adjusted to have the parallel STS model consistent with the new coupled anastomoses configuration, since the flow is bifurcated with the same proportion through the coronary artery and the graft at the STS component (on average within each cycle).

The governing equations for the blood flow and their computational solutions methodology are as provided earlier in “[Computational Model and Flow Conditions](#)” section.

Results

Flow Behavior and Patterns

The flow field and HPs in all the three base models are studied at 12 instants of time, as shown on the waveform in Fig. 4. At times t_3 of peak systole and t_{11} of late-diastole, samples of the computed streamlines of the flow field at the center plane of the three models are presented in Figs. 5 and 6, respectively, wherein the new SQA design, parallel STS, and conventional ETS models are labeled as (a), (b), and (c), respectively.

FIGURE 4. Average velocity values of the waveform used in this study (labels indicate times at which flow and HP are studied).

FIGURE 5. Streamlines at the symmetry plane at time $t_3 = 0.08$ s, (a) new design, (b) parallel STS model, (c) conventional end-to-side model. Strong impact of flow observed on the artery floor in the conventional ETS anastomosis compared to the flow at the STS anastomosis models.

FIGURE 6. Streamlines at the symmetry plane at time $t_{11} = 0.84$ s, (a) new design, (b) parallel STS model, (c) conventional end-to-side model. Larger vortices and recirculation areas are observed in models (b) and (c) compared to new design model (a).

Acceleration phase: As the flow accelerates from t_1 to t_3 (the peak flow rate), in the conventional ETS anastomosis model, a vortex forms at the heel region, with a stagnation point on the artery floor due to the graft flow impacting the artery bed, as shown in Fig. 5c for time t_3 . However, in our new SQA model (Fig. 5a), the flow at the distal ETS anastomosis is very smooth without any vortex formation. There is no impingement on the artery floor. This is because the partial flow from the STS anastomosis along the coronary artery changes the velocity components of the ETS anastomosis flow toward the toe and the coronary artery axis rather than to the artery floor. This results in having no stagnation point formed on the bed. However, there would be some energy loss due to the collision of the two flows from the graft and coronary artery.

At the STS anastomosis of the new SQA model (Fig. 5a), a vortex forms at the heel region along with a stagnation point on the artery bed, due to the interaction of the flow from the graft with the relatively slow flow in the occluded end of the artery. This is consistent with our findings for the parallel STS anastomosis model (Fig. 5b); Bonert *et al.*⁷ have also shown similar results. At the peak flow rate (t_3) in the

new design, 11% of the graft flow goes through the STS anastomosis, and 89% of that passes through the ETS anastomosis. The diversion of 11% of graft flow into the coronary artery at the STS anastomosis has the effect of smoothing the flow at the distal ETS anastomosis.

Deceleration and reversed flow phases: During the mid-deceleration, partial recirculation and back flow appear in the graft in all the models, particularly at the inner wall of the graft curvatures where the blood flow has low inertia, and exhibits oscillatory characteristics. At the ETS anastomosis of the new SQA model, the graft flow bifurcates into the distal and proximal segments of the coronary artery.

As the net flow rate just becomes negative (t_{11}), the blood flows back toward the aorta through the graft at near wall regions, while it still flows forward at the central regions near the graft axis, as shown in Fig. 6. This is due to the high inertia of the fluid in the central region compared to the fluid near the wall having low inertia, as a result of the friction between the layers of the fluid within the boundary layer. At this time instant (t_{11}), there are large vortices and recirculation areas in all the models. At the ETS anastomosis of the new SQA model, there is a small vortex at the graft inner

wall, upstream of the distal anastomosis as shown in Fig. 6a. However, in the conventional ETS anastomosis (Fig. 6c), the vortex is much larger and occupies most of the anastomosis region and half of the graft near the inner wall. In the parallel STS anastomosis model (Fig. 6b), a large vortex occupies the entire anastomosis region. On the other hand, in the STS anastomosis of the new SQA model, the size of the vortex is remarkably reduced and shifted over the toe of the anastomosis. This is due to the blood flow from the ETS component circulating within the vascular loop of the new SQA model, which eliminates the stagnation point on the artery bed as illustrated in Fig. 6a.

Hemodynamic Parameters Distribution

It has been shown that (i) localized distribution of low-WSS and high-oscillatory shear index (OSI) strongly correlates with the focal locations of atheroma,²⁶ (ii) large spatial WSSG contributes to the elevated wall permeability and atherosclerotic lesions,¹² and (iii) prevailing development of these lesions and growth of plaque formation occur in regions of extreme (either maxima or minima) WSS.^{32,46} Hence, in this study, the distributions of HPs, including time-averaged WSS (TAWSS), nondimensional TAWSSG,⁸ and OSI²⁶ are calculated according to their expressions in Eqs. (5) to (7), respectively, and compared in the three models.

$$TAWSS = \frac{1}{T} \int_0^T |\vec{\tau}_w| dt \quad (5)$$

$$TAWSSG = \frac{D_G}{\tau_0} \frac{1}{T} \int_0^T \sqrt{\left(\frac{\partial \tau_x}{\partial x}\right)^2 + \left(\frac{\partial \tau_y}{\partial y}\right)^2 + \left(\frac{\partial \tau_z}{\partial z}\right)^2} dt \quad (6)$$

$$OSI = \frac{1}{2} \left(1 - \frac{\left| \int_0^T \vec{\tau}_w dt \right|}{\int_0^T |\vec{\tau}_w| dt} \right), \quad (7)$$

where $\vec{\tau}_w$ is the WSS vector (traction), T is the time period of the flow cycle, D_G is the graft diameter, and τ_0 is the WSS for Poiseuille flow at the mean flow Reynolds number, which is obtained as 0.48 Pa for the current study.

In order to compare the distribution of HPs quantitatively at the critical sites of the anastomosis such as toe, heel, bed, and the suture line (see Fig. 7), the segmental averages of the HPs are calculated and listed in Table 2. In this table, the above mentioned calculated parameters are also presented for a few more studied models, which will be introduced later in the following section.

TAWSS: As shown in Table 2 for the base models (with anastomotic angle of 45° and $d = 30$ mm), TAWSS is increased on the artery bed of the ETS anastomosis of the new SQA model to 1.63 Pa, from 1.40 Pa in the conventional ETS model. Although this increase is marginal, Giddens *et al.*²³ have found a critical biological WSS value of 15 dyne/cm² (1.5 Pa) below which IT would develop; based thereon, the moderate improvement of TAWSS on the artery bed of the new SQA design can be deemed to be vital. The TAWSS in the STS anastomoses is generally low, with its peak located at the toe; the TAWSS is lower in the STS component of the new SQA model than in the parallel STS model. This depicts a more moderate distribution of WSS in the STS component of the new SQA model, which can reduce the probability of atherosclerotic lesion development.

TAWSSG: As shown in Table 2, TAWSSG at the heel and bed of the ETS component as well as at the toe and suture line of the STS component of the new

FIGURE 7. Critical regions of ETS and STS anastomoses, which are the susceptible sites of intimal hyperplasia and atherosclerotic lesion formation: 1, 5. Suture line, 2, 6. Toe, 3, 7. Heel, 4, 8. Bed.

FIGURE 8. OSI distribution at the anastomotic regions of the three models. OSI is generally low in the graft and distal segment of the coronary artery, due to the waveform having mostly a forward flow.

SQA model is reduced, compared to the conventional ETS and parallel STS anastomoses, respectively. This manifests a more uniform distribution of WSS in the new SQA design at these critical locations, which can lessen the vessel wall permeability and atherosclerotic lesion development.

OSI: The OSI at the ETS anastomosis of the new SQA model is lower at the heel region and the artery wall and bed opposite to the heel, than in the conventional ETS anastomosis model, as demonstrated in Fig. 8. However, OSI is generally low at the ETS anastomoses, due to the flow having mostly a forward direction within the cycle. At the STS anastomosis region of the new SQA model and in the parallel STS model, the OSI distribution is almost the same in the graft, at the heel, and the proximal part of the artery wall, as shown in Fig. 8 and Table 2 for the base model. However, the OSI is increased on the artery bed and at the toe of the STS component of the new design compared to those of the parallel STS model. As shown in Fig. 8, the OSI is generally low within the graft; yet, there is a high-OSI area on the artery bed and wall just distal to the heel of the STS anastomosis, due to the vortex forming there and the moving stagnation point.

The OSI is also high at the occluded segment of the host artery, as illustrated in Fig. 8; but, this is due to

the very small mean WSS in this area rather than due to large changes in WSS over the cardiac cycle as reported by Bonert *et al.*⁷ The OSI distribution in the segment of the coronary artery between the two anastomoses of the new SQA model differs from that of the distal segment of the coronary artery in the parallel STS anastomosis model. In this segment as shown in Fig. 8, the OSI value increases up to 0.15 in the new design, while it is below 0.05 in the parallel STS model. This increase in OSI can be due to the circulation of blood flow in the vascular loop in the new design.

EFFECTS OF THE DESIGN PARAMETERS ON HEMODYNAMIC PARAMETERS DISTRIBUTION

There are two types of parameters involved in the design of the suggested configuration. One group of parameters can be controlled by the surgeon such as the anastomotic angle at the ETS component, and the distance between the two anastomoses (d). The other group of parameters cannot be controlled, while they are different from one patient to another, such as the diameter of the SV and coronary arteries, and the

percentage and location of stenosis which can result in having parallel (where graft and host artery centerlines are approximately in plane) or diamond configuration (where the centerlines of the host artery and graft cross at approximately 90°) at the STS component.

Adjustable parameters: In order to obtain a better flow field and HP distributions, a number of models are simulated for a range of the adjustable parameters, involving anastomotic angle (of 30°, 45°, and 60°) at the ETS component and the distance ($d = 20$ and 30 mm) between the two STS and ETS components of the new design. Comprehensive information of the flow regime dependence on the design parameters (including the graft and coronary artery diameter) can enable tailoring an optimal design for a specific patient.

Non-planar model: In order to verify the advantage of the suggested design for the left coronary artery (LCA) bypasses (where the graft and coronary arteries cannot be assumed to be in the same plane), a non-planar model with a diamond configuration at the STS component is studied.

Variation in occlusion ratio: Anastomosis models with different percentages of coronary artery stenosis are simulated in order to evaluate the performance of the new SQA graft design in the early postoperative stage. It is well known that during the first weeks following grafting (at least until 2 weeks)⁶ a nonnegligible residual flow remains through the stenosed host artery, which will progressively decrease until the stenosed vessel is completely occluded.²⁸ Hence, anastomosis models with two stenosis severity of 75% and 91%

(equivalent to 50% and 70% diameter stenosis, respectively) are investigated in this study.

For this purpose, an axisymmetric stenosis with a Gaussian profile⁴⁷ is considered to be located 6 mm upstream from the heel in the models (with the ETS anastomotic angle of 30° and $d = 30$ mm). At the coronary artery inlet, Berne and Levy⁵ flow waveform is imposed. According to Speziale⁴⁸ who indicated that the flow rate in an internal thoracic artery graft increases with progressing stenosis of the native coronary artery, the distribution percentage of the flow rates issued from the graft and stenosed coronary artery are allocated to be 75 vs. 25 and 91 vs. 9 in the two studied cases, respectively, to simulate the progressive decrease of residual blood flow from a constricted host artery following the bypass surgery.

The segmental averages of the calculated HPs for the studied models with (i) fully occluded and (ii) partially stenosed coronary arteries are, respectively, presented in Tables 2 and 3.

Inferences Drawn From the Results in Tables 2 and 3

The following can be inferred from the results in Tables 2 and 3.

From Table 2, comparison of the conventional ETS models with different anastomotic angles indicates that the TAWSSG is considerably increased with the anastomotic angle, while the TAWSS is marginally increased (except on the artery bed where it is slightly decreased), and the OSI is almost remained constant. Therefore, a smaller anastomotic angle results in a

TABLE 3. Comparison of segmental average of <HP>s in models with partially occluded host artery and ETS anastomotic angle of 30°.

Occlusion ratio:		75%			91%		
Model	Location	<TAWSS>			<TAWSS>		
		<OSI>	(Pa)	<TAWSSG>	<OSI>	(Pa)	<TAWSSG>
Conventional ETS model ^a	1. Suture line	0.01	2.29	12.4	0.02	2.35	15.0
	2. Toe	0.004	5.59	28.8	0.01	5.78	29.8
	3. Heel	0.03	0.56	4.4	0.04	0.49	5.8
	4. Bed	0.003	1.55	3.5	0.02	1.32	4.0
New design model with $d = 30$ mm	ETS component	1. Suture line	0.01	2.25	12.9	0.02	2.34
		2. Toe	0.004	5.57	28.6	0.01	5.80
		3. Heel	0.04	0.47	4.0	0.05	0.49
		4. Bed	0.04	1.39	3.6	0.05	1.46
	STS component	5. Suture line-sts	0.02	0.64	7.2	0.04	0.60
		6. Toe-sts	0.03	0.52	5.4	0.04	0.59
		7. Heel-sts	0.02	0.52	4.4	0.03	0.41
		8. Bed-sts	0.03	0.38	0.4	0.11	0.18
Parallel STS model ^a	5. Suture line	0.01	0.93	16.5	0.02	0.67	10.5
	6. Toe	0.01	0.85	20.8	0.01	0.75	14.4
	7. Heel	0.02	0.52	4.9	0.03	0.41	4.7
	8. Bed	0.005	0.69	1.1	0.05	0.32	0.7

^aReference models.

more favorable HP distribution. This is in agreement with the results reported by Fei *et al.*¹⁷ who studied the flow in distal ETS anastomoses with anastomotic angles of 20°, 30°, 40°, 45°, 50°, 60° and 70°, and suggested that grafts should be placed with a minimal distal anastomotic angle.

Comparing the six planar SQA design models: As shown in Table 2, when the model anastomotic angle is changed from 30° to 60°, the TAWSSG is drastically increased mainly at the toe and suture line of the ETS component (by 169% and 230%, respectively), while generally the TAWSS is negligibly increased (8% and 32%, respectively) and OSI is not changed. This implies that the TAWSSG is the over-riding factor in the selection of the preferred anastomotic angle, which makes the case for the smaller anastomotic angle for the new design.

A change in the distance between the two components (d), has affected the TAWSSG mainly at the toe of the ETS component, with a different trend in each model depending on the anastomotic angle. A decrease in d (from 30 to 20 mm), has caused the TAWSSG (primarily at the toe) to (i) increase in the model with the anastomotic angle of 30°, (ii) decrease in the model with the anastomotic angle of 60°, and (iii) stay almost unchanged in the model with the anastomotic angle of 45°.

Neither the anastomotic angle, nor the distance between the two components has any obvious effect on the HP distribution at the STS component of the new design.

The nonplanar model with a diamond configuration at the STS component (with ETS anastomotic angle of 30° and $d = 20$ mm): This nonplanar model (illustrated in Fig. 9) depicts a lower TAWSSG distribution at the ETS component than the corresponding planar model, as shown in Table 2. On the artery bed of the STS component of this nonplanar model, while the TAWSS and TAWSSG are slightly increased (to 0.23 and 1.3 from 0.18 and 0.4, respectively), the OSI is reduced to half (from 0.2 to 0.09) as compared to that of the corresponding planar model; this is beneficial to prevent the coincidence of low-WSS and high-OSI on the bed. However, on the suture line of the STS component of the nonplanar model, the OSI becomes almost double (from 0.04 to 0.09), while TAWSS and TAWSSG are slightly decreased (from 0.64 and 11 to 0.49 and 9.4, respectively) compared to the corresponding planar model. In addition, the segmental average of TAWSSG on the graft wall across the STS anastomosis of the nonplanar model is increased to 1.6 from 1 in the corresponding planar model (these latter values are not given in Table 2).

This is in agreement with the results reported by Bonert *et al.*,⁷ who demonstrated that the parallel

FIGURE 9. TAWSS distribution in the nonplanar model. TAWSS is low in the graft and proximal segments of the coronary artery, and it is increased at the ETS component and downstream of the coronary artery, with its peak at the toe of the ETS anastomosis.

configuration is more favorable than the diamond configuration for maintaining the graft patency at the STS anastomosis, while the diamond one is favorable for maintaining the host artery patency. Since graft patency is vital for the STS anastomosis of the new design, this design can be more beneficially applicable for the right CABG, wherein the graft and the coronary artery are approximately in the same plane. This fact is further proven by comparing the HP distributions in the STS component of the nonplanar SQA model with the isolated diamond STS model, where all the HP distributions are more favorable both on the suture line and bed of the anastomosis, as shown in Table 2.

The models with partially stenosed coronary arteries: Comparison of the STS component of each new design model with the corresponding parallel STS model (in Table 3) indicates that the suggested SQA design configuration affects the distribution of HPs at the STS anastomosis of the partially occluded models with exactly the same trend as in the fully occluded models (shown in Table 2).

Comparison of the ETS component of each new design model with the corresponding conventional ETS model (in Table 3), indicates that in the case of 91% stenosed coronary artery, the change in the TAWSSG and TAWSS distributions due to the new design configuration has the same trend as in the fully

stenosed models (shown in Table 2). Yet, it does not hold for the OSI at the heel and bed of the coronary artery.

In the case of 75% stenosed coronary artery, none of the advantages which were observed in the distribution of HPs in the fully occluded and 91% stenosed models of the new design are present anymore. The TAWSSG on the bed and suture line, and the TAWSS and OSI on the heel and bed of the ETS component of the new design are inferior compared to those of the corresponding conventional ETS model.

This suggests that if the occlusion percentage of the stenosed artery is below a certain level, the overall advantages of the new configuration might be affected during the first few days following the bypass surgery, due to the competitive flows problem. This is in agreement with the results of the earlier studies,^{14,19,52,54} which have confirmed the existence of a critical value for stenosis severity, below which the graft failure is expected, and above that, the recipient artery will be progressively occluded.

In summary, the effects of the above studied parameters can be concluded as follows.

Comparison of each new SQA model with the corresponding conventional ETS model depicts that in all the new design models the HP distribution is improved on the bed, heel, and (in most of the models) suture line of the ETS component.

The variation of the design parameters of the new SQA graft design demonstrates that the combination of a smaller anastomotic angle at the ETS component and a longer distance between the two components results in a better flow field and distribution of HPs. Yet, there are restrictions which inhibit surgeons from implementing a very acute anastomotic angle and adopting a long distance between the two components practically. Although some innovative suturing methods are proposed to obtain an acute anastomotic angle using prosthetic grafts,²⁵ it is impractical in the standard clinical practice to perform a very small anastomotic angle due to the large cross-sectional area of the graft section resulted in such an anastomosis.

Moreover, the lengths of coronary arteries are limited: the LAD coronary artery measures from 10 to 13 cm in length, whereas the LCx artery measures about 6–8 cm, and the dominant RCA is about 12–14 cm in length.⁵¹ Therefore, taking into account the length of the coronary artery located proximal to the stenosis plus the distance of grafting (required distance between the stenosis and the STS anastomosis), in addition to the lengths of the two anastomoses of the new SQA design, there would be a restricted length of the coronary artery left to be adopted as the distance between the two STS and ETS components of the new graft design practically.

Hence, in this study, the minimum anastomotic angle and maximum distance between the two components are adopted to be 30° and 30 mm, respectively, which result in a better flow field and distribution of HPs than the other models investigated.

The simulation results for the models with partially stenosed coronary arteries further confirm that there is a critical value for stenosis severity, below which graft failure is expected due to the competitive flow problem. Note that the effect of the partial flow through the coronary artery is only studied on the models with anastomotic angle of 30° and $d = 30$ mm, whose results are shown to be the most favorable among the investigated models.

DISCUSSION

In this paper, an out-of-plane sequential bypass graft model is investigated, and a new SQA model design for the distal CABG anastomoses is suggested accordingly. The flow fields and HPs are studied within the model, and compared to those of the conventional ETS distal anastomosis by means of CFD simulation. Finally, sensitivity analysis for the suggested SQA design is conducted by simulation and comparison of several models within the physiological range of the parameters involved.

Evaluation of Model Assumptions, Methods, and Limitations

The effects of the elasticity of the vessel walls and fluid–structure interaction are not investigated in this study, and are left as future work.

The wall motion is ignored in this investigation, as it is shown that the motion of the RCA has minor effect on TAWSS patterns, and hemodynamic aspects of the cardiac motion are dominated by the effects of flow pulsatility.⁵⁵ In addition, it is indicated that the use of a static geometry to predict the mean wall shear rates would yield reasonably accurate results and the dynamic behavior is not significant at the base cardiac frequency of 1 Hz.⁴⁴

The non-Newtonian rheology of blood is not considered in this study. This is because there is only a small variation of less than 6% observed in the peak WSS magnitude between the Newtonian model and the non-Newtonian Carreau model (as computed by us). Besides, numerical simulations of non-Newtonian flow in a two-dimensional ETS anastomosis, investigated by Ballyk *et al.*² under pulsatile conditions, have also shown only minor effects on WSS distributions.

In this study, the outflow boundary conditions at the exits of OM branches are prescribed flow rates,

according to Murray's law. However, in reality, there is a complex interaction between the flow and pressure fields within the coronary arteries as the distal pressure changes with cardiac contraction. Since the choice of the outflow boundary conditions can affect the flow distribution, velocity, and pressure fields,⁵⁰ in order to obtain more realistic results, this should be accounted for in the outflow boundary conditions (for instance, by a lumped parameter model).^{30,45,50}

Evaluation of Results: Novelty and Features of the Coupled STS–ETS Graft Design

In the new design, during the acceleration and early deceleration phases, part of the graft flow is diverted into the coronary artery at the STS anastomosis. When this flow in the coronary artery reaches the ETS anastomosis, it lifts up the flow coming from the graft and helps to direct the graft flow smoothly into the coronary artery, as shown in Fig. 5. Thereby, there is no impact on the artery bed. It is to be borne in mind that the impact on the floor is believed to be a contributing factor to the graft failure, since Bates *et al.*⁴ have shown evidence of the change in the flow character once it has impacted against the junction floor. Hence, having a smoothened flow and no impact on the floor of the coronary artery is a positive feature of the new SQA CABG design.

In the new SQA design, the stagnation point is vanished at either one or both of the ETS and STS anastomoses at different time intervals compared to the conventional ETS and parallel STS anastomoses, as illustrated in Figs. 5 and 6. Stagnation point is always associated with a low-WSS and high spatial WSSG region, contributing to IT and atherosclerosis development and increasing the risk of the aggregation of red blood cells. Hence, the absence of stagnation point is another positive feature of the coupled SQA design.

In the new SQA design, there is no vortex formed at the heel of the ETS anastomosis within the coronary artery, as shown in Figs. 5 and 6, resulting in a relatively higher forward WSS along the artery walls and bed. The presence of a vortex can increase the contact between the blood and the wall surface, which may result in platelet activation.²⁷ The absence of vortex formation is also a positive feature of the coupled STS–ETS graft design.

In the planar new SQA design, the HPs are improved to some extent, especially at the heel and coronary artery bed of the ETS, and at the toe and suture line of the STS anastomosis of the new design, compared to the conventional ETS and parallel STS models, respectively, as shown in Table 2.

In the nonplanar new SQA design, although the HP distribution is improved on the heel, bed, and suture line of the ETS component compared to the conventional ETS model, the inferior distribution of HPs on the suture line and in the graft (compared to isolated diamond STS model and the STS component of the corresponding planar SQA model, as shown in Table 2) makes the advantage of this new design debatable for a nonplanar bypass grafting.

This new SQA design provides a spare route for the blood flow to the coronary artery in order to avoid re-operation in case of re-stenosis in either of the anastomoses. In case that re-stenosis happens first in the STS anastomosis of the (planar) new design, it is predicted that occlusion would occur within the coronary artery rather than in the graft, based on the low-WSS and high-OSI on the coronary artery wall and bed opposite to the heel of the STS anastomosis as shown in Fig. 8. Furthermore, it is demonstrated by Bonert *et al.*⁷ that the parallel configuration is preferred for the graft patency. Therefore, in case of re-stenosis at the STS anastomosis of the new SQA design, the graft would be still patent and the blood can still flow to the ETS anastomosis, eliminating the need for re-operation.

In the ETS anastomosis of the new SQA model, the flow field and distributions of HPs are generally improved at the heel region, the bed and wall of the coronary artery opposite to the heel (but not at the toe), as shown in Table 2. However, there is (i) a vortex formation along the graft inner wall at some time intervals as illustrated in Fig. 6, and (ii) a stagnation point at the heel, during the reversed flow. Hence, in case that re-stenosis happens first in the ETS anastomosis of the new SQA design, it is deemed that the occlusion would happen within the graft above the heel region stretched on the suture line toward the toe of the ETS anastomosis (rather than in the coronary artery). Therefore, the passage for the blood flow would be still open through the STS anastomosis and the coronary artery, without the need for re-operation.

CONCLUSION

A new CABG coupled-sequential anastomosis configuration is designed in this paper, and its flow fields and distributions of various WSS parameters are studied, and compared to those of the conventional distal anastomosis.

Although this design does involve one additional anastomosis (and prolonged operation time), some distinct advantages are observed in the flow field and distribution of HPs in this new coupled SQA design. Simulation results demonstrate that the new sequential

anastomoses model provides: (i) a more uniform and smooth flow at the ETS anastomosis, without any stagnation point on the artery bed and vortex formation in the heel region of the ETS anastomosis within the coronary artery; (ii) a spare route for the blood flow to the coronary artery, to avoid re-operation in case of re-stenosis in either of the anastomoses; and (iii) improved distribution of HPs at the coronary artery bed and in the heel region of the ETS anastomosis, with more moderate shear stress indices.

By investigating the effect of the partial flow through the proximal host artery in the case of partially stenosed coronary arteries, our results further confirm the existence of a critical value for stenosis severity, below which the distributions of HPs might be undesirably affected by the competitive flow problems.

Upon varying the new design parameters of the anastomotic angle and distance between the STS and ETS components, and comparing the out-of-plane design version with the in-plane design version, the superior design is found to be the planar SQA model with the anastomotic angle of 30° and distance of 30 mm.

So now while an innovative CABG design is provided, its flow-simulation benefits would need to be validated by *in vivo* animal experiments, in order to proceed further to the clinical adoption of this new design.

REFERENCES

- ¹Archie, J. P., S. Hyun, C. Kleinstreuer, P. W. Longest, G. A. Truskey, and J. R. Buchanan. Hemodynamic parameters and early intimal thickening in branching blood vessels. *Crit. Rev. Biomed. Eng.* 29(1):1–64, 2001.
- ²Ballyk, P. D., D. A. Steinman, and C. R. Ethier. Simulation of non-Newtonian blood flow in an end-to-side anastomosis. *Biorheology* 31(5):565–586, 1994.
- ³Bartley, T. D., J. C. Bigelow, and U. S. Page. Aortocoronary bypass grafting with multiple sequential anastomoses to a single vein. *Arch. Surg.* 105(6):915–917, 1972.
- ⁴Bates, C. J., D. M. O'Doherty, and D. Williams. Flow instabilities in a graft anastomosis: a study of the instantaneous velocity fields. *Proc. Inst. Mech. Eng. H* 215(6):579–587, 2001.
- ⁵Berne, R. M., and M. N. Levy. *Cardiovascular Physiology*, 8th edn. St. Louis, MO: Mosby, 2001, p. 231.
- ⁶Bertolotti, C., and V. Deplano. Three-dimensional numerical simulations of flow through a stenosed coronary bypass. *J. Biomech.* 33(8):1011–1022, 2000.
- ⁷Bonert, M., J. G. Myers, S. Fremes, J. Williams, and C. R. Ethier. A numerical study of blood flow in coronary artery bypass graft side-to-side anastomoses. *Ann. Biomed. Eng.* 30(5):599–611, 2002.
- ⁸Buchanan, J. R., C. Kleinstreuer, S. Hyun, and G. A. Truskey. Hemodynamics simulation and identification of susceptible sites of atherosclerotic lesion formation in a model abdominal aorta. *J. Biomech.* 36(8):1185–1196, 2003.
- ⁹Chua, L. P., W. F. Ji, C. M. Yu, T. M. Zhou, and Y. S. Tan. Particle image velocimetry measurements of three proximal anastomosis models under a pulsatile flow condition. *Proc. Inst. Mech. Eng. H* 222(3):249–263, 2008.
- ¹⁰Chua, L. P., T. M. Tong, and J. H. Zhou. Numerical simulation of steady flows in designed sleeve models at distal anastomoses. *Int. Commun. Heat Mass Transfer* 32:707–714, 2005.
- ¹¹Chua, L. P., J. M. Zhang, S. C. M. Yu, D. N. Ghista, and Y. S. Tan. Numerical study on the pulsatile flow characteristics of proximal anastomotic models. *Proc. Inst. Mech. Eng. H* 219(5):361–379, 2005.
- ¹²DePaola, N., M. A. Gimbrone, P. F. Davies, and C. F. Dewey. Vascular endothelium responds to fluid shear stress gradients. *Arterioscler. Thromb.* 12(11):1254–1257, 1992.
- ¹³Dodge, J. T., B. G. Brown, E. L. Bolson, and H. T. Dodge. Intrathoracic spatial location of specified coronary segments on the normal human heart. Applications in quantitative arteriography, assessment of regional risk and contraction, and anatomic display. *Circulation* 78(5 I):1167–1180, 1988.
- ¹⁴Einav, S., J. Avidor, and B. Vidne. Haemodynamics of coronary artery-saphenous vein bypass. *J. Biomed. Eng.* 7(4):305–309, 1985.
- ¹⁵Ethier, C. R. Computational modeling of mass transfer and links to atherosclerosis. *Ann. Biomed. Eng.* 30(4):461–471, 2002.
- ¹⁶Ethier, C. R., D. A. Steinman, X. Zhang, S. R. Karpik, and M. Ojha. Flow waveform effects on end-to-side anastomotic flow patterns. *J. Biomech.* 31(7):609–617, 1998.
- ¹⁷Fei, D. Y., J. D. Thomas, and S. E. Rittgers. The effect of angle and flow rate upon hemodynamics in distal vascular graft anastomoses: a numerical model study. *J. Biomech. Eng.* 116(3):331–336, 1994.
- ¹⁸Fleming, R. J., W. D. Johnson, and D. Lepley. Triple aorto-coronary vein bypass as treatment for coronary insufficiency. *Arch. Surg.* 103(1):82–83, 1971.
- ¹⁹Furuse, A., E. H. Klopp, R. K. Brawley, and V. L. Gott. Hemodynamics of aorta-to-coronary artery bypass. Experimental and analytical studies. *Ann. Thorac. Surg.* 14(3):282–293, 1972.
- ²⁰Galjee, M. A., A. C. van Rossum, T. Doesburg, M. B. Hofman, T. H. Falke, and C. A. Visser. Quantification of coronary artery bypass graft flow by magnetic resonance phase velocity mapping. *Magn. Reson. Imaging* 14(5):485–493, 1996.
- ²¹Galjee, M. A., A. C. van Rossum, T. Doesburg, M. J. van Eenige, and C. A. Visser. Value of magnetic resonance imaging in assessing patency and function of coronary artery bypass grafts. An angiographically controlled study. *Circulation* 93(4):660–666, 1996.
- ²²Ganong, W. F. *Review of Medical Physiology*. Stamford, CT: Appleton & Lange, 1999.
- ²³Giddens, D., S. Zarins, and C. K. Glagov. Response of arteries to near-wall fluid dynamics behavior. *Appl. Mech. Rev.* 43(2):S98–S102, 1990.
- ²⁴Grondin, C., and R. Limet. Sequential anastomoses in coronary artery grafting: technical aspects and early and late angiographic results. *Ann. Thorac. Surg.* 23:1–8, 1977.
- ²⁵Hakaim, A. G., M. N. Nalbandian, J. K. Heller, A. C. Chowla, and W. A. Oldenburg. Improved patency of prosthetic arteriovenous grafts with an acute anastomotic

- angle and flow diffuser. *J. Vasc. Surg.* 37(5):1032–1035, 2003.
- ²⁶He, X., and D. N. Ku. Pulsatile flow in the human left coronary artery bifurcation: average conditions. *J. Biomech. Eng.* 118(1):74–82, 1996.
- ²⁷Hughes, P. E., and T. V. How. Flow structures at the proximal side-to-end anastomosis. Influence of geometry and flow division. *J. Biomech. Eng.* 117(2):224–236, 1995.
- ²⁸Kakos, G. S., H. N. Oldham, S. H. Dixon, R. W. Davis, P. O. Hagen, and D. C. Sabiston. Coronary artery hemodynamics after aorto-coronary artery vein bypass. An experimental evaluation. *J. Thorac. Cardiovasc. Surg.* 63(6):849–853, 1972.
- ²⁹Kerem, M., E. Sener, and O. Tasdemir. Long-term patency of sequential and individual saphenous vein coronary bypass grafts. *Eur. J. Cardiovasc. Surg.* 19:140–144, 2001.
- ³⁰Kim, H. J., I. E. Vignon-Clementel, C. A. Figueroa, K. E. Jansen, and C. A. Taylor. Developing computational methods for three-dimensional finite element simulations of coronary blood flow. *Finite Elem. Anal. Des.* 46(6):514–525, 2010.
- ³¹Kleinstreuer, C., M. Lei, and J. P. Archie. Flow input waveform effects on the temporal and spatial wall shear stress gradients in a femoral graft-artery connector. *J. Biomech. Eng.* 118(4):506–510, 1996.
- ³²Kleinstreuer, C., M. Nazemi, and J. P. Archie. Hemodynamics analysis of a stenosed carotid bifurcation and its plaque-mitigating design. *J. Biomech. Eng.* 113(3):330–335, 1991.
- ³³Ku, D. N., D. P. Giddens, C. K. Zarins, and S. Glagov. Pulsatile flow and atherosclerosis in the human carotid bifurcation. Positive correlation between plaque location and low oscillating shear stress. *Arteriosclerosis* 5(3):293–302, 1985.
- ³⁴Lei, M., C. Kleinstreuer, and G. A. Truskey. Numerical investigation and prediction of atherogenic sites in branching arteries. *J. Biomech. Eng.* 117(3):350–357, 1995.
- ³⁵Lei, M., C. Kleinstreuer, and G. A. Truskey. A focal stress gradient-dependent mass transfer mechanism for atherogenesis in branching arteries. *Med. Eng. Phys.* 18(4):326–332, 1996.
- ³⁶Malek, A. M., S. L. Alper, and S. Izumo. Hemodynamic shear stress and its role in atherosclerosis. *JAMA* 282(21):2035–2042, 1999.
- ³⁷Matsuo, S., M. Tsuruta, M. Hayano, Y. Imamura, Y. Eguchi, T. Tokushima, and S. Tsuji. Phasic coronary artery flow velocity determined by Doppler flowmeter catheter in aortic stenosis and aortic regurgitation. *Am. J. Cardiol.* 62(13):917–922, 1988.
- ³⁸Murray, C. D. The physiological principle of minimum work: I. The vascular system and the cost of blood volume. *Proc. Natl Acad. Sci. USA* 12(3):207–214, 1926.
- ³⁹O'Neill, M. J., P. D. Wolf, T. K. O'Neill, R. M. Montesano, and J. A. Waldhausen. A rationale for the use of sequential coronary artery bypass grafts. *J. Thorac. Cardiovasc. Surg.* 81(5):686–690, 1981.
- ⁴⁰Perktold, K., M. Hofer, G. Rappitsch, M. Loew, B. D. Kuban, and M. H. Friedman. Validated computation of physiologic flow in a realistic coronary artery branch. *J. Biomech.* 31(3):217–228, 1998.
- ⁴¹Qiao, A., Y. Liu, S. Li, and H. Zhao. Numerical simulation of physiological blood flow in 2-way coronary artery bypass grafts. *J. Biol. Phys.* 31:161–182, 2005.
- ⁴²Sankaranarayanan, M., D. N. Ghista, L. P. Chua, T. Y. Seng, and G. S. Kassab. Analysis of blood flow in an out-of-plane CABG model. *Am. J. Physiol. Heart Circ. Physiol.* 291(1):H283–H295, 2006.
- ⁴³Sankaranarayanan, M., D. N. Ghista, L. P. Chua, Y. S. Tan, K. Sundaravadeivel, and G. S. Kassab. Blood flow in an out-of-plane aorto-left coronary sequential bypass graft. In: *Computational Cardiovascular Mechanics: Modeling and Applications in Heart Failure*, edited by J. M. Guccione, G. S. Kassab, and M. Ratcliffe. New York: Springer-Verlag, in press.
- ⁴⁴Santamarina, A., E. Weydahl, J. Siegel, Jr, and J. Moore, Jr. Computational analysis of flow in a curved tube model of the coronary arteries: effects of time-varying curvature. *Ann. Biomed. Eng.* 26(6):944–954, 1998.
- ⁴⁵Segers, P., N. Stergiopulos, N. Westerhof, P. Wouters, P. Kolh, and P. Verdonck. Systemic and pulmonary hemodynamics assessed with a lumped-parameter heart-arterial interaction model. *J. Eng. Math.* 47(3–4):185–199, 2003.
- ⁴⁶Shahcheraghi, N., H. A. Dwyer, A. Y. Cheer, A. I. Barakat, and T. Rutaganira. Unsteady and three-dimensional simulation of blood flow in the human aortic arch. *J. Biomech. Eng.* 124(4):378–387, 2002.
- ⁴⁷Siouffi, M., V. Deplano, and R. Pélissier. Experimental analysis of unsteady flows through a stenosis. *J. Biomech.* 31(1):11–19, 1998.
- ⁴⁸Speziale, G. *Competitive Flow and Steal Phenomenon in Coronary Surgery. Intraoperative Graft Patency Verification in Cardiac and Vascular Surgery*. New York: Futura Publishing, 2001.
- ⁴⁹Suo, J., Y. Yang, J. Oshinski, A. Tannenbaum, J. Gruden, and D. Giddens. Flow patterns and wall shear stress distributions at atherosclerotic-prone sites in a human left coronary artery—an exploration using combined methods of CT and computational fluid dynamics. In: *26th Annual Int. Conf. IEEE EMBS*, San Francisco, 2004.
- ⁵⁰Vignon-Clementel, I. E., C. A. Figueroa, K. E. Jansen, and C. A. Taylor. Outflow boundary conditions for three-dimensional finite element modeling of blood flow and pressure in arteries. *Comput. Methods Appl. Mech. Eng.* 195(29–32):3776–3796, 2006.
- ⁵¹Waller, B., and R. Schlant. *Anatomy of the Heart, Hurst's the Heart*. London: McGraw-Hill, pp. 84–86, 1986.
- ⁵²Wiesner, T. F., M. J. Levesque, E. Rooz, and R. M. Nerem. Epicardial coronary blood flow including the presence of stenoses and aorto-coronary bypasses—II: Experimental comparison and parametric investigations. *J. Biomech. Eng.* 110(2):144–149, 1988.
- ⁵³Womersley, J. Method for the calculation of velocity, rate of flow and viscous drag in arteries when the pressure gradient is known. *J. Physiol.* 127:553–563, 1955.
- ⁵⁴Yasuura, K., Y. Takagi, Y. Ohara, Y. Takami, A. Matsuura, and H. Okamoto. Theoretical analysis of right gastroepiploic artery grafting to right coronary artery. *Ann. Thorac. Surg.* 69(3):728–731, 2000.
- ⁵⁵Zeng, D., Z. Ding, M. H. Friedman, and C. R. Ethier. Effects of cardiac motion on right coronary artery hemodynamics. *Ann. Biomed. Eng.* 31(4):420–429, 2003.
- ⁵⁶Zhang, J. M., L. P. Chua, D. N. Ghista, S. C. M. Yu, and Y. S. Tan. Numerical investigation and identification of susceptible sites of atherosclerotic lesion formation in a complete coronary artery bypass model. *Med. Biol. Eng. Comput.* 46(7):689–699, 2008.

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Compliant model of a coupled sequential coronary arterial bypass graft: Effects of vessel wall elasticity and non-Newtonian rheology on blood flow regime and hemodynamic parameters distribution

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ABSTRACT

We have recently developed a novel design for coronary arterial bypass surgical grafting, consisting of coupled sequential side-to-side and end-to-side anastomoses. This design has been shown to have beneficial blood flow patterns and wall shear stress distributions which may improve the patency of the CABG, as compared to the conventional end-to-side anastomosis. In our preliminary computational simulation of blood flow of this coupled sequential anastomoses design, the graft and the artery were adopted to be rigid vessels and the blood was assumed to be a Newtonian fluid. Therefore, the present study has been carried out in order to (i) investigate the effects of wall compliance and non-Newtonian rheology on the local flow field and hemodynamic parameters distribution, and (ii) verify the advantages of the CABG coupled sequential anastomoses design over the conventional end-to-side configuration in a more realistic bio-mechanical condition.

For this purpose, a two-way fluid–structure interaction analysis has been carried out. A finite volume method is applied to solve the three-dimensional, time-dependent, laminar flow of the incompressible, non-Newtonian fluid; the vessel wall is modeled as a linearly elastic, geometrically non-linear shell structure. In an iteratively coupled approach the transient shell equations and the governing fluid equations are solved numerically.

The simulation results indicate a diameter variation ratio of up to 4% and 5% in the graft and the coronary artery, respectively. The velocity patterns and qualitative distribution of wall shear stress parameters in the distensible model do not change significantly compared to the rigid-wall model, despite quite large side-wall deformations in the anastomotic regions. However, less flow separation and reversed flow is observed in the distensible models. The wall compliance reduces the time-averaged wall shear stress up to 32% (on the heel of the conventional end-to-side model) and somewhat increases the oscillatory nature of the flow. It is found that the effects of wall compliance and non-Newtonian rheology are not independent, and they interact with each other. In spite of the modest influence of wall compliance and non-Newtonian rheology on the hemodynamic parameters distribution, the inclusion of these properties has unveiled further advantages of the coupled sequential anastomoses model over the conventional end-to-side anastomosis which had not been revealed in the previous study with the rigid-wall and Newtonian fluid models. Hence, the inclusion of wall compliance and non-Newtonian rheology in flow simulation of blood vessels can be essential in quantitative and comparative investigations.

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Abbreviations: CABG, coronary arterial bypass graft; CFD, computational fluid dynamic; CT, computed tomography; DV, diameter variation; ETS, end-to-side; FSI, fluid–structure interaction; HP, hemodynamic parameter; IT, intimal thickening; LAD, left anterior descending; LDL, low-density lipoprotein; OSI, oscillatory shear index; RCA, right coronary artery; SQA, sequential anastomoses; STS, side-to-side; TAWSS, time-averaged wall shear stress; TAWSSG, time-averaged wall shear stress gradient; WSS, wall shear stress; WSSG, wall shear stress gradient.

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Nomenclature

a	Yasuda exponent
$\mathbf{D}$	rate of deformation tensor
D_A	coronary artery diameter
D_G	graft diameter
d	distance between the two anastomoses
d_{nj}	differential Cartesian components of the outward normal surface vector
E_θ	circumferential elastic modulus
$\mathbf{F}$	load vector
$\mathbf{K}$	structural stiffness matrix
L_D	length of the distal section of the host artery
L_{ETS}	length of the ETS anastomosis
L_P	length of the proximal section of the host artery
L_{STS}	length of the STS anastomosis
$\mathbf{M}$	structural mass matrix
n	power law index
P	pressure
$Q_{\max}$	peak flow rate
$Re_{\max}$	maximum Reynolds number
S	surface regions of integration
$\mathbf{U}$	flow velocity vector
$\mathbf{U}_j$	flow velocity components
$\mathbf{u}$	nodal displacement vector
$\ddot{\mathbf{u}}$	nodal acceleration vector
V	volume region of integration
$\mathbf{W}_j$	control volume boundary velocity (mesh velocity) components
$\alpha_{\max}$	maximum Womersley number
$\dot{\gamma}$	shear rate
η	dynamic viscosity of the fluid
η_0	low shear viscosity
η_∞	high shear viscosity
λ	time constant
ν	Poisson's ratio
ρ	density
ω	angular frequency of oscillation

1. Introduction

In coronary arterial bypass grafts (CABGs), hemodynamic pulsatile shear stress parameters are widely believed to be a highly important factor, implicated in the formation and progression of intimal hyperplasia (IH), the major cause of graft failure [1–7]. Although the underlying mechanism for IH has not yet been fully understood, Caro's "shear-dependent mass transfer" theory [2] suggests that low oscillating wall shear stress (WSS) and enhanced particle residence time in flow separation and flow recirculation zones influence the endothelial function and cause a disturbed mass transfer, which results in intimal thickening (IT).

IT is shown to occur predominantly at the heel and toe of the anastomosis, on the artery floor opposite the anastomosis, and on the suture line in a conventional end-to-side (ETS) anastomosis configuration [8–10]. In order to achieve higher patency rates in bypass grafts, several studies have been conducted to improve the hemodynamics at the aforementioned critical regions of the downstream anastomosis by modification of CABG geometrical factors, including anastomotic angle [11,12], shape of distal anastomosis [13–15], out-of-plane graft [16,17], and graft-to-host artery diameter ratio [18,19].

We have designed a new CABG coupled-sequential anastomosis (SQA) configuration [20], and have shown that it provides: (i) a more uniform and smooth flow at the ETS anastomosis,

without impingement of blood flow on the artery bed and vortex formation in the heel region of the ETS anastomosis within the coronary artery; (ii) improved distribution of hemodynamic parameters (HPs) at the coronary artery bed and in the heel region of the ETS anastomosis, with more moderate shear stress indices; and (iii) a spare route for the blood flow to the coronary artery, to avoid re-operation in case of re-stenosis in either of the anastomoses. This configuration (illustrated in Fig. 1a) brings about a less disturbed flow environment compared to other modified ETS anastomosis designs.

Due to difficulties of solving the coupled fluid flow–structural deformation problem, in the vast majority of earlier computational studies of blood flow in arteries including our previous works, the blood vessels are treated as rigid tubes. However, the arterial wall is a viscoelastic deformable tissue, and its deformation interacts with the pulsatile blood flow. As a result of this interaction, hemodynamic factors of the blood flow are influenced by the mechanical behavior of the wall, and the dynamic properties of the wall are affected by the transient behavior of the blood flow.

In recent years, due to advances in computational methods, performing fluid–structure interaction (FSI) simulations has been facilitated, and more coupled FSI computational studies have been conducted. Perktold and Rappitsch [21,22] simulated the blood flow in compliant models of carotid artery bifurcations and showed a quantitative influence of the wall compliance on the flow patterns and WSS magnitude.

Tang et al. [23] conducted FSI simulations of a nonlinear thick-wall model of carotid arteries with an asymmetric stenosis to quantify the effects of stenosis severity, eccentricity, and pressure conditions on blood flow and wall behaviors to determine conditions under which artery compression and plaque rupture might occur.

By numerical modeling of blood flow and low-density lipoprotein (LDL) transport in a porohyperelastic arterial wall model, Koshiba et al. [24] have demonstrated that the blood flow, arterial wall deformation, and filtration flow all affect the LDL concentration, and that LDL accumulation is due to stagnation and the presence of filtration flow. Hence, they concluded that FSI analysis is indispensable for realistic simulation of a flow field and the LDL concentration patterns in both the lumen and wall.

Although FSI is found to be important in coronary arterial flow simulations by some investigations (including the above reviewed study), there are also studies indicating that the effect of arterial wall deformation on arterial flow can be insignificant. Leuprecht et al. [15] investigated pulsatile flow patterns and vessel wall mechanics in conventional and Miller-cuff types of distal ETS anastomoses of bypass grafts. Their results of the flow studies in distensible vessel wall models showed a rather small influence on the flow field relative to the rigid wall models, despite rather large side wall deformations in the anastomotic region.

Therefore, we have undertaken this study primarily in the light of estimating the significance of vessel wall compliance effect on HPs distribution in our CABG coupled SQA design (shown in Fig. 1a). Further, the effect of non-Newtonian rheology is investigated in this novel SQA configuration.

In our previous study (wherein the vessel walls were assumed to be rigid and the blood was taken to be a Newtonian fluid) [20], by varying the design parameters of the anastomotic angle and distance between the two anastomoses, the superior coupled side-to-side (STS)–ETS anastomoses design was found to have the anastomotic angle of 30° and 30 mm distance between the two (STS and ETS) anastomoses.

Consequently, in this study, the effects of wall elasticity and non-Newtonian rheology are investigated in the superior SQA model and its corresponding conventional ETS model to verify the previously observed advantages of this novel coupled sequential CABG

Fig. 1. (a) Coupled STS–ETS sequential anastomoses model. S_1 to S_{10} and P_1 to P_7 indicate, respectively, the cross-sections and the points at which velocity profiles and WSS variations are discussed and (b) conventional ETS anastomosis model.

design over the conventional ETS configuration in a more realistic bio-mechanical condition. For this purpose, the transient wall equations and the flow equations are solved in an implicitly coupled approach, using an iterative procedure.

2. Computational models and boundary conditions

A two-way (bi-directional) fluid–structure interaction simulation of blood flow in compliant-wall CABG models is conducted using the commercial computational software ANSYS Workbench (ANSYS Inc.) for the coupling of the finite-element-based software, ANSYS, with the finite-volume-based software, ANSYS CFX. Therein, the calculated displacements of the solid (vessel) structure are transferred to the boundary walls of the fluid domain and the computed forces in CFX are sent back to the solid domain during each stagger (coupling) iteration.

2.1. Geometric parameter values

The coupled SQA model and the conventional ETS model are shown in Fig. 1, in which the dimensions of the graft diameter (D_G), coronary artery diameter (D_A), length of the STS anastomosis (L_{STS}), distance between the two anastomoses (d), length of the ETS anastomosis (L_{ETS}), and length of the distal section of the host artery (L_D) are, respectively, 4, 2, 9, 30, 10, and 48 mm. The length of the proximal section of the host artery, located between the stenosis and the anastomosis (L_P) is 6.5 and 10 mm in the SQA model (Fig. 1a) and the conventional ETS model (Fig. 1b), respectively.

Both the SQA model (Fig. 1a) and the conventional ETS anastomosis model (Fig. 1b) have an ETS anastomotic angle of 30° , and are designed to be planar, with smooth graft inner walls [25] and the proximal segment of the coronary artery fully occluded.

2.2. Vessel wall model

Blood vessels experience large strain in vivo, particularly near branches and graft artery junctions [26]. However, as the focus of this investigation is on the flow fields and HPs distribution rather than the intramural stress distributions, a small strain (large deformation) approximation of blood vessel mechanics is utilized, as commonly used in other earlier studies [27–29]. The transient structural equilibrium equation is

$$\{F(t)\} = [M]\{\ddot{u}(t)\} + [K]\{u(t)\} \quad (1)$$

where $\{F\}$ is the load vector, $[M]$ is the structural mass matrix, $[K]$ is the structural stiffness matrix, $\{u\}$ is the nodal displacement vector, and $\{\ddot{u}\}$ is the nodal acceleration vector.

The equilibrium equations for the vessel wall structure are solved with stress boundary conditions (the calculated pressure and WSS values from the fluid domain) at the fluid–structure interface and constraint conditions (at the graft inlet and the coronary artery outlet to prevent rigid body motion), in order to estimate the vessel wall displacements.

The vessel walls are assumed to be isotropic, incompressible, and homogeneous with a density of 1060 kg/m^3 [30], and modeled as a linearly elastic, geometrically non-linear shell structure [6,22]. Poisson's ratio is regarded as $\nu \approx 0.5$ to express the incompressibility of the isotropic vessel wall material.

The stiffness of venous walls is highly nonlinear, exhibiting an increasing elastic modulus for higher strains. At low (venous) pressures, veins have a lower stiffness than arteries; however, at arterial pressures, stiffness of arterialized vein grafts increases to a level even higher than that of arteries. Wesley et al. [31] have measured the incremental elastic moduli (Young's modulus) of human saphenous vein in both longitudinal and circumferential directions at different transmural pressures. As the vessels are strongly restricted in the axial direction under in vivo conditions [32], the value of circumferential elastic modulus at a mean physiologic transmural arterial wall pressure of 100 mmHg, is interpolated (to be $E_\theta = 2.2 \text{ MPa}$) in this study, and used as the Young's modulus for the isotropic graft wall material. Also, as the arterial wall stiffness is increased in atherosclerotic arteries and in this study we are not investigating the effects of compliance mismatch, the same value of elastic modulus is employed for the arterial wall too.

The wall thickness of human left anterior descending (LAD) coronary artery has been measured in atherosclerotic patients both by high-frequency, two-dimensional transthoracic echocardiography (to be $t = 1.9 \pm 0.3 \text{ mm}$) and by high-frequency epicardial echocardiography (to be $t = 1.8 \pm 0.2 \text{ mm}$) [33]. Further, it has been demonstrated that autogenous veins undergo medial thickening when used as arterial bypass grafts [34]. Accordingly, the wall thickness of both the graft and artery is taken to be 2 mm in this investigation.

2.3. Blood flow model

Blood flow through the CABG is assumed to be a three-dimensional, time-dependent, incompressible, isothermal, and laminar flow. In distensible models, the modified equations of motion for fluid mechanics computations (with corrected

convective velocity due to moving boundaries [35]), which are obtained by applying the Leibnitz Rule on the integral conservation equations, are as follows:

$$\frac{d}{dt} \int_{V(t)} \rho dV + \int_s \rho(\mathbf{U}_j - \mathbf{W}_j) dn_j = 0 \quad (2)$$

$$\begin{aligned} \frac{d}{dt} \int_{V(t)} \rho \mathbf{U}_i dV + \int_s \rho(\mathbf{U}_j - \mathbf{W}_j) \mathbf{U}_i dn_j \\ = - \int_s P dn_j + \int_s \eta \left(\frac{\partial U_i}{\partial x_j} + \frac{\partial U_j}{\partial x_i} \right) dn_j \end{aligned} \quad (3)$$

where $\mathbf{U}_j$ and $\mathbf{W}_j$ are the components of the flow velocity and the velocity of the control volume boundary (mesh velocity), respectively, ρ is density (assumed to be 1050 kg/m³ for blood in this study), P is pressure, and η is the dynamic viscosity of the fluid. V and S denote volume and surface regions of integration, respectively, and dn_j are the differential Cartesian components of the outward normal surface vector.

The mesh velocity at an inner point of the flow domain is calculated from the wall movement by a “Displacement Diffusion” mesh motion model, in which, the displacements applied on the boundaries are diffused to other mesh points in a way that the relative mesh distribution of the initial mesh is preserved. For instance, as the initial mesh is relatively fine in boundary layers, it remains comparatively fine after the mesh motion model is applied.

To model the shear thinning behavior of blood, the Carreau–Yasuda model [36] is employed

$$\eta = \eta_\infty + (\eta_0 - \eta_\infty) [1 + (\lambda \dot{\gamma})^a]^{(n-1)/a} \quad (4)$$

where $\dot{\gamma}$ represents a scalar measure of the rate of deformation tensor ($\mathbf{D} = [\nabla \mathbf{U} + (\nabla \mathbf{U})^T]/2$), defined as

$$\dot{\gamma} = \sqrt{2 \text{tr}(\mathbf{D}^2)} \quad (5)$$

and the other parameters are obtained from the experimental data of a blood analogue by Gijzen et al. [37] to be: $\eta_0 = 22 \times 10^{-3}$ Pa s, $\eta_\infty = 2.2 \times 10^{-3}$ Pa s, $\lambda = 0.11$ s, $a = 0.644$, and $n = 0.392$. In the case of Newtonian flow, the dynamic viscosity of blood is taken to be $\eta = 0.00408$ Pa s.

The proximal anastomosis of the graft to the aorta is not considered in this study, and the focus is only on the distal anastomosis. Hence, a fully developed pulsatile flow is applied at the graft inlet. The flow waveform is based on measurements by magnetic resonance phase velocity mapping within a coronary artery bypass graft [38]. The original waveform has been measured in grafts with an average diameter of 6 mm [38]; hence, the corresponding cross sectional average velocity values for a graft diameter of 4 mm are calculated by similitude so as to have the same Reynolds number. Also, some modifications are made to obtain the smoothened waveform with the time period of $T = 0.9$ s adapted for this study, as demonstrated in Fig. 2. The systolic peak flow rate is $Q_{\max} = 70$ ml/min, and the maximum Reynolds and Womersley numbers are calculated to be $Re_{\max} = 79$ and $\alpha_{\max} = 2.45$ respectively, based on the graft diameter of 4 mm. The Womersley solution [39] is assumed for the inlet axial velocity profile, which is derived as a fully developed pulsatile flow and implemented as the inlet boundary condition. At the coronary artery outlet, the traction-free outflow boundary condition is applied. Also, the no-slip boundary condition is applied to all walls.

The governing equations are solved numerically by a finite volume method and the computational fluid dynamic (CFD) software, ANSYS CFX, using a fully implicit second-order backward Euler differencing scheme.

Fig. 2. Average velocity values of the waveform used in the present study. Labels indicate the times at which the flow field and HPs are discussed.

The convergence criterion (a normalized residual, obtained based on the imbalance in the linearized system of discrete equations) is set to 10^{-5} in this study.

The mesh sensitivity is tested on the velocity and WSS, by varying the number of grid cells. The computational domain is considered to be sufficient for this study, when further mesh refinement can only result in less than 2% change in velocity and 1% change in WSS at some examined sections.

The time-step size is taken to be 0.01 s, and the results are recorded at the end of each time-step. In order to eliminate the start-up effects of transient flow, the computation is carried out for 5 periods, and the fifth period results are presented.

3. Results

3.1. Wall deformation

The mesh displacement contour in the SQA model at the peak internal pressure during diastole ($t/T = 0.43$) is shown in Fig. 3. The wall deformation pattern remains qualitatively unchanged during the cardiac cycle. The maximum mesh displacement is about 0.5 mm, occurring at the side walls of the STS anastomosis of the SQA model in the middle of the suture line, where the normal pressure causes the maximum moment (about axes X and Z) on the artery and the graft wall structure, due to the high pressure and long scissor ($L_{\text{STS}} = 9$ mm) on the blood vessels at this location. Likewise, at the ETS component of the SQA model and in the conventional ETS model, the maximum displacement occurs on the side walls of the anastomosis, nearer to the heel rather than to the toe.

At the peak internal pressure, the increase in the diameter of the graft and of the coronary artery at locations immediately proximal and distal to the anastomosis of the conventional ETS model is about 0.16, 0.06, and 0.04 mm (equivalent to 4%, 3%, and 2% diameter variation (DV) ratio) respectively. This value increases up to 5% in the coronary artery of the SQA model proximal to the STS anastomosis. Schaar et al. [40] reported up to 2% circumferential strain (equivalent to 2% DV) in human coronary arteries using three-dimensional ultrasound-based intravascular palpography. Zeng et al. [41] measured 15% of maximum temporal cross-sectional area variation averaged along the RCA (which corresponds to about 8% DV) using multi-slice CT. Also, canine elastic arteries have been reported to experience 6–10% DV over a cardiac cycle driven by the pressure pulse [42,43]. Hence, the calculated diameter variations in the present FSI simulation are comparable to experimental findings.

Fig. 3. Mesh displacement contour in the SQA model at the peak pressure ($t/T=0.43$), with the maximum value occurring at the side walls of the STS anastomosis. The wall deformation pattern remains qualitatively unchanged during the cardiac cycle.

3.2. Flow patterns

The flow patterns in the rigid-wall model have been discussed in detail in our previous study [20]. However, there are substantial differences between certain flow characteristics of the rigid-wall–Newtonian-fluid and compliant-wall–non-Newtonian-fluid models, which are manifested in this section.

Less flow separation is observed in the compliant models. This is consistent with the results of earlier studies; Perktold and Rappitsch [21,22] reported reduction of flow separation at the outer wall of a distensible carotid artery bifurcation model in comparison with the corresponding rigid-wall model. The very advantages which had been observed in the flow fields of the SQA configuration in comparison with that of the conventional ETS anastomosis in the case of rigid-wall model with Newtonian fluid [20] are present in the compliant model as well. For instance, during the acceleration and early deceleration phases, part of the graft flow is diverted into the coronary artery at the STS anastomosis; and when this flow in the coronary artery reaches the ETS anastomosis, it lifts up the flow coming from the graft and directs it smoothly into the coronary artery, as shown in Fig. 4. Thereby, there is no impact on the artery bed; while the impact on the floor is believed to be a contributing factor to the graft failure. Bates et al. [44] have shown evidence of the change in the flow character once it has impacted against the junction floor.

In order to investigate the effect of non-Newtonian rheology of blood on the flow field, the axial velocity profiles at various sections in the symmetry plane of the SQA model at the end of systole ($t_4=0.32$ s) are demonstrated in Fig. 5 for both the Newtonian and non-Newtonian fluid models. The axial velocity profile of the

non-Newtonian fluid is somewhat flattened due to its shear thinning behavior, and is less skewed towards the outer wall of the graft curvature, as compared to that of the Newtonian fluid, especially at sections S_3 , S_4 , and S_5 at the STS component (Fig. 5a) and at section S_6 at the ETS component (Fig. 5b) of the SQA model.

To exemplify the effect of wall compliance and non-Newtonian rheology of blood on the reversed flow, the axial velocity profile at section S_{10} , located distal to the ETS anastomosis of the SQA model, at time $t_5=0.84$ s, when the graft net flow rate just becomes negative, is shown in Fig. 6. Comparison between the Newtonian and non-Newtonian fluid models (in both the rigid and compliant models) demonstrates that the velocity profile of the non-Newtonian fluid is somewhat flattened, due to its shear-thinning behavior. Comparison between the rigid and compliant models (for both the Newtonian and non-Newtonian fluid models) illustrates a considerable reduction of reversed flow in the distensible model. This is because when the graft flow rate decreases during the deceleration phase, in order to satisfy the fluid's mass conservation in the rigid-wall model, this decrease can be compensated for, only by means of reducing the flow velocity. However, in the compliant model, the vessel's contraction partially compensates the flow rate drop by reducing the cross sectional area; consequently, less would be left to be compensated for, by reducing the velocity. As a result, less reversed flow is present in the distensible-wall models. These results are consistent with those of earlier studies [6,45].

Fig. 7 shows the secondary flows at two cross sections (S_3 and S_9) in the SQA model for both the Newtonian and non-Newtonian fluid models at the peak flow rate ($t_2=0.13$ s). At both sections, counter-rotating vortices (Dean vortices) are evident, with nearly symmetric streamlines due to the planarity of the models. At

Fig. 4. Flow streamlines in the SQA model at the peak flow rate ($t_2 = 0.13$ s). No impact of the flow observed on the artery floor at the ETS anastomosis, as the partial flow from the coronary artery segment located between the two anastomoses changes the velocity components of the graft flow and smoothly directs it into the coronary artery.

section S_3 , the secondary flows are weakened in the case of non-Newtonian fluid as compared to those of Newtonian fluid, which is consistent with the results of earlier studies [45]. However, as the cross sectional area is reduced at section S_9 , the velocity, and consequently, the near-wall shear rates are increased at this section where the flows from the coronary artery and the graft are merged.

Hence, the shear-thinning property of the non-Newtonian fluid reveals an opposing effect on the secondary flows at different locations of this section: the secondary velocity is increased at locations near to the wall; but, it is slightly decreased in the central region as compared to the case of Newtonian fluid model. This is because in the near-wall region of this section at this time instant, the fluid shear rate is higher than the threshold value (calculated to be $= 382 \text{ s}^{-1}$ in this study), above which the viscosity of the non-Newtonian fluid falls below the constant viscosity of the Newtonian fluid; however, in the central region, the shear rate is below the threshold. In all cases, the secondary flows are weakened along the coronary artery (distal to the ETS anastomosis) owing to the effect of the fluid viscosity.

3.3. Temporal and spatial variations of WSS

The temporal variations of WSS are investigated at some particular points on the vessel wall (P_1 to P_8 whose locations are shown in Fig. 1a) throughout the cardiac cycle, and are compared for the non-Newtonian fluid between the rigid and compliant models, as demonstrated in Fig. 8. Among all the points studied (including those whose graphs are not shown in Fig. 8), P_7 , located at the toe of the ETS anastomosis, shows the minimum disparity between the WSS time–history of the rigid and compliant models where the two graphs are almost identical (Fig. 8a). On the other hand, P_6 , located on the graft outer wall proximal to the ETS anastomosis, demonstrates the most discrepancy with up to 21% increase in the WSS magnitude in the rigid model compared to that of the distensible model (Fig. 8b), which can be attributable to the higher DV in the graft than in the coronary artery.

The profile of the WSS curves at proximal locations such as P_1 is more analogous to the calculated pressure waveform (see Fig. 8c), than those at distal locations. The overall shape of the

Fig. 5. Axial velocity profiles at various sections in the symmetry plane of the SQA model at the end of systole ($t_4 = 0.32$ s) for the non-Newtonian (continuous line) and Newtonian (dashed line) fluid models. (a) STS anastomosis of the SQA model and (b) ETS anastomosis of the SQA model.

Fig. 6. Axial velocity profiles in different models at section S_{10} , located distal to the ETS anastomosis of the SQA model, at time $t_5 = 0.84$ s, when the graft net flow rate has just become negative. A considerable decrease of the reversed flow is obvious in the distensible model, compared to that in the rigid-wall model.

WSS time–history curves is similar between the rigid and distensible models, with the WSS magnitude being generally higher in the rigid-wall model due to its smaller vessel diameter and the consequent higher velocity. However, at point P_8 , located on the ceiling wall of the coronary artery just distal to the toe of the ETS anastomosis, the magnitude of the WSS in the compliant model is higher than that in the rigid model (Fig. 8d), unlike the other points. This is due to the higher flow separation at this point in the rigid-wall model compared to the distensible model, which results in a significant reduction of WSS magnitude, and is in agreement with the aforementioned observations.

Fig. 9 demonstrates instantaneous WSS distributions along the coronary artery bed of the SQA model for the four cases of the rigid and compliant wall with the Newtonian and non-Newtonian fluid models at four different time points. During the systolic acceleration phase ($t_1 = 0.06$ s) as shown in Fig. 9a, on the artery bed before the middle of the ETS anastomosis ($x \leq 0.0941$ m), the WSS is higher for the non-Newtonian fluid due to its shear thinning behavior and the low shear rate in this region (in both the rigid and compliant models). However, on the artery bed opposite to the ETS anastomosis and further distal, the shear thinning behavior causes the WSS for the non-Newtonian fluid to become smaller than that for the Newtonian fluid, owing to the high shear rate in this region caused by the flow from the graft merging with that from the coronary artery at the ETS anastomosis. The WSS is somewhat higher in the rigid-wall model than that in the distensible

Fig. 7. Secondary flows at two cross sections in the SQA model (S_3 at the middle of the STS anastomosis (upper panel) and S_9 located distal to the ETS anastomosis (lower panel)) for the Newtonian (on the left) and non-Newtonian (on the right) fluid models at the peak flow rate ($t_2 = 0.13$ s). The shape of the rigid wall model is shown by dashed lines to illustrate the deformation of the vessel walls. The contours demonstrate the magnitude of the secondary flow, and they have the same scale for both the sections to facilitate the comparison.

Fig. 8. Temporal variations of WSS throughout the cardiac cycle at various points on the wall. (a) At P_7 , located at the toe of the ETS anastomosis, (b) at P_6 , located on the graft outer wall proximal to the ETS anastomosis, (c) at P_1 , located on the artery bed in the middle of the STS anastomosis, and (d) P_8 , located on the ceiling wall of the coronary artery just distal to the toe of the ETS anastomosis. The calculated pressure waveform is shown by dashed line in panel c.

model for both the Newtonian and non-Newtonian fluid models. At this time instant, the shear rate in the segment of the coronary artery located between the two anastomoses, and at the location distal to the ETS anastomosis is, respectively, lower and higher than the aforementioned threshold (above which the viscosity of non-Newtonian fluid becomes lower than that of the Newtonian fluid). Therefore, as the flow rate increases to its peak value ($t_2 = 0.13$ s), the difference between the WSS magnitudes (for the Newtonian and non-Newtonian fluids) decreases in the former region, while it increases in the latter one, as shown in Fig. 9b. Nevertheless, the qualitative distribution of WSS on the artery bed at the peak flow rate is similar to that during the acceleration phase, with the peak value occurring opposite to the toe of the ETS anastomosis.

Fig. 9c demonstrates the WSS distribution on the artery bed at the end of systole ($t_4 = 0.32$ s). The magnitude of the WSS for the non-Newtonian fluid is generally higher than that for the Newtonian fluid in both the compliant and rigid-wall models, as a result of the low shear rate at this time instant (negative values of WSS indicate reversed flow). At locations distal to the ETS anastomosis, the WSS magnitude in the rigid-wall model is higher than that in the compliant model for both Newtonian and non-Newtonian fluids. However, in the coronary artery segment located between the two anastomoses, the WSS magnitude in the distensible model is higher than that in the rigid model. This is because at this moment (late systolic deceleration), the low pressure results in the coronary artery contraction and reduction of the vessel diameter (to a value even smaller than that of the rigid model in this segment), and consequently, an increase in the WSS magnitude. The same phenomenon occurs in the late diastole too (not shown here). This is in agreement with the results of earlier FSI simulation studies of the blood flow in the right coronary artery reported by Zeng et al. [41] and Torii et al. [46]. Also, similar result can be observed in an ETS anastomosis FSI study by Hofer et al. [6], albeit this aspect (the

opposing effect of wall distensibility on WSS distribution) has not been pointed out.

At the peak reversed flow ($t_6 = 0.87$ s), the WSS magnitude for the non-Newtonian fluid is considerably higher than that for the Newtonian fluid along the artery bed in both the rigid and distensible models, due to the low shear rate at this time instant, as shown in Fig. 9d. Also, the WSS magnitude is slightly higher in the rigid-wall model than in the compliant model.

3.4. Hemodynamic parameters distribution

In order to investigate the effect of wall distensibility and non-Newtonian rheology on the distribution of HPs at the critical sites of the anastomosis namely toe, heel, bed, and the suture line (shown in Fig. 10), the segmental averages of the HPs, including time-averaged WSS (TAWSS), non-dimensional time-averaged WSS gradient (TAWSSG) [1], and oscillatory shear index (OSI) [20], are calculated and presented in Table 1. The following can be inferred from the tabulated results.

3.4.1. TAWSS

Comparison of the TAWSS between the rigid and compliant models (both for the Newtonian and non-Newtonian fluid models) demonstrates a decrease in the TAWSS at all critical locations in the compliant model, which ranges between 3% (on the suture line) and 32% (on the heel) in the conventional ETS model, and from 4% (at the toe of the STS anastomosis) to 27% (on the suture line of the STS anastomosis) in the SQA model. This is consistent with the results of earlier studies reporting that wall motion reduces the mean WSS in a straight elastic tube model [47], and in an elastic abdominal aortic bifurcation model [48].

Upon comparing the TAWSS between the Newtonian and non-Newtonian fluid models (in both compliant and rigid-wall models),

Fig. 9. Instantaneous WSS distributions along the coronary artery bed of the SQA model at different time points. (a) During systolic acceleration phase ($t_1 = 0.06$ s), (b) at systolic peak flow ($t_2 = 0.13$ s), (c) end of systole ($t_4 = 0.32$ s), and (d) at peak reversed flow ($t_6 = 0.87$ s). The shape of the vessel wall is shown by dashed line in panel (a).

Table 1
Comparison of the segmental averages of <HP>s.

Anastomosis model	Location	Rigid ^a			Distensible ^a			Distensible ^a			Distensible ^a		
		Newtonian ^b			Non-Newtonian ^b			Newtonian ^b			Non-Newtonian ^b		
		<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>	<OSI>	<TAWSS> (Pa)	<TAWSSG>
Conventional ETS model	1- Toe	0.01	6.69	34.02	0.01	5.65	28.47	0.01	6.14	31.00	0.02	5.23	26.34
	2- Heel	0.09	0.56	8.29	0.07	0.71	9.57	0.11	0.38	6.10	0.09	0.52	7.97
	3- Bed	0.09	1.67	5.46	0.08	1.55	4.64	0.11	1.47	5.01	0.09	1.40	4.29
	4- Suture line	0.04	2.12	15.09	0.04	2.06	14.94	0.05	2.05	13.30	0.04	1.99	13.66
Coupled sequential anastomoses model													
ETS component	1- Toe	0.01	6.33	36.95	0.02	5.36	31.23	0.01	5.85	29.71	0.02	5.01	25.24
	2- Heel	0.08	0.49	4.39	0.07	0.69	6.26	0.08	0.40	3.52	0.07	0.61	5.50
	3- Bed	0.05	1.86	4.93	0.05	1.76	4.05	0.06	1.76	5.02	0.06	1.59	3.88
	4- Suture line	0.03	2.51	15.12	0.03	2.39	15.00	0.03	2.10	11.44	0.04	2.05	11.61
STS component	5- Toe-STs	0.04	0.70	6.03	0.05	0.80	6.00	0.04	0.67	7.32	0.05	0.77	7.44
	6- Heel-STs	0.08	0.41	4.42	0.08	0.54	5.38	0.09	0.32	3.44	0.07	0.45	4.89
	7- Bed-STs	0.22	0.17	0.40	0.18	0.25	0.50	0.24	0.15	0.45	0.18	0.22	0.55
	8- Sutureline-STs	0.05	0.65	5.94	0.05	0.80	6.54	0.05	0.47	5.37	0.05	0.62	6.39

^a Wall model.

^b Fluid model.

it is seen that at the ETS anastomosis (of both the conventional and SQA models) in the case of non-Newtonian fluid, the TAWSS is decreased at the toe, suture line, and on the bed, while it is increased at the heel. On the other hand, at the STS anastomosis, the TAWSS is increased at all the critical locations. This reduction at the ETS anastomosis and increase at the STS anastomosis is due to the shear thinning behavior of the non-Newtonian fluid, as the shear rate is generally high at the ETS anastomosis (except at the heel) while it is low at the STS anastomosis.

3.4.2. TAWSSG

Comparison of the TAWSSG between the rigid and compliant models (both for the Newtonian and non-Newtonian fluid models) indicates that the TAWSSG is generally decreased in compliant models at the ETS anastomosis of both the conventional and SQA models (except on the artery bed of ETS anastomosis of SQA model in the case of Newtonian fluid). At the STS anastomosis of the SQA model, the TAWSSG is decreased at the heel and on the suture line, while it is increased at the toe and on the artery bed of the distensible models.

Comparison of the TAWSSG between the Newtonian and non-Newtonian fluid models (in both compliant and rigid-wall models), demonstrates that the TAWSSG at the ETS anastomosis (of both the conventional and SQA models) is reduced at the toe and on the artery bed, while it is increased at the heel, and is negligibly (<3%) changed on the suture line in the case of the non-Newtonian fluid model. At the STS anastomosis, the TAWSSG is increased on the artery bed, suture line, and at the heel, while it has experienced less than 2% change at the toe in the case of non-Newtonian fluid.

3.4.3. OSI

As shown in Table 1, the wall compliance somewhat increases the OSI in all the models, albeit the OSI value is generally low due to the waveform having mostly a forward flow during the cardiac cycle. The non-Newtonian rheology has an opposing effect on the OSI, in accordance with the shear thinning behavior. At locations with high shear rate where the shear thinning effect reduces the fluid viscosity and facilitates the oscillation of the flow (such as at the toe of the anastomosis), the OSI is increased in the case of non-Newtonian fluid model. Conversely, at locations with low shear rate where the shear thinning effect increases the fluid viscosity and impedes the flow oscillation (for instance at the heel and on the artery bed), the non-Newtonian rheology reduces the OSI. This effect is mostly pronounced on the artery bed at the STS anastomosis of the SQA model, where the OSI is reduced from 0.24 to 0.18 in the distensible model and from 0.22 to 0.18 in the rigid-wall model.

The OSI is slightly lower at the heel and on the artery bed of the ETS anastomosis of the SQA model, than in the conventional ETS anastomosis. Moreover, the OSI on the artery bed at the STS anastomosis of the SQA configuration is lower in the case of compliant model with non-Newtonian fluid, than in the case of the rigid-wall model with Newtonian fluid.

4. Discussion

In the present study, a two-way coupled FSI analysis of a novel CABG SQA is performed. The effects of vessel wall compliance and shear thinning property of blood are investigated on the flow field and HP distributions and the performance of this coupled SQA configuration in comparison with the conventional ETS anastomosis is evaluated in a more realistic bio-mechanical condition.

4.1. Model assumptions and limitations

As the focus of this investigation is on the flow fields and HPs distribution rather than the intramural stress distributions, a small

strain (large deformation) approximation of blood vessel mechanics is utilized. The vessel walls are assumed to be isotropic and homogeneous, and modeled as a linearly elastic, geometrically non-linear shell structure [6,22], and the same value of elastic modulus is employed for both the graft and the arterial wall.

The cardiac motion is ignored in this investigation, as it is indicated that a static geometry can predict the mean wall shear rates with a reasonable accuracy and the dynamic behavior is not significant at the base cardiac frequency of 1 Hz [49], and the motion of the RCA has minor effect on TAWSS patterns [50].

4.2. Evaluation of results

As described above in Section 3, the velocity profiles of non-Newtonian flow are flattened (as illustrated in Figs. 5 and 6) and the TAWSS is reduced at high shear rates due to shear thinning behavior of the blood (as shown in Table 1). In simple language, the blood has the property of losing its viscosity at high variations of velocity, which makes it less sticky and more fluent, and let the fluid layers flow more easily over each other.

Since the change in the velocity is higher in the near wall region and lower in the core region, this characteristic facilitates the flow in the former region and impedes it in the latter one. Hence, the velocity profile is flattened as compared to the parabolic velocity profile of a Newtonian fluid.

Likewise, in the case of high velocity gradients at the wall, the less sticky layers of the fluid can easily flow over each other near to the wall and induce less shear forces to the wall than in the case of low velocity gradients where the flow of the viscous fluid layers exerts higher shear forces onto the wall. When a non-Newtonian fluid is approximated by a Newtonian model, the constant viscosity of the Newtonian model represents the average viscosity of the non-Newtonian fluid within its working range of shear rates. Thus, comparison of the two fluids results in lower viscosity (and WSS values) at high shear rates and higher viscosity (and WSS values) at low shear rates for the non-Newtonian fluid as compared to the equivalent Newtonian fluid.

As observed and discussed in Section 3, at some locations, the effects of wall compliance and non-Newtonian rheology on the HPs distribution are in line, while at some other locations these effects are opposing. For instance, the wall compliance and non-Newtonian rheology both decrease the TAWSSG at the toe of the ETS anastomosis (from 36.95 to 29.71 and from 36.95 to 31.23, respectively, in the SQA model), which result in a further reduction (to 25.24) when comparing the “compliant wall with non-Newtonian fluid” model with the “rigid-wall with Newtonian fluid” model, due to the accumulation of these effects. However, at the heel of the ETS anastomosis, for example, the non-Newtonian rheology increases the TAWSS (from 0.56 Pa to 0.71 Pa in the rigid model), while the wall compliance decreases this parameter (from 0.56 Pa to 0.38 Pa in the case of Newtonian fluid); and the accumulation of these opposing effects results in a negligible overall change (from 0.56 Pa to 0.52 Pa) when a comparison between the above mentioned models is made.

Nevertheless, the interesting point is that at some particular locations, the accumulation of the two effects does not result in an expected outcome as above. For instance, at the toe of the STS anastomosis of the SQA model, the non-Newtonian rheology slightly decreases the TAWSSG in the rigid model from 6.03 to 6, while the wall compliance increases this HP from 6.03 to 7.32. Nonetheless, the accumulation of the two effects does not result in a value between 6 and 7.32, but in a higher value of 7.44. This fact demonstrates that the effect of one parameter (either non-Newtonian rheology or wall compliance) is not independent from the other one. As in this example, the non-Newtonian rheology has slightly decreased the TAWSSG in the rigid-wall model (from 6.03 to 6),

Fig. 10. Critical regions of the ETS (left panel) and STS (right panel) anastomoses, which are the susceptible sites of IH and atherosclerotic lesion formation. 1,5: toe, 2,6: heel, 3,7: artery bed, and 4,8: suture line.

while it has increased this HP in the compliant model (from 7.32 to 7.44). Likewise, on the artery bed of the ETS anastomosis of the SQA model for instance, the wall compliance has slightly increased the TAWSSG (from 4.93 to 5.02) in the case of the Newtonian fluid model, while it has decreased this HP (from 4.05 to 3.88) in the case of the non-Newtonian fluid model.

This phenomenon might be attributable to the interaction of the shear thinning property of the blood with the sudden, local variations of shear rate due to expansions and contractions of the compliant vessel wall during the cardiac cycle. As the vessel wall moves, the shear rate may increase or decrease at different points, depending on the relative movement of the wall and the fluid. This results in some instantaneous local variations of WSS which consequences in some extreme (high or low) spatial WSSG that unexpectedly affects the value of TAWSSG over the cardiac cycle. This phenomenon suggests that it is essential to study and incorporate the effects of these parameters (wall compliance and non-Newtonian rheology) simultaneously, rather than discretely and individually, as they are not independent and cannot be super-imposed.

The HPs distribution illustrates that the advantages of the SQA model over the conventional ETS anastomosis, which had been observed in the rigid-wall model with the Newtonian fluid previously and reported in our earlier study [20], are present in the compliant model with the non-Newtonian fluid too. The TAWSS is increased on the artery bed of the ETS anastomosis of the SQA model to 1.59 Pa, from 1.40 Pa in the conventional ETS model. Although this increase is marginal, a critical biological WSS value of 1.5 Pa has been reported [51,52] below which intimal thickening would develop. Based thereon, the moderate improvement of TAWSS on the artery bed of the SQA design is deemed to be vital. In addition, the TAWSS at the heel of the ETS anastomosis is slightly reduced in the conventional ETS anastomosis (from 0.56 to 0.52), while it is increased in the SQA configuration (from 0.49 to 0.61) in the compliant model with non-Newtonian fluid, as compared to those in the rigid-wall model with Newtonian fluid. This results in having the TAWSS at the heel of the ETS anastomosis in the SQA model to be higher than that in the conventional ETS model, while it is opposite in the rigid-wall model with Newtonian fluid. This reveals another advantage of the SQA configuration over the conventional

ETS anastomosis which had not been disclosed in our previous study.

As shown in Table 1, the TAWSSG is decreased at all the critical locations of the ETS anastomosis in the SQA configuration as compared to the conventional ETS anastomosis in the case of compliant model with non-Newtonian fluid, while this advantage can be observed only at the heel and on the artery bed in the case of the rigid-wall model with Newtonian fluid. This manifests a more uniform distribution of WSS at the ETS anastomosis of the SQA configuration, which can lessen the vessel wall permeability and atherosclerotic lesion development, and further unveils the advantages of the SQA design over the conventional ETS anastomosis.

4.3. Surgical aspects

The surgical procedure required to perform the coupled SQA configuration is the same as that of a typical sequential bypass grafting; the only difference is that both the anastomoses are sutured on the same coronary artery. Usually surgeons start the suturing with the furthest anastomosis; for instance, in the case of left coronary

Fig. 11. Comparison of analytical solution due to Zamir [53] and the current numerical solution at $t = 6.26$ s, 6.45 s, 6.75 s, and 7.00 s. The symbols are due to the current numerical solution and the solid lines are due to the analytical solution.

arteries, the distal ETS anastomosis is performed first, and then the STS anastomosis is sutured.

The angle at which a surgeon cuts the graft end determines the angle of implantation (ETS anastomotic angle) which can be adjusted to an optimum. The length of arteriotomy is about 5 mm, and most superficial coronary arteries have at least 2–3 cm of visible course on the surface of the heart. Hence, the proposed grafting configuration would be technically feasible in certain cases.

This design does involve one additional anastomosis which results in a prolonged operation time. However, apart from the distinct advantages it brings about in the flow field and distribution of HPs, it provides a spare route for the blood flow to the coronary artery, to avoid re-operation in case of re-stenosis in either of the anastomoses.

5. Conclusion

A two-way coupled FSI analysis of a novel CABG SQA is carried out in conjunction with the shear thinning property of blood to investigate the performance of this coupled SQA configuration in comparison with the conventional ETS anastomosis in a more realistic bio-mechanical condition, with an emphasis on the effects of wall compliance and non-Newtonian rheology on the HPs distribution.

The simulation results indicate that the velocity patterns and qualitative distribution of WSS parameters do not change significantly in the compliant model despite quite large side-wall deformations in the anastomotic regions. The WSS magnitude is generally reduced in the distensible model, as compared to that in the rigid-wall model, resulting in a lower TAWSS in the compliant model. The wall compliance has generally decreased the TAWSSG, while it has somewhat increased the oscillatory nature of the flow.

The effect of non-Newtonian rheology on the HPs is heterogeneous. The ETS anastomosis (of both the conventional and SQA models) experiences mostly a decrease in the TAWSS (except at the heel), while the STS anastomosis of the SQA model undergoes an increase in this HP. The flow oscillation is increased at the toe of the anastomosis, whereas it is decreased at the heel and on the artery bed, due to the shear thinning behavior of the blood.

It is observed that the effects of wall compliance and non-Newtonian rheology are not independent, and that they influence each other. Hence, it is essential to investigate the effects of these parameters simultaneously (and not individually) in each particular model.

Although vessel wall compliance and non-Newtonian rheology have shown modest influence on the HPs in each model, they have unveiled further advantages of the coupled SQA model over the conventional ETS anastomosis which had not been revealed in our previous study with the rigid-wall and Newtonian fluid models [20]. Therefore, we conclude that the inclusion of wall compliance and non-Newtonian rheology in flow simulation of blood vessels can be essential in quantitative and comparative analyses. This investigation further verifies the hemodynamic benefits of the blood flow in the coupled SQA configuration in a more realistic bio-mechanical condition.

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A.1. Validation of FSI methodology

In order to validate the FSI simulations and the method used in this study, a simple sinusoidal flow in a straight compliant tube is modeled and the numerical results are compared with the corresponding analytical solution due to Zamir [53].

The length and radius of the tube, and the thickness and elastic modulus of the wall are, respectively, 0.42 m, 0.005 m, 0.0005 m, and 20 MPa; and the fluid has the same properties as the Newtonian blood in the present study. The frequency of oscillation is set to be 1 Hz.

The applied boundary pressure waveforms are:

$$P_{\text{inlet}} = 30 + 1000 \sin(2\pi t) \text{ Pa} \quad (\text{A1})$$

$$P_{\text{outlet}} = 1000 \sin(2\pi t - 0.0139456) \text{ Pa} \quad (\text{A2})$$

Fig. 11 demonstrates the comparison of the calculated non-dimensional velocity profiles at a cross section located at 0.4 m distance from the entrance of the tube. The velocity is normalized using $R^*\omega$ as the characteristic scale, where R^* is the radius of the tube plus half the thickness of the tube wall and ω is the angular frequency of oscillation. There is an excellent agreement between the analytical solution and the obtained numerical solution with an average relative error of 5.1%.

Based on these validation results, hence, it is concluded that the fluid–structure interaction method used in the present study is accurate in predicting the fluid dynamics of the coronary arterial bypass graft models investigated.

Conflict of interest statement

The authors affirm that there are no financial and personal relationships or involvement with any commercial organization that could inappropriately influence or bias the present manuscript.

References

- [1] Buchanan JR, Kleinstreuer C, Hyun S, Truskey GA. Hemodynamics simulation and identification of susceptible sites of atherosclerotic lesion formation in a model abdominal aorta. *Journal of Biomechanics* 2003;36:1185–96.
- [2] Caro CG, Fitz-Gerald JM, Schroter RC. Atheroma and arterial wall shear. Observation, correlation and proposal of a shear dependent mass transfer mechanism for atherogenesis. *Proceedings of the Royal Society of London Series B, Biological Sciences* 1971;177:109–59.
- [3] Caro CG, Parker KH. In: Olsson AG, editor. The effect of hemodynamics factors on the arterial wall. Edinburgh: Churchill Livingstone; 1987. p. 183–95.
- [4] Friedman MH, Barger CB, Deters OJ, Hutchins GM, Mark FF. Correlation between wall shear and intimal thickness at a coronary artery branch. *Atherosclerosis* 1987;68:27–33.
- [5] Fry DL. Acute vascular endothelial changes associated with increased blood velocity gradients. *Circulation Research* 1968;22:165–97.
- [6] Hofer M, Rappitsch G, Perktold K, Trubel W, Schima H. Numerical study of wall mechanics and fluid dynamics in end-to-side anastomoses and correlation to intimal hyperplasia. *Journal of Biomechanics* 1996;29:1297–308.
- [7] Nerem RM, Cornhill JF. The role of fluid mechanics in atherogenesis. *Journal of Biomechanical Engineering* 1980;102:181–9.
- [8] Bassiouny HS, White S, Glagov S, Choi E, Giddens DP, Zarins CK. Anastomotic intimal hyperplasia: mechanical injury or flow induced. *Journal of Vascular Surgery* 1992;15:708–17.
- [9] Sottiurai VS, Yao JST, Batson RC, Sue SL, Jones R, Nakamura YA. Distal anastomotic intimal hyperplasia: histopathologic character and biogenesis. *Annals of Vascular Surgery* 1989;3:26–33.
- [10] Trubel W, Schima H, Moritz A, Raderer F, Windisch A, Ullrich R, et al. Compliance mismatch and formation of distal anastomotic intimal hyperplasia in externally stiffened and lumen-adapted venous grafts. *European Journal of Vascular and Endovascular Surgery* 1995;10:415–23.
- [11] Fei DY, Thomas JD, Rittgers SE. The effect of angle and flow rate upon hemodynamics in distal vascular graft anastomoses: a numerical model study. *Journal of Biomechanical Engineering* 1994;116:331–6.
- [12] Staalsen NH. The anastomosis angle does change the flow fields at vascular end-to-side anastomoses in vivo. *Journal of Vascular Surgery* 1995;21:460–71.
- [13] How TV, Rowe CS, Gilling-Smith GL, Harris PL. Interposition vein cuff anastomosis alters wall shear stress distribution in the recipient artery. *Journal of Vascular Surgery* 2000;31:1008–17.

- [14] Lei M, Kleinstreuer C, Archie Jr JP. Geometric design improvements for femoral graft–artery junctions mitigating restenosis. *Journal of Biomechanics* 1996;29:1605–14.
- [15] Leuprecht A, Perktold K, Prosi M, Berk T, Trubel W, Schima H. Numerical study of hemodynamics and wall mechanics in distal end-to-side anastomoses of bypass grafts. *Journal of Biomechanics* 2002;35:225–36.
- [16] Sankaranarayanan M, Ghista DN, Chua LP, Tan YS, Kassab GS. Analysis of blood flow in an out-of-plane CABG model. *American Journal of Physiology–Heart and Circulatory Physiology* 2006;291:H283–95.
- [17] Sherwin SJ, Shah O, Doorly DJ, Peiró J, Papaharilaou Y, Watkins N, et al. The influence of out-of-plane geometry on the flow within a distal end-to-side anastomosis. *Journal of Biomechanical Engineering* 2000;122:86–95.
- [18] Bonert M, Myers JG, Fremes S, Williams J, Ethier CR. A numerical study of blood flow in coronary artery bypass graft side-to-side anastomoses. *Annals of Biomedical Engineering* 2002;30:599–611.
- [19] Qiao A, Liu Y. Influence of graft–host diameter ratio on the hemodynamics of CABG. *Bio-Medical Materials and Engineering* 2006;16:189–201.
- [20] Kabinejadian F, Chua LP, Ghista DN, Sankaranarayanan M, Tan YS. A novel coronary artery bypass graft design of sequential anastomoses. *Annals of Biomedical Engineering* 2010;38:3135–50.
- [21] Perktold K, Rappitsch G. In: Tarbell JM, editor. *Advances in bioengineering*, vol. 26. New York: ASME; 1993. p. 127–30.
- [22] Perktold K, Rappitsch G. Computer simulation of local blood flow and vessel mechanics in a compliant carotid artery bifurcation model. *Journal of Biomechanics* 1995;28:845–56.
- [23] Tang D, Yang C, Kobayashi S, Zheng J, Vito RP. Effect of stenosis asymmetry on blood flow and artery compression: a three-dimensional fluid–structure interaction model. *Annals of Biomedical Engineering* 2003;31:1182–93.
- [24] Koshiba N, Ando J, Chen X, Hisada T. Multiphysics simulation of blood flow and LDL transport in a porohyperelastic arterial wall model. *Journal of Biomechanical Engineering* 2007;129:374–85.
- [25] Kabinejadian F, Chua LP, Ghista DN, Tan YS. CABG models flow simulation study on the effects of valve remnants in the venous graft. *Journal of Mechanics in Medicine and Biology* 2010;10:593–609.
- [26] Ballyk PD, Walsh C, Ojha M. Effect of intimal thickening on the stress distribution at an end-to-side graft–artery junction. *Hull*, vol. 31. San Francisco, CA: ASME; 1995.
- [27] Aoki T, Ku DN. Collapse of diseased arteries with eccentric cross section. *Journal of Biomechanics* 1993;26:133–42.
- [28] Salzar RS, Thubrikar MJ, Eppink RT. Pressure-induced mechanical stress in the carotid artery bifurcation: a possible correlation to atherosclerosis. *Journal of Biomechanics* 1995;28:1333–40.
- [29] Vorp DA, Raghavan ML, Borovetz HS, Greisler HP, Webster MW. Modeling the transmural stress distribution during healing of bioresorbable vascular prostheses. *Annals of Biomedical Engineering* 1995;23:178–88.
- [30] Nichols WW, O'Rourke MF. In: Nichols WW, O'Rourke MO, editors. *McDonald's blood flow in arteries. Theoretical, experimental and clinical principles*. 3rd ed. London: Edward Arnold; 1990. p. 89.
- [31] Wesly RLR, Vaishnav RN, Fuchs JCA, Patel DJ, Greenfield Jr JC. Static linear and nonlinear elastic properties of normal and arterialized venous tissue in dog and man. *Circulation Research* 1975;37:509–20.
- [32] Hasegawa H, Kanai H. Measurement of elastic moduli of the arterial wall at multiple frequencies by remote actuation for assessment of viscoelasticity. *Japanese Journal of Applied Physics, Part 1: Regular Papers and Short Notes and Review Papers* 2004;43:3197–203.
- [33] Gradus-Pizlo I, Bigelow B, Mahomed Y, Sawada SG, Rieger K, Feigenbaum H. Left anterior descending coronary artery wall thickness measured by high-frequency transthoracic and epicardial echocardiography includes adventitia. *American Journal of Cardiology* 2003;91:27–32.
- [34] Dobrin PB, Littooy FN, Endean ED. Mechanical factors predisposing to intimal hyperplasia and medial thickening in autogenous vein grafts. *Surgery* 1989;105:393–400.
- [35] Hughes TJR, Liu WK, Zimmermann TK. Lagrangian–Eulerian finite element formulation for incompressible viscous flows. *Computer Methods in Applied Mechanics and Engineering* 1981;29:329–49.
- [36] Bird RB, Armstrong RC, Hassager O. *Dynamics of polymer liquids*, vol. 1, 2nd ed. New York: Wiley; 1987.
- [37] Gijzen FJH, Van De Vosse FN, Janssen JD. The influence of the non-Newtonian properties of blood on the flow in large arteries: steady flow in a carotid bifurcation model. *Journal of Biomechanics* 1999;32:601–8.
- [38] Galjee MA, Van Rossum AC, Doesburg T, Hofman MBM, Falke THM, Visser CA. Quantification of coronary artery bypass graft flow by magnetic resonance phase velocity mapping. *Magnetic Resonance Imaging* 1996;14:485–93.
- [39] Womersley JR. Method for the calculation of velocity, rate of flow and viscous drag in arteries when the pressure gradient is known. *The Journal of Physiology* 1955;127:553–63.
- [40] Schaar JA, Regar E, Mastik F, McFadden EP, Saia F, Disco C, et al. Incidence of high-strain patterns in human coronary arteries: assessment with three-dimensional intravascular palpography and correlation with clinical presentation. *Circulation* 2004;109:2716–9.
- [41] Zeng D, Boutsianis E, Ammann M, Boomsma K, Wildermuth S, Poulidakos D. A study on the compliance of a right coronary artery and its impact on wall shear stress. *Journal of Biomechanical Engineering* 2008;130:1–11.
- [42] Atabek HB, Ling SC, Patel DJ. Analysis of coronary flow fields in thoracotomized dogs. *Circulation Research* 1975;37:752–61.
- [43] Patel DJ, Fry DL. In situ pressure–radius–length measurements in ascending aorta of anesthetized dogs. *Journal of Applied Physiology* 1964;19:413–6.
- [44] Bates CJ, O'Doherty DM, Williams D. Flow instabilities in a graft anastomosis: a study of the instantaneous velocity fields. *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine* 2001;215:579–87.
- [45] Chen J, Lu XY, Wang W. Non-Newtonian effects of blood flow on hemodynamics in distal vascular graft anastomoses. *Journal of Biomechanics* 2006;39:1983–95.
- [46] Torii R, Wood NB, Hadjiloizou N, Dowsey AW, Wright AR, Hughes AD, et al. Fluid–structure interaction analysis of a patient-specific right coronary artery with physiological velocity and pressure waveforms. *Communications in Numerical Methods in Engineering* 2009;25:565–80.
- [47] Wang DM, Tarbell JM. Nonlinear analysis of oscillatory flow, with a nonzero mean, in an elastic tube (artery). *Journal of Biomechanical Engineering* 1995;117:127–35.
- [48] Lee CS, Tarbell JM. Wall shear rate distribution in an abdominal aortic bifurcation model: effects of vessel compliance and phase angle between pressure and flow waveforms. *Journal of Biomechanical Engineering* 1997;119:333–42.
- [49] Santamarina A, Weydahl E, Siegel Jr JM, Moore Jr JE. Computational analysis of flow in a curved tube model of the coronary arteries: effects of time-varying curvature. *Annals of Biomedical Engineering* 1998;26:944–54.
- [50] Zeng D, Ding Z, Friedman MH, Ross Ethier C. Effects of cardiac motion on right coronary artery hemodynamics. *Annals of Biomedical Engineering* 2003;31:420–9.
- [51] Giddens DP, Zarins CK, Glagov S. Response of arteries to near-wall fluid dynamics behavior. *Applied Mechanics Review* 1990;43:S98–102.
- [52] Lieber BB, Giddens DP. Post-stenotic core flow behavior in pulsatile flow and its effects on wall shear stress. *Journal of Biomechanics* 1990;23:597–605.
- [53] Zamir M. *The physics of pulsatile flow*. New York: Springer-Verlag; 2000. p. 113–145.

CABG MODELS FLOW SIMULATION STUDY ON THE EFFECTS OF VALVE REMNANTS IN THE VENOUS GRAFT

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Venous valves and sinuses are frequently observed in vein grafts in the coronary artery bypass grafts (CABG). However, from the biomedical engineering viewpoint, vein grafts are always assumed as smooth tubes in the existing simulations, and no effort has been made to investigate the effects of jaggedness of the graft inner wall due to the valve cusps remnants and valve sinus (in case of valve-stripped saphenous vein (SV) grafts) on the blood flow patterns and hemodynamic parameters (HPs). In this paper, the effects of the inner surface irregularities of a vein graft on the blood flow is investigated in the graft as well as in the distal anastomotic region, with a more realistic geometry of valve-stripped SV, by means of numerical simulation of pulsatile, Newtonian blood flow. The simulation results demonstrate that the valve remnants and sinuses cause disturbances in the flow field within the graft (due to vortices formation within the valve sinuses) and undesirable distribution of HPs, which can result in early atherosclerotic lesion development in the graft.

Keywords: Coronary artery bypass grafting (CABG); saphenous vein; venous valve remnants; hemodynamics; stenosis; computational fluid dynamics (CFD).

Nomenclature

B_n	Fourier coefficients
D_A	Coronary artery diameter
D_G	Graft diameter
J_0, J_1	First kind Bessel functions of order zero and one respectively
L_1	Distance between the anastomosis and the nearest valve

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L_2	Distance between two valves
L_B	Length of anastomosis bed
L_D	Length of distal section of the host artery
L_P	Length of occluded proximal section of the host artery
L_V	Length of the valve region
p	Pressure
R	Tube radius
t	Time
T	Time period of the flow cycle
$\mathbf{u}$	Velocity vector

Greek symbols

α	Womersley number
μ	Dynamic viscosity of the blood
ρ	Density
τ_0	Wall shear stress for Poiseuille flow at the mean flow Reynolds number
$\vec{\tau}_w$	Wall shear stress vector (traction)

1. Introduction

Coronary artery bypass grafts (CABG) flow modeling and computational fluid dynamic (CFD) investigations have played an important role in attempts to prevent acute and late graft occlusion, by correlating abnormal flow dynamics to sites of cell proliferation, in order to identify the etiology of anastomotic neointimal hyperplasia and feasibility of its prevention.

It is well documented that hemodynamic parameters (HPs) are associated with intimal hyperplasia (IH) and hypothesized as a cause of bypass graft failure.^{1–3} In order to investigate and improve the HP distributions in CABG, many studies have been undertaken and effects of different geometrical parameters have been evaluated on both proximal and distal anastomoses, as well as total CABG models.^{4–10} Yet, in all earlier investigations, the graft inner wall surface is assumed to be smooth. Hence, we have undertaken to investigate the effects of the inner surface irregularities of a vein graft on the blood flow in the case of valve-stripped saphenous vein (SV) grafts, by comparing CFD-simulated flows in models of valve-stripped SV grafts with a smooth-walled graft model.

1.1. Valve-stripped SV grafting

In reversed vein grafts, the pressure trap, caused by competent valves in the distal segment of the grafts, can result in segmental hypertension, which can play an important role in graft stenosis.^{11,12} Moreover, abnormal venous valves may cause obstruction to flow unrelated to technical error or poor run-off.¹³ Therefore, the alternative procedure to reversed vein grafting is the valve-stripped vein grafting, where surgeons remove the venous valves before grafting a commonly used SV.

Nevertheless, this method is not devoid of complications. Apart from the probable internal vein trauma caused by valvulotomes, the valve sinus and remnants of the valve cusps cause irregularities on the vein inner wall, and deviate its geometry from an ideal, smooth, and regular tube, which may affect the hemodynamics in the graft.

Hence, in this paper, the effects of the valve sinus and remnants of the valve cusps on the blood flow at the distal anastomosis of a CABG with a valve-stripped vein graft are studied by means of numerical simulation of pulsatile Newtonian blood flow.

2. Model of Vein Graft with Stripped Valves

It is of interest for us to more realistically model vein graft with stripped valves, and study the effect of irregularities of the graft inner wall on the flow field and HP distributions. Since the study of a complete CABG model has demonstrated that IH would be more prone to form in the distal anastomosis than in the proximal anastomosis,¹⁰ this effect of unevenness of graft inner wall is investigated at the distal anastomosis models of a CABG for the valve-stripped SV grafting.

2.1. Occurrence and distribution of venous valves

The average distance between valves in the superficial veins of the shank is 40 mm. The average number of valves in the thigh region of the long SV is 3.5, and in the lower leg region is 4.¹⁴ Depending upon the length of the graft, up to seven pairs of valves have been identified in a single vein graft.¹⁵

2.2. Geometry of the models

Based on the medical data on occurrence and distribution of venous valves in SV grafts, three distal anastomosis models of the right coronary artery (RCA) bypass graft are designed for CFD simulation as follows: one distal anastomosis model with a smooth inner wall vein graft having neither valve nor its remnants (as earlier simulations); another model with a vein graft containing one valve sinus and the valve remnants; and finally, one distal anastomosis model with a vein graft containing two valve sinus and the valve remnants, namely model 1, model 2, and model 3, respectively. The last model is considered due to evidences that the presence of more than one valve in a graft may cause flow disturbance.¹⁶

The dimensions of the models are listed in Table 1, where D_G , D_A , L_P , L_B , L_D , L_1 , L_2 , and L_V stand for the graft diameter, coronary artery diameter, length of occluded proximal section of the host artery, length of anastomosis bed, length of distal section of the host artery, distance between the anastomosis and the nearest valve, distance between two valves, and length of the valve region, respectively, as shown in Fig. 1. The proximal segment of the coronary artery is fully occluded since

Table 1. Dimension of different models' geometry (all lengths are in mm).

Model	D _G	D _A	L _P	L _B	L _D	L ₁	L ₂	L _V
1 (No valve remnant)	4	2	14	12	24	N.A.	N.A.	N.A.
2 (One valve remnant)	4	2	14	12	24	7	N.A.	8.5
3 (Two valve remnants)	4	2	14	12	24	7	30	8.5

Fig. 1. A schematic view and definition of various parts of the distal anastomotic model.

it generally becomes occluded within a month after surgery; and the models are designed to be planar according to Galjee *et al.*¹⁷ who demonstrated that the typical location and course of RCA bypass graft could be assumed to be approximately planar.

2.3. CFD model formulation and boundary conditions

The governing equations for three-dimensional (3D), transient, incompressible, and laminar blood flow are Continuity and Navier–Stokes equations:

$$\nabla \cdot \mathbf{u} = 0 \quad (1)$$

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

where $\mathbf{u}$ is the velocity vector, t the time, and p is the pressure. The density (ρ) and dynamic viscosity (μ) of the blood are assumed to be 1050 kg/m^3 and $0.00408 \text{ Pa}\cdot\text{s}$, respectively.^{8,9}

The commercial CFD software, FLUENT (Fluent User's Guide, Fluent, Lebanon, NH), is used to solve the governing equations by a finite volume method. The semi-implicit SIMPLEC algorithm is used as the pressure-velocity coupling scheme. Time stepping employs a fully implicit scheme, and the time step size is taken to be 0.01 s . The convergence criterion, which is the scaled residual, is set to be required to decrease to 5×10^{-5} in this study. The scaled residual computed by FLUENT's segregated solver for the continuity equation is the total absolute rate of mass creation in all the computational cells divided by its maximum value obtained in the first five iterations. For the Navier–Stokes equation, the residual is defined

as the imbalance in the momentum conservation equation for each discretized cell, summed over all the computational cells.

In order to eliminate the start-up effects of transient flow, the computation is carried out for five periods, and the fifth period results are presented.

A fully developed pulsatile flow is applied at the graft inlet, whose flow waveform and the velocity profile are based on the measurements (by magnetic resonance phase velocity mapping) within a CABG;¹⁸ however, some modifications are made to smoothen the waveform. The resulting waveform, with the period of 0.9 s and average velocity values adapted for this study, is demonstrated in Fig. 2.

The Womersley solution^{19,20} is assumed for the inlet axial velocity profile, which is derived as a fully developed pulsatile flow, and implemented as the inlet boundary condition to calculate the velocity for the pulsatile flow:

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

where i is the imaginary unit, R is the tube radius, α is the Womersley number, J_0 and J_1 are the first kind Bessel functions of order zero and one, respectively, B_n Fourier coefficients, and $\text{Real}\{\}$ represents the real part of the complex expression. A user-supplied C program is provided to implement the above equation, and calculate the velocity profiles for the pulsatile flow, as the inlet boundary condition within FLUENT.

The exit flow is assumed to be in a fully developed condition. Thereby, the FLUENT's outflow boundary condition is set to assume a zero normal gradient for all flow variables except pressure. In this study, the vein and arteries are considered

Fig. 2. Average velocity waveform adapted for the present study (labels indicate times at which flow and HP are studied).

as rigid tubes, and the no-slip boundary condition is applied to all walls. This is because the effects of wall elasticity are minor on overall wall shear stress (WSS) patterns and less pronounced than those of arterial geometry and flow conditions.^{21–23}

In order to optimize the computational time, only one symmetric half of the distal anastomosis models is built and meshed. The mesh independency is tested on the velocity and WSS distributions by increasing the number of grid cells. For instance, for the model containing two valve remnants, the mesh with 106976 cells is found to be sufficient, since finer meshes of 129163 and 173590 cells did not show considerable change in the results.

3. Results

3.1. Flow behavior

The flow field and HPs in all models are studied at 12 instants of time, as shown on the waveform in Fig. 2, some of which are presented here. The streamlines of the flow field in the center plane of the three models are presented from Fig. 3 to Fig. 7, where model 1 (with the smooth graft), model 2 (with one valve remnant), and model 3 (with two valve remnants) are labeled as (a), (b), and (c), respectively.

At the early systolic acceleration phase (t_1), as observed in Fig. 3, the flow in the graft maintains its flow path smoothly toward the anastomosis in all models, and it is well conformed to the shape of the graft at the valve remnant and sinus. There is also a vortex formed at the occluded segment of the coronary artery in all the models.

As the flow further accelerates, in models containing valve remnants (see Figs. 4(b) and 4(c), a vortex appears in each valve sinus due to the flow separation at the valve remnant located at the beginning of the valve sinus; this vortex size increases with the flow rate, and occupies all around the graft perimeter within the valve sinus at the peak flow rate (t_3). The vortex in the occluded segment of the coronary artery shifts toward the heel of the anastomosis with the flow rate increment, in all the models as demonstrated in Fig. 4.

During the systolic deceleration phase, the size of the vortices in the valve sinuses increases with flow deceleration (as compared to the systolic acceleration phase) due to the fluid momentum decrease within the graft, as shown in Fig. 5 for the time t_6 , the first valley in the velocity cycle. There is also a small vortex formed at the graft inner wall, proximal to the valve remnant in models 2 and 3. At this time, the vortex at the heel of the anastomosis is about combining with the vortex at the valve sinus of the closer valve remnant to the anastomosis. None of these is observed in the model with smooth graft. However, the size of the vortices does not further increase with the diastolic acceleration phase starting at this time.

The flow fields during the diastolic acceleration and early diastolic deceleration phases (t_7 to t_{10}) are similar to those of corresponding systolic phases. Therefore, they are not shown here.

Fig. 3. Streamlines at the symmetry plane at time $t_1 = 0.02$ s: (a) smooth graft model, (b) model with one valve remnant, and (c) model with two valve remnants. Smooth flow pattern is observed in the graft.

Fig. 4. Streamlines at the symmetry plane at time $t_3 = 0.08$ s: (a) smooth graft model, (b) model with one valve remnant, and (c) model with two valve remnants. The size of the vortex in the valve sinus is increased.

Fig. 4. (*Continued*)

Fig. 5. Streamlines at the symmetry plane at time $t_6 = 0.31$ s: (a) smooth graft model, (b) model with one valve remnant, and (c) model with two valve remnants. Enhanced vortices observed in the valve sinus and heel of anastomosis.

Fig. 6. Streamlines at the symmetry plane at time $t_{11} = 0.84$ s: (a) smooth graft model, (b) model with one valve remnant, and (c) model with two valve remnants. Vortices located in the heel of anastomosis, valve sinus near to anastomosis, and the segment proximal to its valve remnant all merging due to large size of vortices and short distance between the valve sinus and the anastomosis. Considerable flow disturbance is observed within the grafts containing valve remnants.

As the graft net flow rate becomes negative (t_{11}), in the model with smooth graft, the size of the vortex at the heel increases immensely and one more vortex appears along the graft outer wall near the toe in addition to the vortex in the occluded segment of the coronary artery, as shown in Fig. 6(a). This is because the low momentum fluid near the wall is flowing backward at this time instant, while the fluid near the graft axis is still flowing forward; therefore, in between of these two reverse direction flows, there would be a zero velocity region, where the new vortex is formed. In models 2 and 3, the vortex in the valve sinus, which has reached to its maximum size, now merges with the vortex located at the heel along the inner wall as well as with the vortex proximal to the valve remnant. Along the outer wall, the vortex near the toe has also merged with the vortex in the valve

sinus, as shown in Figs. 6(b) and 6(c). The flow disturbances in the graft of models 2 and 3 are considerably increased due to the merging of these vortices with those in the anastomotic region, which is because of the short distance between the valve remnant and the anastomosis. This has somewhat blocked the forward flow of the blood.

At the time of reversed flow (t_{12}), the blood is flowing back toward the aorta in all the models, and those two vortices in the anastomotic region are vanished. In models 2 and 3, the vortex in the valve sinus reduces in size and shifts toward the graft axis while the flow streamlines are smooth near the graft wall, as demonstrated in Fig. 7; but in the smooth graft model, the blood is flowing back in the graft without any disturbances near the graft axis.

Fig. 7. Streamlines at the symmetry plane at time $t_{12} = 0.88$ s: (a) smooth graft model, (b) model with one valve remnant, and (c) model with two valve remnants. Backflow in the graft shifts the vortex in the valve sinus and the flow disturbances toward the graft axis in models containing valve remnants.

3.2. HP distribution

The localized distribution of low-WSS-and-high-oscillatory shear index (OSI) strongly correlates with the focal locations of atheroma.^{24,25} Besides, high spatial WSS gradient (WSSG) contributes to the elevated wall permeability and continued growth of atherosclerotic lesions.^{26,27} Hence, in order to evaluate and compare the hemodynamics in the three models, the HPs including time-averaged WSS (TAWSS), nondimensional time-averaged WSS gradient (TAWSSG),²⁴ and OSI²⁵ are investigated, according to their expressions given by the following Eqs. (4)–(6), respectively.

$$\text{TAWSS} = \frac{1}{T} \int_0^T |\vec{\tau}_w| dt \quad (4)$$

$$\text{TAWSSG} = \frac{D_G}{\tau_0} \frac{1}{T} \int_0^T \sqrt{\left(\frac{\partial \tau_x}{\partial x}\right)^2 + \left(\frac{\partial \tau_y}{\partial y}\right)^2 + \left(\frac{\partial \tau_z}{\partial z}\right)^2} dt \quad (5)$$

$$\text{OSI} = \frac{1}{2} \left(1 - \frac{\left| \int_0^T \vec{\tau}_w dt \right|}{\int_0^T |\vec{\tau}_w| dt} \right), \quad (6)$$

where $\vec{\tau}_w$ is the WSS vector (traction), T the time period of the flow cycle, D_G the graft diameter, and τ_0 is the WSS for Poiseuille flow at the mean flow Reynolds number.

Moreover, in order to compare the distribution of HPs quantitatively at the critical sites of the anastomosis, such as suture line, toe, heel, and bed, the segmental average of the HPs are calculated for different models.²⁸

The TAWSS, nondimensional TAWSSG, and OSI contours are presented in Figs. 8–10, respectively.

As illustrated in Figs. 8 and 9, the distributions of TAWSS and TAWSSG in all models are similar, with the maximum value occurring at the toe of the anastomosis. The values of these two HPs do not differ remarkably between the valve remnant containing models (2 and 3) and the smooth graft model (1) even in the valve region of the graft. However, as shown in Fig. 10, OSI is very high in the valve sinus of models 2 and 3 due to the flow recirculation and vortex formation in this region; while OSI value is low in model 1 at the corresponding region. There is also a high-OSI region at the heel of the anastomosis and in the proximal segment of the coronary artery; the latter is due to the very small mean WSS in this area rather than due to large changes in WSS over the cardiac cycle as reported by Bonert *et al.*²⁹

Segmental (area weighted) averages of HPs²⁶ in the valve region of the grafts and critical anastomotic regions (see Fig. 11) are presented in Table 2. The segmental averages of all HPs are similar in the anastomotic regions in all models, as shown in Table 2. This is due to the analogous flow characteristics observed within the similar anastomotic geometry of all models. However, the comparison of the graft

Fig. 8. TAWSS distribution at the anastomotic region of the three models. Distribution of TAWSS is similar in all models, with the maximum value occurring at the toe of the anastomosis.

sections of the three models demonstrates significant differences in HPs distribution between the smooth graft sections and those containing valve remnant and sinus. As shown in Table 2, the segmental average of OSI is increased to more than three times in graft Sec. 2 in models 2 and 3 as compared to the smooth graft segments of model 1. Note that this is the average of OSI over the segment area; otherwise, in some regions of the valve sinus, as demonstrated in Fig. 10, the OSI value has even reached to 0.5, which means a fully oscillatory WSS. Furthermore, the TAWSS has become even smaller in these regions; and at the same time, the TAWSSG is at

Fig. 9. Nondimensional TAWSSG distribution at the anastomotic region of the three models. The peak occurs at the toe of the anastomosis in all models.

least eight times larger in the valve segments than that in corresponding smooth graft segments, although it is still not that large compared to that at the toe of the anastomosis.

4. Discussion and Conclusion

In this paper, we have studied (by means of numerical simulation) the effects of the inner surface unevenness of a graft due to valve remnants and valve sinuses in the case of valve-stripped SV graft on the blood flow in the graft as well as in the distal anastomotic region of a CABG.

Fig. 10. OSI distribution at the anastomotic region of the three models. High OSI values are observed in the valve sinus due to the vortex formation and flow recirculation in the valve remnant containing models. OSI is also high in the occluded segment of the coronary artery in all models.

There are some simplifying assumptions made in this study. The compliance effect of the vessel walls has been neglected, since Tang *et al.*³⁰ and Leuprecht *et al.*³¹ showed that the effects of wall distensibility are less pronounced than those of changes in arterial geometry and flow conditions. Moreover, the blood is assumed to be a Newtonian fluid, since bypass surgery is normally associated with vessels greater than 2 mm in diameter, where non-Newtonian effects are not prevailing. However, taking into account the compliance of the vessel walls and non-Newtonian characteristics of blood flow could make the simulation results to be more realistic.

There are disturbances due to the valve remnants and valve sinus, observed in the graft flow field owing to vortices formation in the valve sinus and proximal to

Fig. 11. Critical anastomotic regions and graft sections, whose segmental average of HPs are calculated and compared in Table 2 for the three models: 1—graft section 1, 2—graft section 2, 3—suture line, 4—toe, 5—heel, and 6—bed.

Table 2. Comparison of segmental average of HPs in different models in the anastomotic regions and graft sections.

Model	Location	TAWSS (Pa)	TAWSSG	OSI
(1): No-valve remnant	1—Graft section 1	0.52	0.08	0.04
	2—Graft section 2	0.54	0.36	0.04
	3—Suture line	2.54	40.5	0.07
	4—Toe	5.81	84	0.01
	5—Heel	0.13	1.5	0.24
	6—Bed	2.44	8.3	0.09
(2): One-valve remnant	1—Graft section 1	0.52	0.03	0.04
	2—Graft section 2	0.29	5.04	0.13
	3—Suture line	2.54	40.9	0.07
	4—Toe	5.81	84.6	0.01
	5—Heel	0.13	1.6	0.24
	6—Bed	2.46	8	0.09
(3): Two-valve remnants	1—Graft section 1	0.34	3.62	0.10
	2—Graft section 2	0.29	3.08	0.13
	3—Suture line	2.55	40.2	0.07
	4—Toe	5.82	84	0.01
	5—Heel	0.13	1.6	0.23
	6—Bed	2.46	7.7	0.09

the valve remnants. These flow disturbances and vortices cause a high OSI in the valve sinus regions, where the TAWSS is very low. This results in a low-WSS-and-high-OSI combination, which can lead to early atherosclerotic lesion development in the graft.²⁴ This is likely to be initiated by internal trauma in veins due to valvulotomes following valve leaflets removal in these regions, which can be even aggravated due to the increase in TAWSSG observed in these regions, which can result in growth of atherosclerotic lesions.^{26,27}

Despite the increase in OSI and TAWSSG and decrease in TAWSS caused in the graft segments by the valve remnant and sinus, yet, the vortex disturbances in the valve sinuses do not apparently reach further downstream to the anastomosis. Hence, as noted in Table 2, the HP distributions in the anastomotic region of the three models are of the same order of magnitude.

Therefore, this study unveils the potential critical role of the valve remnants in the SV grafts in CABG as a cause of atherosclerotic lesion formation within the graft.

References

1. Ando J, Ohtsuka A, Korenaga R, Kawamura T, Kamiya A, Wall shear stress rather than shear rate regulates cytoplasmic Ca^{++} responses to flow in vascular endothelial cells, *Biochem Biophys Res Commun* **190**:716–723, 1993.
2. Kamiya A, Ando J, Shibata M, Roles of fluid shear stress in physiological regulation of vascular structure and function, *Biorheology* **25**:271–278, 1988.
3. Diamond SL, Eskin SG, McIntire LV, Fluid flow stimulates tissue plasminogen activator secretion by cultured human endothelial cells, *Science* **243**:1483–1485, 1989.
4. Chua LP, Ji WF, Yu CM, Zhou TM, Tan YS, Particle image velocimetry measurements of three proximal anastomosis models under a pulsatile flow condition, *Proc Inst Mech Eng H* **222**(3):249–263, 2008.
5. Chua LP, Zhang JM, Yu SCM, Ghista DN, Tan YS, Numerical study on the pulsatile flow characteristics of proximal anastomotic models, *Proc Inst Mech Eng H* **219**(5):361–379, 2005.
6. Anayiotos AS, Pedroso PD, Eleftheriou EC, Venugopalan R, Holman WL, Effect of a flow-streamlining implant at the distal anastomosis of a coronary artery bypass graft, *Ann Biomed Eng* **30**(7):917–926, 2002.
7. Keynton RS, Rittgers SE, Shu MCS, The effect of angle and flow rate upon hemodynamics in distal vascular graft anastomoses: An *in vitro* model study, *J Biomech Eng* **113**(4):458–463, 1991.
8. Sankaranarayanan M, Ghista DN, Chua LP, Tan YS, Kassab GS, Analysis of blood flow in an out-of-plane CABG model, *Am J Physiol Heart Circ Physiol* **291**(1):H283–H295, 2006.
9. Sankaranarayanan M, Chua LP, Ghista DN, Tan YS, Flow studies in three-dimensional aorto-right coronary bypass graft system, *J Med Eng Technol* **30**(5):269–282, 2006.
10. Zhang JM, Chua LP, Ghista DN, Yu SCM, Tan YS, Numerical investigation and identification of susceptible sites of atherosclerotic lesion formation in a complete coronary artery bypass model, *Med Biol Eng Comput* **46**(7):689–699, 2008.

11. Robicsek F, Thubrikar MJ, Fokin A, Tripp HF, Fowler B, Pressure traps in femoropopliteal reversed vein grafts. Are valves culprits? *Cardiovasc Surg* **40**(5):683–689, 1999.
12. Thubrikar MJ, Robicsek F, Fowler BL, Pressure trap created by vein valve closure and its role in graft stenosis, *J Thorac Cardiovasc Surg* **107**(3):707–716, 1994.
13. Dye TE, Izquierdo P, Abnormal venous valves: A cause of early obstruction of saphenous vein bypass grafts, *Tex Heart Inst J* **10**(4):365–369, 1983.
14. Gottlob R, May R, *Venous Valves*, Springer-Verlag/Wien, New York City, NY, 1986.
15. McCaughan Jr. JJ, Doan TB, Nonreversed valve-stripped vein graft, *Am J Surg* **136**(2):212–214, 1978.
16. Singh RN, Flow disturbance due to venous valves: A cause of graft failure, *Catheter Cardio Diag* **12**(1):35–38, 1986.
17. Galjee MA, Van Rossum AC, Doesburg T, Van Eenige MJ, Visser CA, Value of magnetic resonance imaging in assessing patency and function of coronary artery bypass grafts: An angiographically controlled study, *Circulation* **93**(4):660–666, 1996.
18. Galjee MA, Van Rossum AC, Doesburg T, Hofman MBM, Falke THM, Visser CA, Quantification of coronary artery bypass graft flow by magnetic resonance phase velocity mapping, *J Magn Reson Imaging* **14**(5):485–493, 1996.
19. Womersley JR, Method for the calculation of velocity, rate of flow and viscous drag in arteries when the pressure gradient is known, *J Physiol* **127**:553–563, 1955.
20. Mazumdar JN, *Biofluid Mechanics*, World Scientific, Singapore, 1992.
21. Friedman MH, Bargerion CB, Duncan DD, Hutchins GM, Mark FF, Effects of arterial compliance and non-Newtonian rheology on correlations between intimal thickness and wall shear, *J Biomech Eng* **114**(3):317–320, 1992.
22. Friedman MH, Arteriosclerosis research using vascular flow models: From 2-D branches to compliant replicas, *J Biomech Eng* **115**(4B):595–601, 1993.
23. Steinman DA, Ethier CR, The effect of wall distensibility on flow in a two-dimensional end-to-side anastomosis, *J Biomech Eng* **116**(3):294–301, 1994.
24. Buchanan JR, Kleinstreuer C, Hyun S, Truskey GA, Hemodynamics simulation and identification of susceptible sites of atherosclerotic lesion formation in a model abdominal aorta, *J Biomech* **36**(8):1185–1196, 2003.
25. He X, Ku DN, Pulsatile flow in the human left coronary artery bifurcation: Average conditions, *J Biomech Eng* **118**(1):74–82, 1996.
26. Buchanan JR, Kleinstreuer C, Truskey GA, Lei M, Relation between non-uniform hemodynamics and sites of altered permeability and lesion growth at the rabbit aortoceliac junction, *Atherosclerosis* **143**:27–40, 1999.
27. DePaola N, Gimbrone Jr MA, Davies PF, Dewey Jr CF, Vascular endothelium responds to fluid shear stress gradients, *Arterioscler Thromb* **12**(11):1254–1257, 1992.
28. Archie Jr JP, Hyun S, Kleinstreuer C, Longest PW, Truskey GA, Buchanan JR, Hemodynamic parameters and early intimal thickening in branching blood vessels, *Crit Rev Biomed Eng* **29**(1):1–64, 2001.
29. Bonert M, Myers JG, Fremes S, Williams J, Ethier CR, A numerical study of blood flow in coronary artery bypass graft side-to-side anastomoses, *Ann Biomed Eng* **30**(5):599–611, 2002.
30. Tang D, Yang C, Kobayashi S, Ku DN, Steady flow and wall compression in stenotic arteries: A three-dimensional thick-wall model with fluid-wall interactions, *J Biomech Eng* **123**:548–557, 2001.
31. Leuprecht A, Perktold K, Prosi M, Berk T, Trubel W, Schima H, Numerical study of hemodynamics and wall mechanics in distal end-to-side anastomoses of bypass grafts, *J Biomech* **35**:225–236, 2002.