A Coupled CFD-Lumped Parameter Model of the Human Circulation: Elucidating the Hemodynamics of the Hybrid Norwood Palliative Treatment and Effects of the Reverse Blalock-Taussic Shunt Placement and Diameter

2015

Andres Ceballos

University of Central Florida

Find similar works at: https://stars.library.ucf.edu/etd

University of Central Florida Libraries http://library.ucf.edu

Part of the Engineering Commons

STARS Citation


https://stars.library.ucf.edu/etd/654

This Doctoral Dissertation (Open Access) is brought to you for free and open access by STARS. It has been accepted for inclusion in Electronic Theses and Dissertations by an authorized administrator of STARS. For more information, please contact lee.dotson@ucf.edu.

by

ANDRES CEBALLOS
B.S University of Central Florida, 2009
M.S University of Central Florida, 2011

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Mechanical and Aerospace Engineering in the College of Engineering and Computer Science at the University of Central Florida Orlando, Florida

Summer Term 2015

Major Professor: Alain Kassab
ABSTRACT

The Hybrid Norwood (HN) is a relatively new first stage procedure for neonates with Hypoplastic Left Heart Syndrome (HLHS), in which a sustainable univentricular circulation is established in a less invasive manner than with the standard procedure. A computational multiscale model of such HLHS circulation following the HN procedure was used to obtain detailed hemodynamics. Implementation of a reverse-BT shunt (RBTS), a synthetic bypass from the main pulmonary to the innominate artery placed to counteract aortic arch stenosis, and its effects on local and global hemodynamics were studied.

A synthetic and a 3D reconstructed, patient derived anatomy after the HN procedure were utilized, with varying degrees of distal arch obstruction, or stenosis, (nominal and 90% reduction in lumen) and varying RBTS diameters (3.0, 3.5, 4.0 mm). A closed lumped parameter model (LPM) for the peripheral or distal circulation coupled to a 3D Computational Fluid Dynamics (CFD) model that allows detailed description of the local hemodynamics was created for each anatomy.

The implementation of the RBTS in any of the chosen diameters under severe stenosis resulted in a restoration of arterial perfusion to near-nominal levels. Shunt flow velocity, vorticity, and overall wall shear stress levels are inverse functions of shunt diameter, while shunt perfusion and systemic oxygen delivery correlates positively with diameter. No correlation of shunt diameter with helicity was recorded.

In the setting of the hybrid Norwood circulation, our results suggest: (1) the 4.0mm RBTS may be more thrombogenic when implemented in the absence of severe arch stenosis and (2) the 3.0mm and 3.5mm RBTS may be a more suitable alternative, with preference to the latter since it provides similar hemodynamics at lower levels of wall shear stress.
To friends and family and especially to my late father Nestor and my mother Martha.
ACKNOWLEDGMENTS

Special thanks to:

Dr. Eduardo Divo, Dr. Alain Kassab and Dr. William DeCampli for their mentorship, support and inspiration. Dr. Ricardo Argueta and Lauren Blanchette for their important contributions to this work.

This study was supported in part by the Orlando Health Foundation, the American Heart Association under Grant number 11GRNT7940011, and a National Institutes of Health National Research Service Award Doctoral Fellowship under Grant Number 1 F31 HL123280-01.
# TABLE OF CONTENTS

LIST OF FIGURES ........................................................................................................... viii

LIST OF TABLES ................................................................................................................ xi

CHAPTER ONE: INTRODUCTION ................................................................................ 1

CHAPTER TWO: RELEVANT ANATOMICAL AND PHYSIOLOGICAL FEATURES OF
THE CARDIOVASCULAR SYSTEM ...................................................................................... 1

The Heart ......................................................................................................................... 2

The Cardiac Cycle .............................................................................................................. 3

Vessel Anatomy and Physiology ..................................................................................... 6

Arteries ............................................................................................................................... 6

Veins ................................................................................................................................. 8

Flow Characteristics Through the Arterial and Venous Systems ................................ 9

CHAPTER THREE: HLHS AND THE HYBRID NORWOOD ANATOMY ..................... 10

HLHS Anatomy .............................................................................................................. 10

Hybrid Norwood Procedure and Post-Operative Anatomy ........................................ 11

Hybrid Norwood Procedure ........................................................................................... 11

Post-Operative Anatomy ............................................................................................... 12

Post-Operative Complications ....................................................................................... 14

CHAPTER FOUR: MATERIALS AND METHODS ..................................................... 15

Anatomical Model .......................................................................................................... 15

CFD Model ....................................................................................................................... 20
LIST OF FIGURES

Figure 1: HLHS Anatomy (left) [3], Standard Norwood Anatomy (center) [4], Hybrid Norwood Anatomy (right) [5]. ....................................................................................................................... 1

Figure 2: Hybrid Norwood Anatomy with RBTS in place ................................................................. 3

Figure 3: Main systemic and pulmonary circuits in the human anatomy [10]. ................................. 2

Figure 4: Stages of the systemic cardiac cycle [8]. ............................................................................ 5

Figure 5: Arterial and Venous Composition [9]. ................................................................................ 7

Figure 6: HLHS Anatomy [3]. ........................................................................................................... 11

Figure 7: Hybrid Norwood Anatomy [5]. ........................................................................................... 13

Figure 8: Synthetic model anatomical configurations: Nominal(Top Left), Nominal RBTS (Top Right), 90% stenosis (Bottom Left), 90% stenosis RBTS (Bottom Right). ............................. 15

Figure 9: Patient specific anatomical configurations: 90% stenosis shown with RBTS (right) and without RBTS (left). Frontal view. ............................................................................................. 16

Figure 10: Patient specific anatomy with 90% stenosis (left) and nominal stenosis (right). Posterior view. .............................................................................................................................. 17

Figure 11: Dimensions for synthetic models (A) stenotic and (B) Nominal 4.0mm RBTS configurations. Dimensions in millimeters. (Ø = diameter) ........................................................................ 19

Figure 12: Dimensions for patient derived models, Nominal 4.0mm RBTS configuration shown. Dimensions in millimeters. (Ø = diameter) ........................................................................ 19

Figure 13: Multiscale model of the HN circulation, three-dimensional CFD model coupled with lumped parameter model ........................................................................................................... 22

Figure 14: Detailed LPM schematic with RBTS in place. ............................................................... 23
Figure 15: Averaged flow velocity magnitude through shunt during the cardiac cycle. Antegrade and retrograde averaged velocity magnitudes also included. Synthetic (top) and patient derived (bottom) anatomical configurations.

Figure 16: Streamlines through shunt at selected points during cardiac cycle. 4.0mm RBTS configuration, (Top) synthetic, (Bottom) Patient Derived, (A) Nominal, (B) 90% stenosis.

Figure 17: Streamlines through shunt at selected points during cardiac cycle. 3.5mm RBTS configuration, (Top) synthetic, (Bottom) Patient Derived, (A) Nominal, (B) 90% stenosis.

Figure 18: Streamlines through shunt at selected points during cardiac cycle. 3.0mm RBTS configuration, (Top) synthetic, (Bottom) Patient Derived, (A) Nominal, (B) 90% stenosis.

Figure 19: Comparison of shunt flow at time point 3 in late diastole. Nominal patient derived configurations P5 (Top), P4 (Middle), P3 (Bottom).

Figure 20: Flow direction nomenclature. Antegrade flow through the isthmus and mid-aortic arch occurs in the direction from pulmonary root to aortic root. Antegrade flow through the shunt occurs from pulmonary root to innominate artery.

Figure 21: Plane sections used to monitor flow through the ascending aorta and mid-aortic arch in the patient derived anatomy.

Figure 22: Branched arterial flow and pulmonary flow over one cardiac cycle for patient derived, stenosed configurations.

Figure 23: Systemic oxygen delivery for all anatomical configurations and shunt diameters.

Figure 24: Contour plots of cycle averaged wall shear stress magnitude. Nominal stenosis cases shown, synthetic anatomy (Top) and patient derived anatomy (Bottom).

Figure 25: Contour plots of oscillatory shear index. Nominal stenosis cases shown, synthetic anatomy (Top) and patient derived anatomy (Bottom).
Figure 26: Contour plots of cycle averaged wall shear stress magnitude. Severe (90%) stenosis cases shown, synthetic anatomy (Top) and patient derived anatomy (Bottom). ..........................51

Figure 27: Contour plots of oscillatory shear index. Severe (90%) stenosis cases shown, synthetic anatomy (Top) and patient derived anatomy (Bottom). .................................................................52

Figure 28: Volume averaged vorticity and helicity of flow through shunt over one cardiac cycle. ...............................................................................................................................................55

Figure 29 Streamlines colored by velocity, 90% Stenosis Nominal CVR..................................................58

Figure 30: Streamlines colored by velocity, 90% Stenosis CVR +50% ..................................................59

Figure 31: Streamlines colored by velocity, 90% Stenosis CVR +100%.................................................59

Figure 32: Streamlines colored by velocity, 90% Stenosis CVR +200%................................................60

Figure 33: CFD-LP model coupling scheme flow chart. .................................................................65
LIST OF TABLES

Table 1: Eight models for each of the two anatomical configurations: (a) synthetic (S1-8), and (b) patient-derived (P1-8). ................................................................. 18

Table 2: Cardiac output, arterial flow rates and relative flow changes. Synthetic (top) and patient derived (bottom) anatomical configurations................................................................. 32

Table 3: Flow in Patient derived configurations through various plane sections located along the ascending aorta and mid-aortic arch (see Figure 21). Isthmus flow is that crossing through the stenosis site. Branched arterial flow is the sum of all flow through the branched arteries’ outlet boundaries (LcorA, RcorA, LSA, LCA, RSA, RCA, DA). Pulmonary flow is the sum of the flow through the LPA and RPA outlet boundaries........................................... 44

Table 4: Cardiac output, arterial flow rates and flow changes for the synthetic severe stenosis case without RBTS (S2). .............................................................................................................. 57
CHAPTER ONE:
INTRODUCTION

Congenital heart disease is the leading cause of death for infants born with birth defects, with more than a 30% mortality attributed to this disease. One of the most complex forms of congenital heart disease is HLHS and occurs in 4 to 8 percent of infants born with cardiac malformations [1]. The main complications of HLHS are severely malformed anatomies of the left ventricle, mitral and aortic valves, and ascending aorta (Figure 1). There are currently two approaches to therapy for children with HLHS: heart transplantation or surgical intervention to establish univentricular circulation. Unfortunately heart transplantation is often not an alternative due to the low number of donors at this early age [2]. Surgical techniques such as the Norwood operation are then the most common method to establish an early blood circulation that is compatible with life. The Norwood operation consists of removal of the atrial septum, reconstruction the malformed aorta, and connection of a bypass (BT-shunt) from the innominate artery to the right pulmonary artery (RPA) to allow for pulmonary perfusion (Figure 2).

Figure 1: HLHS Anatomy (left) [3], Standard Norwood Anatomy (center) [4], Hybrid Norwood Anatomy (right) [5].
Successful recovery of the patient from the Norwood operation is often followed by subsequent surgical procedures to establish a more normal circulatory system where pulmonary perfusion is achieved with deoxygenated blood. A relatively new alternative to the first-stage Norwood procedure is the Hybrid Norwood procedure, which consists of removal of the atrial septum, implantation of a stent in the patent ductus arteriosus, and banding of the pulmonary arteries. The PDA, a small vessel that connects the pulmonary arteries with the aortic arch and normally closes shortly after birth, is enlarged with the use of the stent to allow circulation from the right ventricle into the systemic circulation through the aortic arch. The pulmonary banding is put in place to prevent excessive pulmonary circulation, with an ideal adjustment providing a pulmonary to systemic flow ratio of 1 [6]. The Hybrid Norwood is a less invasive procedure that avoids the use of a heart-lung machine as well as deliberate cardiac and circulatory arrest. Though there are numerous surgical advantages of the Hybrid versus the conventional method, there are also different complications that may arise with this method. The most important to surgeons participating in this study is the obstruction of flow due to stenosis of the aortic arch proximal to the stent. This condition is fatal if coronary and/or carotid flow is critically low. With the expectation of increasing perfusion to these vessels, a bypass called Reverse BT-shunt (RBTS) is placed connecting the pulmonary root to the innominate artery (Figure 2).
The resulting hemodynamics are very complex since the flow reaching the innominate artery is both antegrade and retrograde, meaning part of the circulation flows downstream through the innominate and part upstream to feed the coronary and remaining aortic branches. Furthermore, flow reversal and secondary motions have been detected throughout the cardiac cycle, making this circulatory configuration far from intuitive [8]. Surgeons are therefore deeply interested in understanding the local hemodynamics of the with RBTS in place Hybrid Norwood anatomy and the potential benefits of the reverse BT shunt, especially when severe stenosis is present. The main objectives of this study are therefore: 1) To develop a closed-loop, multiscale model of the cardiovascular system able to describe detailed local hemodynamics and its effects on the global circulation; 2) assess the performance of the RBTS in increasing perfusion to the coronary and carotid circulation.
CHAPTER TWO:
RELEVANT ANATOMICAL AND PHYSIOLOGICAL FEATURES OF THE CARDIOVASCULAR SYSTEM

In humans, the cardiovascular system is composed of the heart and a closed system of vessels constituted by the arteries, veins and capillaries. The primary function of the cardiovascular system is the transport of oxygen, carbon dioxide, nutrients, hormones and other life essential nutrients [9]. There are two primary blood circuits, the pulmonary and the systemic circuits. The pulmonary circuit is composed of the pulmonary arteries and its branches that deliver blood from the right ventricle to the lungs, the capillaries in the lungs where gas exchange occurs, and the pulmonary veins that deliver oxygen rich blood to the left atrium. The systemic circuit supplies nutrients to all tissues in the body and its vessels include the aorta and branching arteries which distribute the blood coming from the left ventricle, the capillary system through which material exchange occurs, and the systemic veins that return the blood to the heart [10].
Figure 3: Main systemic and pulmonary circuits in the human anatomy [11].

The Heart

The heart is a muscular pump that sustains the flow of blood through the body. It does so in a periodic cycle of events denominated the cardiac cycle. It has four chambers, two atria and two ventricles; the left supports the systemic circulation and the right the pulmonary circulation. The left and right side of the heart are separated by the respective atrial and ventricular septum. In a healthy heart, the systemic and pulmonary circulations occur in parallel, with deoxygenated blood flowing through the right heart and oxygenated blood through the left heart. The heart's
walls are mainly composed of three layers of tissue and muscle. The outermost layer is the epicardium, a serous membrane which is not easily distensible and thus restricts excessive and rapid expansion of the cardiac chambers. Lining the interior chambers of the heart is the endocardium, a smooth layer of tissue extending over the heart valves. In between the epicardium and endocardium is the myocardium, the muscle that enables the heart's contraction and is made of muscular fibers of variable thicknesses within the different chambers. The left ventricle is much more developed than the right ventricle, with a thicker wall allowing for higher ventricular pressures required to provide adequate systemic perfusion. Four valves allow filling of the chambers and prevent regurgitation. The right atrium is supplied by the inferior and superior venae cava and blood flows through the mitral valve into the right ventricle. Blood is then pumped through the pulmonary valve into the main pulmonary artery. Similarly, the left atrium is supplied by the pulmonary veins and blood flows through the tricuspid valve into the left ventricle. Blood is then pumped through the aortic valve into the ascending aorta. The myocardium is perfused by the coronary arteries, relatively narrow vessels that feed from the root of the ascending aorta, immediately above the aortic valve. There are two principal coronary arteries, the left and right coronary arteries, that branch around their respective ventricles [10].

The Cardiac Cycle

The cardiac cycle can be briefly defined as the sequential contraction and relaxation of the atria and ventricles[9]. The periods of contraction and relaxation are denominated systole and diastole, respectively. Below is a description of the cardiac cycle stages.
**Ventricular Systole**

- **Isovolumic Contraction:** this is the period after the ventricle has just been filled and the atrioventricular and semi-lunar valves are closed. There is marked intraventricular pressure increase at constant volume.

- **Ejection:** begins when the intraventricular pressure exceeds the arterial pressure and the semi-lunar valve opens. Immediately after the valve opening there is rapid ejection and a continued rise in ventricular and aortic pressure. Due to the arterial wall compliance, some of the pulse energy is stored in the arterial walls and then released after peak systolic pressure. Flow inertia drives a subsequent period of reduced ejection from the ventricle, in which the ventricular-aortic pressure gradient starts reversing and the arterial walls begin contracting. Eventually the arterial pressure exceeds that of the ventricle and the semi-lunar valve closes. A small amount of flow reverses through the aortic valve as it closes, producing a small region of negative cardiac output as seen in Figure 4.

**Ventricular Diastole**

- **Isovolumic Relaxation:** the closure of the aortic valve after the period of reduced ejection produces the incisura, also called the anacrotic notch, on the onset of diastole. The pressure within the ventricle is still higher than that in the atrium, therefore both valves are closed and the sharp reduction of pressure is isovolumic.

- **Rapid Filling:** at the end stages of ventricular relaxation the pressure in the ventricle becomes less than that in the atrium causing the atrioventricular valves to open. The blood that had filled the ventricle during ventricular diastole now rushes into the ventricle rapidly and there is a marked increase in ventricle pressure and volume.
• Diastasis: as the ventricle fills its pressure increases gradually until it reaches the atrial pressure at which point the atrioventricular valve begins to close.

Atrial Systole

This is the period of atrial contraction, which elevates the atrial pressure beyond that of the ventricle allowing the atrioventricular valve to open and the filling of the ventricle. Usually this produces an additional 20% of ventricular filling after diastole during rest and even a higher percentage during exercise due to higher flow inertia.

Figure 4: Stages of the systemic cardiac cycle illustrated in the Wiggers diagram [9].
Vessel Anatomy and Physiology

Arteries

There are three types of vessels that transport oxygenated blood through the body: the arteries, arterioles, and capillaries. All arteries have a basic composition of an internal or intimal layer that is directly in contact with the circulation, a middle layer containing smooth muscle cells, and an outer layer composed of elastin, collagen fibers, and other connective tissue (Figure 5). The intimal layer, or tunica intima, is mainly composed of the endothelium, a thin layer of cells that facilitate the flow of blood and are responsible for the release of anticoagulation and vasoregulatory substances. The middle layer, or tunica media, is responsible for the contraction or dilation of the vessel under stimuli. It also has a layer of elastic tissue that supports and allows the vessel to contract after a pressure pulse. The outer layer or tunica adventitia maintains the vessel in place.
The arteries can be subdivided in two major groups:

- Elastic arteries: these are the largest arteries in the body and are typically 1 to 2.5 cm in diameter. Arteries within this group include the pulmonary artery, aorta and its major branching arteries. The higher proportion of elastine in the tunica media in these vessels gives them higher compliance than in vessels of smaller diameter and therefore can “store” flow during systole.
• Muscular arteries: these are vessels in the range of 1mm to 1cm in diameter. The tunica media in these vessels contains a higher proportion of smooth muscle, which allows them to constrict or distend to regulate blood flow.

The arterioles are smaller in diameter (0.01 - 1 mm) than muscular arteries and contain less elastic and connective tissue. These vessels control to great extent the regulation of blood pressure and do so with a relatively higher amount of smooth muscle that varies the cross-sectional area of the lumen.

The smallest vessels in the body (0.005 mm, - 0.01mm) are the capillaries through which material exchange occurs. Their walls are very thin, about 1 cell thin to enable diffusion. Flow velocity through the capillaries is very slow relative to arterial flow due to the increased equivalent cross-sectional area of their lumen.

Veins

The vessels that return blood flow from the arterial system to the heart can be divided into two groups, the veins and venules. Venules are the smallest vessels in the venous system (0.005mm - 0.1mm) and their walls are continuous with those of the capillaries. They share some of the physiological properties and are very similar wherever material exchange occurs. The venules transport the blood to larger vessels, the veins, which increase in diameter, wall thickness, and composition as they approach the heart (0.1mm - 20mm). Typically veins have thinner walls when compared to arteries of the same lumen since they are subjected to much lower pressures and wave amplitudes. At the point where blood reaches the veins, much of the mechanical energy that drives the flow has been spent. To aid the return of blood to the heart,
most veins have valves that prevent retrograde flow. Contraction of muscles in the extremities and the changes in pressure in the torso due to breathing also help to drive the flow to the heart.

Flow Characteristics Through the Arterial and Venous Systems

As described earlier, the composition of the arterial and venous walls varies depending on their size and location. As the composition of the vessels change so do their mechanical properties. Elasticity is perhaps the most important property of the blood vessels in the present study. In the arterial system, the relatively high elasticity in the larger arteries allows them to store some kinetic energy of the flow during systole, as evidenced by their distension, and release it during diastole. This property, which will be referred to as compliance, will be explained further in the Lumped Parameter Model section. This achieves three things: a more continuous flow to the tissues, a reduction in pressure wave amplitude, and a reduction in cardiac workload. The further downstream through the arterial system, the more attenuated is the pressure waveform and the more steady flow becomes. Once the blood reaches the capillary beds it encounters high resistance to flow, as the equivalent vessel cross-sectional area increases and the flow slows down to allow diffusion to occur. The result is near steady flow through the capillary beds. This effect is denominated the “hydraulic filter” in reference to the effects of capacitance and resistance in electrical circuits, which analogous to this case dampen the pressure and flow waveform signals from the heart.
CHAPTER THREE:
HLHS AND THE HYBRID NORWOOD ANATOMY

HLHS Anatomy

As described earlier, Hypoplastic Left Heart Syndrome (HLHS) comprises a group of malformations and underdevelopment of the left side of the heart. These include an underdeveloped left atrium and ventricle, stenosis or atresia of the aortic and mitral valves, and hypoplasia (in this case significant narrowing) of the ascending aorta [12]. As a consequence there is no ejection from the left ventricle to the ascending aorta. The right heart becomes enlarged and hypertrophic, since it has to support both pulmonary and systemic circulations at the same time. In newborns, the patent ductus arteriosus (PDA) connects the pulmonary artery to the mid-aortic arch, allowing the aforementioned univentricular circulation to be possible. The PDA, however, naturally starts to recede and eventually ceases to exist as a blood conduit shortly after birth. Atrial septal defect (ASD), a malformation that allows blood flow between the two atria, is also present. The systemic and pulmonary circulations are in serial with the HLHS anatomy, since all the blood is pumped by the right ventricle into the main pulmonary artery. Blood flows retrograde through the mid-aortic arch and ascending aorta into the branched and coronary arteries.
Hybrid Norwood Procedure and Post-Operative Anatomy

Hybrid Norwood Procedure

The hybrid Norwood procedure was named after Dr. William Norwood, the pioneer of surgical treatment for patients with HLHS. The following is a brief description of the principal objectives of the operation.

Pulmonary Artery Banding

The procedure starts with a median sternotomy and placement of a chest retractor. The pericardium is opened and a suture stay is placed to allow the manipulation of the main pulmonary artery (MPA). Two segments of 3.5 mm polytetrafluoroethylene (PTFE) tube grafts
(same material used in bypasses) are cut to be used as bands for the left (LPA) and right (RPA) pulmonary arteries [12]. The bands are placed around the root of the pulmonary arteries and are sutured. If being implemented, a reverse BT-shunt is anastomosed to the innominate artery from the MPA. An angiogram (flow visualization in arteries using X-ray) is performed to confirm placement and proper amount of occlusion, usually about 50% of original lumen.

**Ductal Stenting**

A puncture is made at the root of the MPA where a sheath, the conduit through which the catheter passes, is introduced. A stent, an expandable metallic mesh, is deployed along the entire length of the ductus arteriosus using the catheter. Proper placement of the stent is confirmed using an angiogram after the sheath/catheter is removed. If there is not enough flow crossing the atrial septum a septostomy is performed or a stent is placed to enlarge it. The sternum is closed and a subcuticular suture finishes the operation.

**Post-Operative Anatomy**

Figure 7 shows the changes to the anatomy performed after the hybrid Norwood procedure. Univentricular circulation is established through the placement of the PDA stent, the banding of the pulmonary arteries, and if required septostomy or atrial stenting. In this configuration, the systemic and pulmonary circulations are in parallel as both circuits are fed from the MPA. Since the left ventricle is hypoplastic and the aortic valve is essentially shut, intercommunication of the atria must exist in order to allow incoming blood from the pulmonary arteries to reach the right ventricle. This is why there must be an ASD of the proper size or septostomy or stenting must be employed to guarantee this intercommunication. Very important to note is the mixing of oxygenated blood returning from the pulmonary veins with deoxygenated blood returning from
the vena cavae in the atria. This results in both pulmonary and systemic circuits feeding from blood with the same oxygen content. Balancing the pulmonary to systemic blood flow ratios (Qp/Qs) is very important to the recovery of the patient. Studies [13], [14] have shown that the optimal Qp/Qs = 1 ratio is 1 for adequate perfusion of the through the systemic circulation and metabolic function.

Figure 7: Hybrid Norwood Anatomy [5].
Post-Operative Complications

The Hybrid Norwood procedure has its unique set of complications that may arise during postoperative care:

- **Pредuctal Stenosis** - since no ascending aorta reconstruction is performed, stenosis prior to the PDA may restrict retrograde flow and produce insufficient cerebral and coronary perfusion. In addition, it is necessary to place the stent protruding from the PDA into the isthmus (proximal region in the aortic arch prior to the PDA) to prevent ductal constriction [6]. This may increase the risk of preductal stenosis since the stent itself promotes neointimal proliferation [15]. The degree of stenosis may vary prior to stage two palliation and is one of the variables that is analyzed in the present study.

- **Atrial Stent Patency** - as reported by Bacha et. al [6], ductal stents are unreliable beyond three months after placement.

- **Stent and Pulmonary Band Migration** - ductal stent migration can occur into the MPA or descending aorta if an incorrect diameter is chosen or the stent is misplaced. Pulmonary band migration can also occur due to size and placement issues.
CHAPTER FOUR:
MATERIALS AND METHODS

Anatomical Model

Synthetic rigid-walled 3D models (SolidWorks, Dassault Systemes, Concord, MA) representative of an infant with HLHS following the HN procedure were constructed assuming atresia of the aortic valve and including the ascending aorta (AA), transverse arch (TA), innominate artery (IA), right and left subclavian arteries (RSA, LSA), right and left carotid arteries (RCA, LCA), main pulmonary artery (MPA), branched pulmonary arteries (BPA, right=RPA, left=LPA), patent ductus arteriosus (PDA), descending aorta (DA), and right and left coronary arteries (RcorA, LcorA). Additionally, a magnetic resonance imaging (MRI) derived, post HN procedure, patient derived anatomy was reconstructed using medical image segmentation software (Mimics, Materialise, Leuven, Belgium).

Figure 8: Synthetic model anatomical configurations: Nominal(Top Left), Nominal RBTS (Top Right), 90% stenosis (Bottom Left), 90% stenosis RBTS (Bottom Right).
Figure 9: Patient specific anatomical configurations: 90% stenosis shown with RBTS (right) and without RBTS (left). Frontal view.
Figure 10: Patient specific anatomy with 90% stenosis (left) and nominal stenosis (right). Posterior view.

Eight rigid-walled models were developed for each of the synthetic (S1-S8) and patient-derived (P1-P8) anatomies for a total of 16 models for this study, see Table 1. Models S1 and P1 are nominal models analogous to the standard HN procedure with “typical” hypoplasia of the distal arch, however, the hypoplasia in the synthetic model is more severe than in the patient-derived anatomy. Models S2 and P2 are stenosed models where part of the computational domain was removed at a point proximal to the PDA and distal to the LSA to decrease the lumen of the transverse aortic arch (90%) representing a severe discrete stenosis. In the synthetic model the stenosis was introduced as a discrete surface emanating from right lateral isthmus wall.
proximal to the RBTS, while it was introduced as an annular constriction in the patient derived model. Models S3-S8 and P3-P8 were constructed by incorporating a RBTS, that is, a 4.0mm, 3.5mm or 3.0mm diameter x 21mm length bypass graft from the MPA to the IA (Figures 1-3, Table 1). Vessel diameters and other important dimensions along the aortic arch and branching arteries are depicted in Figure 11 for synthetic models and in Figure 12 for patient derived models. The synthetic model dimensions were chosen to be representative of a typical HN patient, with typically employed shunt diameter sizes. In the patient-derived models, the coronary arteries were modeled synthetically from their take off of the ascending aorta because the resolution and contrast of the MRI did not allow for an accurate reconstruction. The length of the pulmonary arteries was extended and banded sections of the vessels were added synthetically due to the aforementioned reasons.

Table 1: Eight models for each of the two anatomical configurations: (a) synthetic (S1-8), and (b) patient-derived (P1-8).

<table>
<thead>
<tr>
<th>Baseline Model</th>
<th>RBTS diameter x length added to baseline models</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthetic Nominal (S1)</td>
<td>3mm x 21mm RBTS (S3)</td>
</tr>
<tr>
<td>Synthetic 90% stenosed (S2)</td>
<td>3mm x 21mm RBTS (S6)</td>
</tr>
<tr>
<td>Patient-derived Nominal (P1)</td>
<td>3mm x 21mm RBTS (P3)</td>
</tr>
<tr>
<td>Patient-derived 90% stenosed (P2)</td>
<td>3mm x 21mm RBTS (P6)</td>
</tr>
<tr>
<td></td>
<td>3.5 mm x 21mm RBTS (S4)</td>
</tr>
<tr>
<td></td>
<td>3.5 mm x 21mm RBTS (S7)</td>
</tr>
<tr>
<td></td>
<td>3.5 mm x 21mm RBTS (P4)</td>
</tr>
<tr>
<td></td>
<td>3.5 mm x 21mm RBTS (P7)</td>
</tr>
<tr>
<td></td>
<td>4 mm x 21mm RBTS (S5)</td>
</tr>
<tr>
<td></td>
<td>4 mm x 21mm RBTS (S8)</td>
</tr>
<tr>
<td></td>
<td>4 mm x 21mm RBTS (P5)</td>
</tr>
<tr>
<td></td>
<td>4 mm x 21mm RBTS (P8)</td>
</tr>
</tbody>
</table>
Figure 11: Dimensions for synthetic models (A) stenotic and (B) Nominal 4.0mm RBTS configurations. Dimensions in millimeters. (Ø = diameter)

Figure 12: Dimensions for patient derived models, Nominal 4.0mm RBTS configuration shown. Dimensions in millimeters. (Ø = diameter)
CFD Model

Solid models were imported into Star-CCM+ (CD-Adapco, NY), a commercial Finite Volume-based CFD software. A high quality mesh was obtained for all models providing grid-independence and adequate capture of the boundary layer and detailed flow features. The number of volumes used varied in the range between 1 and 3.1 million, depending on the anatomy. Blood was modeled as an incompressible Newtonian fluid with density of ρ=1060kg/m3 and viscosity of μ=0.004Pa-s. The 3D flow field is obtained by numerically resolving the Navier-Stokes (NS) mass and momentum conservation equations:

\[ \nabla \cdot \vec{V} = 0 \]  

(1)

\[ \rho \frac{\partial \vec{V}}{\partial t} + \rho (\vec{V} \cdot \nabla) \vec{V} = -\nabla p + \mu \nabla^2 \vec{V} \]  

(2)

Here, \( \vec{V} \) is the velocity vector and \( p \) is the pressure field. The NS were solved with an unsteady implicit scheme. The time step of 4.62ms provided time-independent solution for a 130 bpm. Waveforms provided by the LPM are used to impose an unsteady stagnation pressure inlet at the MPA root and prescribe unsteady flow splits as arterial outlet boundary conditions.

Lumped Parameter Model

The LPM is an electrical analog of the circulatory system [16] modeling viscous drag as a resistor (R), flow inertia as an inductor (L), vessel compliance as a capacitor (C), and tricuspid and pulmonary valves as ideal diodes. A pair of differential equations governs each R-L-C compartment model of a vascular bed:

\[ \Delta p = L \frac{dQ}{dt} + RQ \]  

(3)
\[ \Delta Q = C \frac{d(\Delta p)}{dt} \]

where, \( Q \) is the flow-rate and \( \Delta p \) is the pressure difference, while the second equation models vessel wall compliance with \( C = \frac{dV}{dp} \). Previously published work by others provided baseline values of \( R, L, \) and \( C \) \([8, 13, 17, 18]\) which were adjusted iteratively to approach waveforms from catheterization data of a “typical” HN patient. The arterial vascular bed resistance is tuned first, since it is the primary determinant of total flow through any given artery. Compliance and inductance parameters are then tuned to approach the desired waveform. Comparable methods have been successfully utilized in previous CFD studies of palliative strategies in HLHS \([8, 13, 17-19]\)

The right ventricle, modeled as a time varying capacitor, \( C(t) \), is the driving function of the circuit providing pulsatile cardiac output. Its reciprocal, the elastance, \( E_n(t_n)E(t) \), relates ventricular pressure and volume at a given point during the cardiac cycle. We used the form

\[
E(t) = (E_{\text{max}} - E_{\text{min}}) \cdot E_n(t_n) + E_{\text{min}},
\]

where, \( E_n(t_n) \) is the “double hill” normalized elastance function which has been modified from the adult model in \([20]\) to a neonate model as:

\[
E_n(t_n) = \left[ \frac{\left( \frac{t_n}{0.303} \right)^{1.32}}{1 + \left( \frac{t_n}{0.303} \right)^{1.32}} \right] \left[ \frac{1}{1 + \left( \frac{t_n}{0.508} \right)^{21.9}} \right]
\]

where, \( t_n = \frac{t}{t_c}, \ t_c = \frac{60}{HR} \), \( HR \) is the heart rate. The exponential coefficients, \( E_{\text{max}} \), and \( E_{\text{min}} \) were iteratively tuned in Eq. (4) to produce a cardiac output for the nominal model of ~2.0 liters/min. These values were held constant for all subsequent simulations. The right atrium was modeled using a constant elastance. A 32 state variable closed-loop circuit representation of the systemic
and pulmonary circulation (Figure 13, Figure 14) leads to coupled ordinary differential equations that are solved via a 4th order adaptive Runge-Kutta integrator.

BPA banding is achieved using a geometrical restriction in the CFD model supplemented with a resistance placed in pulmonary LPM vascular bed to achieve cycle-averaged ratio of total BPA artery to ductal flow, \( Q_p/Q_s \approx 1 \), in the nominal model. In order for the LPM to account for most of the coronary perfusion during diastole, the coronary arterial bed resistance is assumed to be a normalized exponential function of the time-varying elastance. The nominal LPM parameters are held constant in subsequent simulations in which the RBTS, as well as various levels of stenosis in the isthmus, are introduced into the 3D model.
Figure 14: Detailed LPM schematic with RBTS in place.
Coupling

Coupling refers to the interaction between the Lumped Parameter and the CFD models. A baseline LPM of the Nominal anatomical configuration is constructed and adjusted to approach pressure and flow waveforms derived from a catheterization procedure performed on a “typical” HN patient. This baseline LPM model is tuned as described below, with all vascular bed parameters influencing the output waveforms. In all other anatomical configurations the coupling only affects those parameters that are common in the LPM and CFD, that is, the parameters in the arterial and venous beds, remain constant. This is done to obtain a relative comparison of results among the anatomical configurations; no considerations were given to physiological responses affecting vascular resistance. The coupling is achieved by: (1) tuning the initial circuit to produce target flows and pressure waveforms obtained from catheter data when available supplemented with nominal values for typical HLHS patients, (2) imposing transient flow splits (branching arteries) and stagnation pressure (pulmonary root) boundary conditions to the CFD model from the circuit, (3) carrying out the CFD simulation to obtain the detailed flow field, (4) modifying the CFD equivalent parameters within the circuit to match those derived from the CFD, (5) running the LPM and imposing updated flow splits to CFD, and (6) iterating the system of equations until convergence. Convergence is achieved once the relative change in flow rates at all branch vessels is less than $10^{-2}$, reached typically in 15-20 iterations between the CFD and LPM models. Once the process has converged, the CFD simulation is run for three cardiac cycles to achieve a sustained periodic solution, and post-processing is performed. Our iterative approach provides a convenient and computationally effective way to tune the LPM parameters.
A more specific description as it pertains to the particular codes and software utilized in this study is provided in APPENDIX A: CFD-LPM COUPLING PSEUDOCODES.

**Oxygen Transport Model**

The oxygen transport model is based on the typical uptake, consumption, and conservation equations used in physiology, implemented in the present study using the LPM model. Oxygen transport equations are not calculated for the CFD model since the oxygen concentration entering the pulmonary and systemic arteries is the same in the HN anatomy. The major driver for systemic and pulmonary oxygen concentrations is thus the pulmonary to systemic blood flow ratio (Qp/Qs). The premise of the LPM oxygen transport model can be described using the following equations,

\[ C_{P,venO_2} \cdot Q_p = C_{P,artO_2} \cdot Q_p + S\dot{V}_{O_2} \]  
\[ C_{Sys,venO_2} \cdot Q_{Sys} = C_{Sys,art} \cdot Q_{sys} - C\dot{V}_{O_2} \]

Equation 2 states that the oxygen flow into the pulmonary veins, \( C_{P,venO_2} \cdot Q_p \), is equal to the oxygen flow entering the pulmonary arterial circulation, \( C_{P,artO_2} \cdot Q_p \), plus the oxygen uptake in the lungs, \( S\dot{V}_{O_2} \). Equation 3 states that the oxygen flow out of the systemic venous circulation, \( C_{Sys,venO_2} \cdot Q_{sys} \), is equal to flow of oxygen entering the systemic arterial circulation \( C_{Sys,art} \cdot Q_{sys} \), minus the whole-body oxygen consumption, \( C\dot{V}_{O_2} \). The analysis will assume steady state conditions (maintaining constant oxygen concentration in time), therefore according to the mass conservation for oxygen,
\[ S\dot{V}_{O_2} = C\dot{V}_{O_2} \]  \hspace{1cm} (7)

The systemic oxygen delivery is thus a function of cardiac output, Qp/Qs, pulmonary venous blood oxygen delivery, and the whole-body oxygen consumption as follows,

\[ C_{\text{sys,art}} \cdot Q_{\text{sys}} = C_{\text{sys,veno}_2} \cdot Q_{\text{sys}} \cdot \gamma - C\dot{V}_{O_2} \cdot \frac{1}{Q_p/Q_s} \]  \hspace{1cm} (8)

Where \( \gamma \) is the blood oxygen capacity defined as 0.22 (ml oxygen / ml blood) and the whole-body oxygen consumption, \( C\dot{V}_{O_2} \), as 18 (ml oxygen / min) for a neonate [21].

**Hemodynamic Parameters**

Hemodynamics are investigated in post-processing by examining the velocity vectors, by computing the wall shear stress (WSS), and by computing the oscillatory shear index (OSI), an indicator of cyclic departure of the wall shear stress vector from its predominant axial alignment. The WSS and OSI are defined as:

\[ \text{WSS} = \left| \frac{1}{T} \int_0^T \bar{\tau}_w \, dt \right| \]  \hspace{1cm} (9)

\[ \text{OSI} = \frac{1}{2} \left( 1 - \left| \frac{\int_0^T \bar{\tau}_w \, dt}{\int_0^T |\tau_w| \, dt} \right| \right) \]  \hspace{1cm} (10)

where \( \bar{\tau}_w \) is the instantaneous wall shear stress vector. Equation 9 is the time average of the wall shear stress magnitude [22]. In Equation 10, the numerator of the shear stress fraction represents the magnitude of the time averaged wall shear stress while the denominator represents the time-average of the wall shear stress magnitude. The OSI can vary from 0 or no variation in the stress alignment to 0.5, a complete reversal.
In addition, we studied the vorticity which is a measure of fluid rotation, and helicity which is a measure of how much the velocity field is aligned with vorticity, i.e. corkscrew or helical flow pattern, to further examine flow phenomena in the shunts. These are defined as:

\[
\text{Vorticity} = \nabla \times \vec{V} \quad (11)
\]

\[
\text{Helicity} = \vec{V} \cdot (\nabla \times \vec{V}) \quad (12)
\]

**Effects of Increasing Cerebral Vascular Resistance on HLHS Hemodynamics**

This study also explored the possibility of altering cerebral vascular resistance (CVR) on patients undergoing HN palliation for HLHS in order to increase coronary perfusion. During the course of HN palliation it may be useful to increase coronary blood flow to prevent hypoperfusion of the myocardium, often due to aortic arch atresia and/or the presence of stenosis in the aortic isthmus proximal to the ductus arteriosus after stent placement. Other than implanting an RBTS in patients with severe isthmus stenosis, increasing CVR may offer a way of increasing coronary perfusion. CVR can be modified by adjusting the mechanical ventilation parameters or pharmacologically in HN patients [23-29]. The hypothesis to be tested is the following: *An increase in CVR will produce a reduction in cerebral perfusion that will in turn produce an important increase in coronary perfusion.*

The synthetic anatomy was used to investigate the effects of increasing CVR on hemodynamics and perfusion to the coronary arteries and all major branching arteries. The severe stenosis in the synthetic model created a higher restriction of flow than in the patient derived model and thus the effects of CVR should be more impactful. The analysis was performed using the synthetic severe stenosis case without RBTS (S2) for this reason. Keeping
all other vascular bed parameters constant, the carotid arterial bed resistances were raised to provide a 50%, 100%, and 200% increase in CVR. The percent increases in CVR were chosen arbitrarily to capture a feasible range of resistance increase achievable by modifying mechanical ventilation parameters.
CHAPTER FIVE: RESULTS AND DISCUSSION

Pressure and flow-rate waveforms were obtained for the major arteries and all configurations, a comparison of the major phenomena in non-RBTS and RBTS configurations was performed in our previous study for the synthetic anatomy [30]. Although the standard and hybrid Norwood basic objectives are the same, the resulting anatomical configurations are clearly different. This raises the possibility of distinct differences in the resulting hemodynamics and physiology and unique effects on the various arterial segments of the reconstruction. Additionally, the HN is subject to unique complications such as distal arch obstruction, ductal stenosis, stent migration, atrial septal restriction, and under- or over-circulation to one or both lungs, all of which are known to have a substantial impact on early and intermediate term morbidity and mortality. Distal aortic arch obstruction occurs in 15-25% [2, 6, 31] of patients who have undergone the HN procedure. Causes may include juxtaductal intimal or ductal cell proliferation, stent malposition, or chronic flow disturbance. Caldarone et al [32] first proposed treating, or even preventing the effects of distal arch obstruction by suturing a graft (RBTS) from the pulmonary trunk or bifurcation area to the IA. Understanding the hemodynamic properties of the HN circulation is thus of paramount importance.  

Whereas clinical imaging and catheter measurements provide some understanding, CFD has the power to elucidate hemodynamic behavior in a controlled manner and at sub-millimeter level of detail [8-12]. Corsini et al [33] examined the effects of various degrees of branch pulmonary artery banding and ductal stent diameter on cardiac output and oxygen delivery in the HN model.

---

They found that these parameters were much more sensitive to changes in the percentage constriction of the BPA than to the same percentage change in ductal diameter, and suggested that a banded BPA lumen diameter of 2mm was optimal. Subsequently Hsia et al [19] compared cardiac output, systemic and cerebral oxygen delivery in two variants of the standard Norwood and the HN circulations. Controlling for all other characteristics of cardiac function and peripheral beds, they found that cardiac output and oxygen delivery were significantly lower in the HN circulation, despite the presence of an unobstructed aortic arch. These findings are consistent with the clinical reports [34, 35]. This illustrates the power of CFD to demonstrate underlying mechanisms, not necessarily intuitive, for the clinical findings in this case that the combination of diastolic flow reversal in the ductus, plus obligatory retrograde (albeit unobstructed) arch flow was responsible for reductions in both cardiac output and cerebral blood flow.²

In general, stenosed configurations have an important reduction in flow (around a 30% or 15% reduction in all branching arteries with 90% stenosis in the synthetic and patient-derived configurations, respectively) and a loss in pressure and pulsatility. It is noted however, that flow through the RBTS as a percentage of cardiac output remained almost the same (within 1%) in stenosed configurations for both anatomies (Table 2).

In the stenosed RBTS cases, the RBTS compensated for the distal arch obstruction, restoring cardiac output, coronary and arch branch flow and pressure to near nominal levels. Models including arch stenosis have lower cardiac output due to the increased afterload resulting from the reduction of the isthmus lumen. Individual cycle-averaged flow rates are provided in

² Some content in this paragraph also in [30] ibid.
Table 2 as a percentage of cardiac output as well percentage of change from those of Nominal. Cycle-averaged velocities through the shunt, as well as averaged retrograde and antegrade flow, are provided in Figure 15.
Table 2: Cardiac output, arterial flow rates and relative flow changes. Synthetic (top) and patient derived (bottom) anatomical configurations.

<table>
<thead>
<tr>
<th>Patient Specific</th>
<th>Cardiac Output (ml/min)</th>
<th>Flow Rate as Percentage of Cardiac Output</th>
<th>Percentage Change from Nominal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Qp/Qs</td>
<td>DA</td>
</tr>
<tr>
<td>Nominal</td>
<td></td>
<td>2022</td>
<td>0.95</td>
</tr>
<tr>
<td>Nominal-3mmRBTS</td>
<td></td>
<td>2029</td>
<td>0.94</td>
</tr>
<tr>
<td>Nominal-3.5mmRBTS</td>
<td></td>
<td>2047</td>
<td>0.95</td>
</tr>
<tr>
<td>Nominal-4mmRBTS</td>
<td></td>
<td>2055</td>
<td>0.94</td>
</tr>
<tr>
<td>Stenosed</td>
<td></td>
<td>1942</td>
<td>1.01</td>
</tr>
<tr>
<td>Stenosed-3mmRBTS</td>
<td></td>
<td>2031</td>
<td>0.96</td>
</tr>
<tr>
<td>Stenosed-3.5mmRBTS</td>
<td></td>
<td>2041</td>
<td>0.96</td>
</tr>
<tr>
<td>Stenosed-4mmRBTS</td>
<td></td>
<td>2051</td>
<td>0.96</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Synthetic</th>
<th>Cardiac Output (ml/min)</th>
<th>Flow Rate as Percentage of Cardiac Output</th>
<th>Percentage Change from Nominal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Qp/Qs</td>
<td>DA</td>
</tr>
<tr>
<td>Nominal</td>
<td></td>
<td>2015</td>
<td>0.94</td>
</tr>
<tr>
<td>Nominal-3mmRBTS</td>
<td></td>
<td>2072</td>
<td>0.93</td>
</tr>
<tr>
<td>Nominal-3.5mmRBTS</td>
<td></td>
<td>2077</td>
<td>0.94</td>
</tr>
<tr>
<td>Nominal-4mmRBTS</td>
<td></td>
<td>2085</td>
<td>0.93</td>
</tr>
<tr>
<td>Stenosed</td>
<td></td>
<td>1983</td>
<td>1.10</td>
</tr>
<tr>
<td>Stenosed-3mmRBTS</td>
<td></td>
<td>1998</td>
<td>0.55</td>
</tr>
<tr>
<td>Stenosed-3.5mmRBTS</td>
<td></td>
<td>2016</td>
<td>0.55</td>
</tr>
<tr>
<td>Stenosed-4mmRBTS</td>
<td></td>
<td>2035</td>
<td>0.55</td>
</tr>
</tbody>
</table>
Figure 15: Averaged flow velocity magnitude through shunt during the cardiac cycle. Antegrade and retrograde averaged velocity magnitudes also included. Synthetic (top) and patient derived (bottom) anatomical configurations.
Incorporating the RBTS in the absence of stenosis results in a slight increase in cardiac output for increasingly larger shunt diameters in the nominal cases (Table 2) without causing significant changes in the overall flowrates and pressures. This supports the notion of implanting the shunt as a preventative measure in case stenosis develops with time after the initial procedure, reducing or eliminating the need for re-intervention. However, the prophylactic use of the 4.0mm RBTS in the absence of distal arch stenosis may have negative implications due to abnormal hemodynamic patterns that are potentially thrombogenic sites, as will be discussed below.

**Synthetic Anatomy Hemodynamics**

The synthetic anatomy features the more severe hypoplastic features. In the Nominal 4.0mm RBTS configuration, prominent recirculation and stagnation zones are observed, particularly at the origin of the IA caused by the confluence of retrograde flow from the PDA and the RBTS through the IA, as well as at the distal anastomosis of the RBTS (Figure 16A). In this configuration, the RBTS flow features a chaotic swirl in early diastole which progressively increases in mid to late diastole, at which point the flow stagnates and reverses in direction. This finding is consistent with our previous report [30]. The 3.0mm RBTS configurations exhibit a higher velocity and more organized shunt flow throughout the cardiac cycle. The Nominal 3.0mm and 3.5mm RBTS configurations do not exhibit the helical flow through the shunt present in the 4.0mm model (Figure 17 and Figure 18), presumably due to the higher momentum of the flow disrupting the formation of vortical structures seen in the lower velocity flow. Of particular interest are the changes in the flow to the LPA and RPA during the late diastolic period. At this point in the cardiac cycle, the flow through these arteries is mainly delivered by the RBTS in the
4.0mm configuration. In the 3.0mm and 3.5mm configuration, however, the contribution of flow from the rest of the branching arteries (LCA, LSA, in addition to the DA) is important.

Figure 16: Streamlines through shunt at selected points during cardiac cycle. 4.0mm RBTS configuration, (Top) synthetic, (Bottom) Patient Derived, (A) Nominal, (B) 90% stenosis.
Figure 17: Streamlines through shunt at selected points during cardiac cycle. 3.5mm RBTS configuration, (Top) synthetic, (Bottom) Patient Derived, (A) Nominal, (B) 90% stenosis.
Figure 18: Streamlines through shunt at selected points during cardiac cycle. 3.0mm RBTS configuration, (Top) synthetic, (Bottom) Patient Derived, (A) Nominal, (B) 90% stenosis.

The 90% stenosis 4.0mm RBTS configuration exhibits more organized flow through the shunt and reduced recirculation zones (Figure 16). The chaotic swirling seen through the shunt in the Nominal 4.0mm RBTS configuration is not present in the 90% stenosis configurations. This
is, again, a consequence of the higher flow velocity through the RBTS. All of the 90% stenosis RBTS configurations have very similar flow structure and velocities. This indicates that the a larger shunt diameter (graft size) should be carefully considered in the absence of distal aortic arch obstruction, as it may result in undesirable flow conditions such as impingement, stagnation and recirculation zones. Characteristically, such zones have low shear stress promoting platelet activation, aggregation and thrombosis, especially within the lumen of a synthetic graft [36, 37].

Patient-Derived Anatomy Hemodynamics

The hypoplastic features of the patient-derived anatomy are less severe than the synthetic model. Nominal 4.0mm RBTS configuration has a more uniform flow through the shunt as compared to its synthetic analogous during most of the cardiac cycle, with less helical structures forming. There are multiple areas of flow recirculation, of which the most prominent are the root of the IA and the ascending aorta, the latter being significantly larger and more proximal to the atretic aortic valve than in the synthetic case and thus creates flow stagnation of ample duration throughout the cardiac cycle. Shunt flow in late diastole exhibits an interesting phenomenon in which both antegrade and retrograde flow exist within the lumen. The portion of shunt wall corresponding to the larger radius of curvature (distal to the PA) is in contact with a swirling antegrade flow, while the wall portion corresponding to the inner radius of curvature is in contact with a more uniform retrograde flow. See Figure 19 for a close-up of late diastolic shunt flow during mid-diastole (corresponding to time point 3 as indicated in Figure 18) for patient-derived nominal cases with RBTS.
Figure 19: Comparison of shunt flow at time point 3 in late diastole. Nominal patient derived configurations P5 (Top), P4 (Middle), P3 (Bottom)
For all patient derived configurations, the flow velocity is significantly higher in the LCA due to it being severely narrowed in this particular anatomy as compared to the other branching arteries (an outlet RCA to LCA area ratio of 9.5). Nominal RBTS cases exhibit similar hemodynamics but with a less prevalent recirculation zone at the IA root and a more uniform shunt flow throughout the cardiac cycle in the P3 and P4 configurations. There is also a slight tendency of shunt flow to the mid-aortic arch during mid diastole as the shunt is decreased in diameter. The antegrade shunt velocity with the 3.5mm RBTS is lower than in the 3.0mm RBTS configuration (Figure 15); the difference in lumen area between the two shunts does not produce significantly different flow-rates.

Severely stenosed cases exhibit pronounced impingement and recirculation zones at the root of the IA. In general, shunt flow is more uniform as the shunt is reduced in diameter. Interestingly, when compared to the analogous Nominal cases, the proportion of RBTS retrograde to antegrade flow increases in the severely stenosed cases (Table 3). The increase of RBTS antegrade flow over the cardiac cycle in severely stenosed cases relative to nominal stenosis cases of same diameter is 62%, 69%, and 59% respectively for 3.0mm, 3.5mm, and 4.0mm shunts. This compared to retrograde flow over the cardiac cycle, where the increase in flow through the RBTS relative to the nominal cases is 145%, 166%, and 148% respectively for 3.0mm, 3.5mm, and 4.0mm shunts. Mid-aortic arch and aortic isthmus flow results from the confluence of flows coming through the RBTS and the stenosis site. The average location of this confluence, or point where these flows that travel in opposing directions meet during systole, changes with RBTS diameter Figure 20. For P6 and P7 configurations, net LCA flow is a result of this confluence occurring at the LCA root (52% and 85% RBTS flow contribution for P6 and P7, respectively). In the P8 configuration the confluence is located at the LSA root with a 15%
RBTS contribution to net LSA flow. Implantation of the RBTS in severely stenosed cases reduces flow magnitude (both antegrade and retrograde flow considered) along the mid-aortic arch anywhere from 60%-80% relative to the non-RBTS stenosed configuration (P2) independently of RBTS diameter. Flow magnitude through the stenosis, however, does not decrease as sharply, with a decline of 14%, 23%, and 25% relative to the P2 configuration as a percentage of CO respectively for the P6, P7, and P8 configurations. It is thus LSA flow, whether antegrade or retrograde, that mostly determines the flow that crosses the stenosis in RBTS cases.

Another important result from the stenosed RBTS cases is that systemic flow and pressure waveform amplitudes increase relative to the Nominal RBTS and non-RBTS cases (Figure 22). The opposite is true for the pulmonary arterial waveforms. This results in higher forward flow during systole and higher reverse flow during diastole for the branched arteries, with a net gain in cycle arterial perfusion. Pulmonary flow on the other hand is always forward regardless of the configuration but becomes steadier in RBTS cases, with a higher flow contribution from the branched arteries during diastole.
Figure 20: Flow direction nomenclature. Antegrade flow through the isthmus and mid-aortic arch occurs in the direction from pulmonary root to aortic root. Antegrade flow through the shunt occurs from pulmonary root to innominate artery.
Figure 21: Plane sections used to monitor flow through the ascending aorta and mid-aortic arch in the patient derived anatomy.
Table 3: Flow in Patient derived configurations through various plane sections located along the ascending aorta and mid-aortic arch (see Figure 21). Isthmus flow is that crossing through the stenosis site. Branched arterial flow is the sum of all flow through the branched arteries’ outlet boundaries (LcorA, RcorA, LSA, LCA, RSA, RCA, DA). Pulmonary flow is the sum of the flow through the LPA and RPA outlet boundaries.

<table>
<thead>
<tr>
<th>Net Flow (ml/min)</th>
<th>Isthmus Flow</th>
<th>Branched Arterial Flow</th>
<th>Pulmonary Flow</th>
<th>LSA_LCA_section</th>
<th>LCA_IA_section</th>
<th>IA_section</th>
<th>CorA Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>90p</td>
<td>-93.65</td>
<td>-108.31</td>
<td>0.00</td>
<td>-14.07</td>
<td>-41.19</td>
<td>-0.54</td>
<td>-0.45</td>
</tr>
<tr>
<td>90p, 3mmRBTS</td>
<td>-190.86</td>
<td>-407.22</td>
<td>0.00</td>
<td>-55.10</td>
<td>-54.45</td>
<td>-1.96</td>
<td>-1.76</td>
</tr>
<tr>
<td>90p, 3.5mmRBTS</td>
<td>-179.78</td>
<td>-432.04</td>
<td>0.00</td>
<td>-30.35</td>
<td>-95.10</td>
<td>-2.41</td>
<td>-2.01</td>
</tr>
<tr>
<td>90p, 4mmRBTS</td>
<td>-168.24</td>
<td>-456.32</td>
<td>0.00</td>
<td>-38.33</td>
<td>-139.80</td>
<td>-2.52</td>
<td>-1.95</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Flow Magnitude (ml/min)</th>
<th>Isthmus Flow</th>
<th>Branched Arterial Flow</th>
<th>Pulmonary Flow</th>
<th>LSA_LCA_section</th>
<th>LCA_IA_section</th>
<th>IA_section</th>
<th>CorA Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>90p</td>
<td>574.19</td>
<td>603.61</td>
<td>975.88</td>
<td>392.43</td>
<td>207.61</td>
<td>63.64</td>
<td>65.16</td>
</tr>
<tr>
<td>90p, 3mmRBTS</td>
<td>518.77</td>
<td>1257.02</td>
<td>996.65</td>
<td>154.41</td>
<td>60.25</td>
<td>75.66</td>
<td>73.62</td>
</tr>
<tr>
<td>90p, 3.5mmRBTS</td>
<td>407.16</td>
<td>1310.58</td>
<td>1001.63</td>
<td>88.03</td>
<td>110.50</td>
<td>73.82</td>
<td>74.80</td>
</tr>
<tr>
<td>90p, 4mmRBTS</td>
<td>456.77</td>
<td>1762.31</td>
<td>1005.85</td>
<td>64.63</td>
<td>170.08</td>
<td>74.78</td>
<td>75.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antegrade Flow (ml/min)</th>
<th>Isthmus Flow</th>
<th>Branched Arterial Flow</th>
<th>Pulmonary Flow</th>
<th>LSA_LCA_section</th>
<th>LCA_IA_section</th>
<th>IA_section</th>
<th>CorA Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>90p</td>
<td>489.54</td>
<td>495.31</td>
<td>975.88</td>
<td>349.16</td>
<td>266.42</td>
<td>63.07</td>
<td>64.71</td>
</tr>
<tr>
<td>90p, 3mmRBTS</td>
<td>327.92</td>
<td>849.80</td>
<td>996.65</td>
<td>99.31</td>
<td>5.80</td>
<td>73.70</td>
<td>71.85</td>
</tr>
<tr>
<td>90p, 3.5mmRBTS</td>
<td>287.38</td>
<td>878.54</td>
<td>1001.63</td>
<td>50.98</td>
<td>15.41</td>
<td>71.41</td>
<td>72.59</td>
</tr>
<tr>
<td>90p, 4mmRBTS</td>
<td>268.54</td>
<td>905.96</td>
<td>1005.85</td>
<td>25.28</td>
<td>30.78</td>
<td>72.26</td>
<td>73.37</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Retrograde Flow (ml/min)</th>
<th>Isthmus Flow</th>
<th>Branched Arterial Flow</th>
<th>Pulmonary Flow</th>
<th>LSA_LCA_section</th>
<th>LCA_IA_section</th>
<th>IA_section</th>
<th>CorA Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>90p</td>
<td>19.49</td>
<td>231.87</td>
<td>0.00</td>
<td>12.61</td>
<td>15.66</td>
<td>0.85</td>
<td>0.69</td>
</tr>
<tr>
<td>90p, 3mmRBTS</td>
<td>58.20</td>
<td>436.92</td>
<td>0.00</td>
<td>55.48</td>
<td>938.54</td>
<td>2.66</td>
<td>2.45</td>
</tr>
<tr>
<td>90p, 3.5mmRBTS</td>
<td>62.56</td>
<td>441.18</td>
<td>0.00</td>
<td>72.68</td>
<td>617.18</td>
<td>3.38</td>
<td>2.74</td>
</tr>
<tr>
<td>90p, 4mmRBTS</td>
<td>70.10</td>
<td>450.37</td>
<td>0.00</td>
<td>155.63</td>
<td>452.57</td>
<td>3.48</td>
<td>2.65</td>
</tr>
</tbody>
</table>
Figure 22: Branched arterial flow and pulmonary flow over one cardiac cycle for patient derived, stenosed configurations.

**Oxygen Transport**

The maximum systemic oxygen delivery increase afforded by the implantation of the shunt is 2.2% in Nominal configurations and 8.5% in Stenosis 90% configurations for the patient derived anatomy. Similarly, the increase is 4.0% in Nominal configurations and 18.1% in Stenosis 90% configurations for the synthetic anatomy (Figure 23). The diameter used for the shunt has little effect on overall systemic oxygen delivery; all RBTS cases are within 2.3% of each other in both anatomies.
Figure 23: Systemic oxygen delivery for all anatomical configurations and shunt diameters.

**Wall Shear Stress and Oscillatory Shear Index**

Of particular interest in this study is how the vessel WSS changes depending on shunt diameter. Studies [38-41] have shown a strong correlation in the magnitude of shear stress, endothelial cell function, and vessel wall remodeling. Low levels of shear stress promote platelet activation and coincide with areas of low flow velocity, typically the outer walls of bifurcations and recirculation zones. Varying levels of shear stress through the ductus arteriosus, where a metallic stent is placed to prevent it ductus closure, affect the formation of neointimal
hyperplasia and stenosis formation. Flow characteristics surrounding the RBTS anastomosis are also of great interest since there has been early evidence of pulmonary root hyperplasia and studies have suggested there is an optimal shunt diameter as a function of shear stress that achieves greater shunt patency and reduction in graft thrombosis [36, 42]. Figure 24 through Figure 27 depict WSS and OSI for all RBTS configurations.

Both synthetic and patient derived configurations exhibit very similar trends with respect to the effects of shunt diameter on WSS and OSI. The prominent areas of high WSS in all models include shunt anastomosis sites, pulmonary banding region, stenosis region, and the root of the LSA. Areas of high OSI in all models include the mid-RBTS, left and right carotid roots, stenosis region, and the DA. For both anatomical models, configurations with the 4.0mm shunt exhibit less wall shear stress in critical regions such as the shunt anastomosis sites and stenosis surroundings (Figure 24). However, there is higher flow residence time and decreased velocity in the 4.0mm shunt which encourage thrombogenesis.

In all configurations there is a region of progressively higher WSS as the RBTS diameter decreases extending from the stenosis site retrograde through the aortic isthmus into the LCA root. The distal shunt anastomosis as well as the shunt wall also exhibit larger regions of higher WSS as the shunt diameter decreases. There are no considerable changes in OSI in all Nominal configurations.

In the 90% Stenosis RBTS cases (Figure 26) there is a sharp increase in WSS near the shunt anastomosis sites as well as the proximal half of the shunt in the 3.0mm case relative to the 4.0mm and 3.5mm case. Higher WSS is also seen at the root of the LSA as shunt diameter decreases; this is due to the higher flow rate through the stenosis site impinging at the distal side of the LSA root. An interesting deduction that can be made based on the WSS plot in Figure 26
is that most of the flow through the LSA and LCA comes from the shunt/innominate in the 4.0mm case as opposed to most of the flow coming retrograde form the stenosis site in the 3.0mm case. In the 3.5mm RBTS case there is a compromise between the competing flows through the mid-aortic arch. There is a notable decrease in OSI through the mid-artic arch region and branching arteries as shunt diameter decreases in severely stenosed cases.

Regions of peak OSI for both synthetic and patient derived anatomies include the descending aorta, pulmonary arteries distal to the banding, and root of the LSA and LCA (Figure 25 and Figure 27). Generally, there are no considerable changes in OSI due to shunt diameter for the two anatomical cases. In the patient derived, severely stenosed cases there is a considerable reduction in OSI in the ascending aorta and descending aorta relative to nominal configurations. A reduction in OSI is seen in the descending aorta for the synthetic, severely stenosed cases relative to nominal configurations.

Our results suggest that the 3.0mm RBTS maintains the same flow-rates as the 4.0mm RBTS without the deleterious hemodynamic patterns experienced with the larger shunt. The disordered flow patterns seen in late diastole with the larger shunt can cause acute thrombosis. On the other hand, the smaller shunts are at higher risk of stenosis. The smaller 3.0mm shunt does, however, exhibit a higher level of shear stress along the suture lines and this has been associated with suture line stenosis, which develops over time to gradually restrict flow. Such a phenomenon, because of the time scale of its manifestation, can be detected and corrected by balloon dilation and stenting. As such, our results suggest that the 4.0mm shunt is a generous shunt diameter choice that may be problematic particularly when implemented as a prophylactic measure, and that the 3.5mm shunt may be a more suitable alternative as it provides the more organized hemodynamics from the 3.0mm configurations with lower levels of WSS.
Figure 24: Contour plots of cycle averaged wall shear stress magnitude. Nominal stenosis cases shown, synthetic anatomy (Top) and patient derived anatomy (Bottom).
Figure 25: Contour plots of oscillatory shear index. Nominal stenosis cases shown, synthetic anatomy (Top) and patient derived anatomy (Bottom).
Figure 26: Contour plots of cycle averaged wall shear stress magnitude. Severe (90%) stenosis cases shown, synthetic anatomy (Top) and patient derived anatomy (Bottom).
Other Hemodynamic Parameters

In an effort to better describe the particular hemodynamic phenomena in shunt flow, we studied the vorticity (a measure of fluid rotation) and helicity (a measure of how much the velocity field is aligned with vorticity, i.e. corkscrew or helical flow pattern). In Figure 28, volume average vorticity and helicity are reported over a cycle. Vorticity increases as the shunt diameter decreases; an increased velocity magnitude through the shunt increases the vorticity generated at the walls. There is a small dip just prior to cardiac ejection. The cycle averaged vorticity over all shunt diameters increases from nominal to severe stenosis by 87% for patient...
derived cases and in the same manner by 65% in synthetic cases. The shunt volume averaged vorticity plots compare similarly for patient derived and synthetic cases, in fact, the difference from synthetic to patient derived cycle averaged vorticity for the combined shunt diameters is 10% in nominal configurations and -1% in severe configurations. In this setting, where perfusion is restored to all arterial beds to near nominal levels (with similar distribution of flow in both anatomies) by the RBTS, these results suggest that shunt flow vorticity has little correlation with the patient anatomy. In other words, vorticity generation can be attributed predominantly to how much flow traverses the shunt and to shunt diameter, and not the anatomical configuration.

In contrast to the behavior of vorticity, helicity is highly dependent on the anatomy under consideration. The motivation for investigating helicity is the potential of helical flow structures to reduce shunt stenosis. Helical flow is seen in many vessels in healthy vasculature including the aortic arch, descending aorta, and common iliac and femoral arteries. Numerous studies have found that this type of flow is more stable, enhances oxygen transport, and reduces thrombogenic particle adhesion in the lumen, among other benefits [43]. The potential advantage of utilizing helical flow in vascular disease treatment was reported in a recent study by Caro et al [44], who found that helical-centerline metallic stents implanted in the common carotid artery of healthy pigs produces significantly less intimal hyperplasia than straight-centerline stents. The authors attributed this finding to the enhanced intraluminal wall shear stress (WSS) and enhanced intraluminal blood-vessel wall mass transport that the helical-centerline stent reportedly provides. The study, however, did not detail the precise hemodynamics sought or the level of WSS enhancement that results in decreased intimal hyperplasia. In the present case, the motivation is to explore the values of helicity with respect to the different anatomies and shunt diameters.
In the synthetic cases, helicity is higher in the nominal configurations, with the opposite occurring in the patient derived cases. Helicity occurs in a clockwise direction for patient derived anatomies and in a counterclockwise direction for synthetic anatomies (Figure 28). Helicity reverses in direction in the P3 configuration during the diastolic phase. Discernible helical structures were only found in the S5 configuration, briefly in the late diastole phase. The presence of helical flow structures does not necessarily translate in higher helicity values in the present case, rather, a better predictor is the degree of the velocity vector alignment with the vorticity in the flow. The results obtained show that there is little correlation between helicity and shunt size in the synthetic case while there is variability in the patient derived case.
Figure 28: Volume averaged vorticity and helicity of flow through shunt over one cardiac cycle.
Effects of Increasing Cerebral Vascular Resistance on HLHS Hemodynamics

Individual cycle-averaged flow rates are provided in Table 4, the values are also presented as a percentage of cardiac output and percentage of change from those the S2 configuration with Nominal CVR. An increase in CVR leads to a reduction in cardiac output due to the increase in afterload. The ratio of pulmonary to systemic circulation (Qp/Qs) is seen to increase as CVR increases. As expected, carotid flow decreases significantly with increased CVR. The reduction in cardiac output and carotid flow is accompanied by an increase in flow for all other arteries. In the most severe case (200% increase in CVR), coronary flow is increased by ~12% with a decrease of ~60% in carotid flow. Figures 1-4 show streamlines superimposed with velocity vectors for the four cases at selected points during the cardiac cycle: 1) peak systole, 2) early diastole, 3) mid-diastole and 4) late diastole. Hemodynamically, there is little difference among all of the cases, with all of them exhibiting the same prominent areas of high/low flow velocity, recirculation zones, and overall flow direction. Given the small gain in increased coronary blood flow with the accompanying reduction in carotid flow, increasing CVR may not be an advantageous approach to increasing coronary blood flow in the case of distal arch obstruction.
Table 4: Cardiac output, arterial flow rates and flow changes for the synthetic severe stenosis case without RBTS (S2).

| Cardiac Output (ml/min) | Flow Rate (ml/min) | Flow Rate as Percentage of Cardiac Output
|-------------------------|--------------------|----------------------------------------------|
|                         | Qp/Qs | DA | LCA | LcorA | LPA | LSA | RCA | RcorA | RPA | RSA | Shunt
| Sten 90% Nominal CVR    | 1919  | 1.11 | 612.1 | 62.0 | 23.9 | 500.6 | 61.6 | 62.0 | 25.7 | 509.1 | 61.9 | NA
| Sten 90% CVR +50%       | 1906  | 1.14 | 616.0 | 43.9 | 25.2 | 503.6 | 67.6 | 45.5 | 27.1 | 512.2 | 65.2 | NA
| Sten 90% CVR +100%      | 1895  | 1.16 | 618.8 | 33.7 | 26.0 | 503.9 | 70.0 | 35.5 | 27.8 | 512.6 | 66.7 | NA
| Sten 90% CVR +200%      | 1885  | 1.18 | 619.7 | 23.4 | 26.8 | 505.4 | 72.8 | 25.5 | 28.9 | 513.9 | 68.9 | NA

| Cardiac Output (ml/min) | Qp/Qs | DA | LCA | LcorA | LPA | LSA | RCA | RcorA | RPA | RSA | Shunt
|-------------------------|-------|-----|-----|-------|-----|-----|-----|-------|-----|-----|-------|
| Sten 90% Nominal CVR    | 1919  | 1.11 | 31.9 | 3.2  | 1.2 | 26.1 | 3.2 | 3.2  | 1.3 | 26.6 | 3.2  | NA
| Sten 90% CVR +50%       | 1906  | 1.14 | 32.3 | 2.3  | 1.3 | 26.4 | 3.5 | 2.4  | 1.4 | 26.9 | 3.4  | NA
| Sten 90% CVR +100%      | 1895  | 1.16 | 32.7 | 1.8  | 1.4 | 26.6 | 3.7 | 1.9  | 1.5 | 27.1 | 3.5  | NA
| Sten 90% CVR +200%      | 1885  | 1.18 | 32.9 | 1.2  | 1.4 | 25.8 | 3.9 | 1.4  | 1.5 | 27.3 | 3.7  | NA

<table>
<thead>
<tr>
<th>Percentage Change from Nominal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qp/Qs</td>
</tr>
<tr>
<td>Sten 90% CVR +50%</td>
</tr>
<tr>
<td>Sten 90% CVR +100%</td>
</tr>
<tr>
<td>Sten 90% CVR +200%</td>
</tr>
</tbody>
</table>
Figure 29 Streamlines colored by velocity, 90% Stenosis Nominal CVR
Figure 30: Streamlines colored by velocity, 90% Stenosis CVR +50%

Figure 31: Streamlines colored by velocity, 90% Stenosis CVR +100%
Figure 32: Streamlines colored by velocity, 90% Stenosis CVR +200%

**Limitations**

The principal limitation of this study is the rigid-walled CFD model, which does not account for arterial elasticity within its domain. The arterial compliances of the LPM model were tuned to compensate for this limitation in regards to absolute flow and pressure waveforms. Additionally, vessel wall elasticity can exaggerate impedance mismatches at vessel junctions or anastomoses, thereby affecting the flow characteristics. WSS is magnified due to the lack of compliance and thus only a relative comparison of its magnitude among the different anatomical configurations is appropriate. An improvement would be the development of a model that incorporates fluid-structure interaction to account for vessel-wall compliance, however, this would entail a significant increase in computational burden.
CHAPTER SIX: CONCLUSIONS

We utilized a multi-scale model to study the hemodynamics of the hybrid Norwood palliative treatment for HLHS. Calculated local hemodynamics derived from the model provide an insight of the effects of severe stenosis and RBTS implantation. This study considered the effects of varying shunt diameters (3.0mm, 3.5mm and 4.0mm) and the effects of severe stenosis of the aortic isthmus by comparing nominal cases with cases with a 90% reduction in lumen. In the stenosed RBTS cases, the RBTS compensated for the distal arch obstruction, restoring cardiac output as well as coronary and arch branch flows and pressures to near nominal levels. Systemic flow and pressure waveform amplitudes increase in severely stenosed cases with RBTS relative to all other cases while the opposite occurs for the pulmonary arterial waveforms. RBTS diameter has little effect on overall systemic oxygen delivery. Consistent trends were observed between the synthetic and patient specific geometries on bed perfusion, vorticity, oscillatory shear index (OSI) and wall shear stress (WSS) levels. Helicity on the other hand is shown to be highly dependent on anatomy and level of stenosis.

The Nominal case with 4.0mm RBTS configuration exhibits low flow velocity and disorganized flow through the shunt, which increase the possibility of thrombogenesis and hyperplasia. Cases with the 3.0mm RBTS exhibit higher shear stress at critical sites such as shunt anastomosis and stenosis sites which may reduce shunt patency and promote vessel wall remodeling. From a clinical perspective, our results indicate that the 3.5mm RBTS maintains acceptable hemodynamics without the deleterious patterns observed with the 3.0 and 4.0mm shunts. The disordered flow patterns seen in late diastole with the larger shunt may lead to thrombosis. On the other hand, the smaller shunts are at higher risk of stenosis. The 3.0mm shunt
does, however, exhibit a higher level of shear stress along the suture lines associated with suture-line-stenosis that develops gradually over time and, therefore, can be detected and corrected by balloon dilation and stenting. Among the three configurations, the most promising seems to be the 3.5mm RBTS which provides a more organized flow similar to that of the 3.0mm configuration with lower levels of wall shear stress. As such, our results suggest that: (1) the 4.0mm shunt is a generous shunt diameter choice that may be problematic particularly when implemented prophylactically in the absence of stenosis, and (2) the 3.5mm shunt may be a more suitable alternative since it exhibits more favorable hemodynamics at lower levels of wall shear stress.
APPENDIX A: CFD-LPM COUPLING PSEUDOCODES
The CFD software Star-CCM+ by CD-Adapco allows for the interaction with other commercial or proprietary codes. Special problems (such as this cardiovascular model) and unsupported physics (such as non-linear, large deformation FSI) require additional capabilities that are not native to Star-CCM+. The coupling scheme employed in this work involves the transfer of data between Star-CCM+ and the user code through file sharing. This is a similar coupling method that is engineered in the software to communicate with other widely available computational mechanics packages. The data passed in between the LPM code developed for this study and Star-CCM+ can include direct specification of boundary conditions as well as direct data-mapping matrices convenient for post-processed quantities such as averaged WSS and OSI.

In the current coupling scheme, Star-CCM+ controls the iterative process with a master routine written in Java, which allows access to all the programming constructs of the language such as loops and conditional constructs. This routine is compiled within the Star-CCM+ environment and allows to the control of all critical simulation parameters (time step size, convergence criteria, solver under-relaxation parameters, etc) as well most post-processing features (scalar, vector or custom plot generation, exportation of face-value or surface mapped quantities, etc). More importantly, this master routine is able to use the resources of the local computer system, which are used to run the LPM routine and make all the necessary post-processing, data parsing, and generation of tables that Star-CCM+ can read as boundary conditions.
Figure 33: CFD-LP model coupling scheme flow chart.
APPENDIX B: MASTER ROUTINE AND LPM PSEUDOCODES
// STAR-CCM+ macro: Coupling_of_CFD_LPM_PSEUDO

// Import all necessary classes
package macro;
import java.util.*;
import star.common. *;

public class Coupling_of_CFD_LPM_PSEUDO extends StarMacro {

    public void execute() {
        int n = 20; // Number of iterations
        Run_RK4(); // RK4 Subroutine
        for (int i = 1; i < (n + 1); i++) {
            StarReady(); // Checks for communication file
            if (i == n)
                PostProcess(); // Runs all post-processing activities
                DirChanger(); // Sorts and stores files in remote dir
        }
    }
}

The LPM code is compiled in C language and performs the operations involving: receiving user input on initial circulation values and parameter values, solving the coupled ordinary differential equations through a Runge-Kutta adaptive algorithm, importing data created by the CFD solver and performing post-processing for updated parameter calculation, and exporting all data necessary for the next CFD iteration.
///**Vascular Circuit Simulator***/

#include<stdio.h>
#include<stdlib.h>
#include<math.h>
#include "CSV_Read_90p.c"

/******************General Information********************
int i,j,k,l,m,n,counter,iter_count,file_count;
double IHR,NC,NS;

//Set Degrees of Freedom of LPM model
#define NDOF 32

/**********************Defining all parameter variables**************

//Heart
double C_RA, R_TRIC, EMAX_RV, EMIN_RV, R_RV;

//Pulmonary Bed
double C_PA, R_PA, L_PA,
R_RPA, R_LPA,
R_Rlung, R_Llung,
C_Rlung, C_Llung,
C_RPVB, C_LPVB,
L_Rlung, L_Llung,
R_RPVB, R_LPVB;

//Aortic Arch
double R_IA, R_AO, R_DA,
C_AO, L_AO;

// Etc, etc, etc*****************************************************************************

//Compliance
double CC, CD, Erv;

//System Matrices
double AC[NDOF][NDOF], BC[NDOF];
//Maximum Tolerance Error
double ERMAX = 1.0e-10;

//Current Solution
double YC[NDOF];

//Cardiac Cycle Interval
double TC;

//Elapsed Time at the Beginning of Cycle
double TE;

//Elapsed Time Within Cycle
double TI;

//Time Sampling Interval
double DTS;

//Sampling Interval Subdivisions
int WSS;

//Integration Step
int WN;

//Estimated Solutions
double Y1[NDOF], Y2[NDOF];

//SOLUTION PARAMETERS for RK4
double YN[NDOF]; //New Solution
double TT, DT, TS;
double YK[NDOF];
double RK[4][NDOF];
double RW[4], RT[4], RY[4];
int WTS;
int KR;
double DTHMIN, ER, DT;
// Function to Read Parameters from File
int Input()
{
    // Skip file read after first iteration
    FILE *ptr_file;
    char string[1000000];

    ptr_file = fopen("File Location", "r");
    if (!ptr_file)
    {
        printf("File Not Found\n\n");
        getchar();
        return 1;
    }

    // General Configuration Info
    for (i=0; i<4; i++)
    {
        fgets (string, 1000000, ptr_file);
        fscanf(ptr_file,"%lf %lf %lf", &IHR, &NC, &NS);
        printf("HR = %lf NC = %lf NS = %lf\n", IHR, NC, NS);
    }

    // Initial Conditions
    for (i=0; i<3; i++)
    {
        fgets (string, 1000000, ptr_file);
        for (i=0; i<NDOF; i++)
        {
            fscanf(ptr_file,"%lf", &YC[i]);
        }
        fgets (string, 1000000, ptr_file);
        fgets (string, 1000000, ptr_file);
    }

    // Right Heart
    fgets (string, 1000000, ptr_file);
    fscanf(ptr_file,"%lf", &C_RA);

    // Repeat for all vascular beds

    fclose(ptr_file);
}
int Assemble()
{
    // compliance();
    for (i=0;i<NOGF;i++)
    {
        for(j=0;j<NOGF;j++)
        {
            if (i==j)
            {
                Ac[i][j] = 0.0;
            }
            if (i!=j)
            {
                Ac[i][j] = 1.0;
            }
        }
    }

    RC[3] = (L/C_B5)*((V[2]-V[3]) - (I*V[3]));
    RC[7] = (L/C_B9)*((V[2]-V[7]) - (I*V[7]));
    RC[8] = (L/C_B10)*((V[2]-V[8]) - (I*V[8]));
    RC[10] = (L/C_B12)*((V[2]-V[10]) - (I*V[10]));
    RC[12] = (L/C_B14)*((V[2]-V[12]) - (I*V[12]));
    RC[14] = (L/C_B16)*((V[2]-V[14]) - (I*V[14]));
    RC[16] = (L/C_B18)*((V[2]-V[16]) - (I*V[16]));
    RC[17] = (L/C_B19)*((V[2]-V[17]) - (I*V[17]));
    RC[18] = (L/C_B20)*((V[2]-V[18]) - (I*V[18]));
    RC[19] = (L/C_B21)*((V[2]-V[19]) - (I*V[19]));
    RC[20] = (L/C_B22)*((V[2]-V[20]) - (I*V[20]));
    RC[21] = (L/C_B23)*((V[2]-V[21]) - (I*V[21]));
    RC[22] = (L/C_B24)*((V[2]-V[22]) - (I*V[22]));
    RC[23] = (L/C_B25)*((V[2]-V[23]) - (I*V[23]));
    RC[26] = (L/C_B28)*((V[2]-V[26]) - (I*V[26]));
    RC[27] = (L/C_B29)*((V[2]-V[27]) - (I*V[27]));
    RC[28] = (L/C_B30)*((V[2]-V[28]) - (I*V[28]));
    RC[29] = (L/C_B31)*((V[2]-V[29]) - (I*V[29]));
    RC[31] = (L/C_B33)*((V[2]-V[31]) - (I*V[31]));

    return 0;
}
Define Elastance function

```c
int compliance()
{
    double Tmax = 60.0/IHR;
    double dt = 1e-10;
    double Tn = TT/Tmax;
    double Tndt = (TT+dt)/Tmax;
    //Print TT withing Compliance execution
    //printf("TT with in Compliance execution = %6.13lf\n", TT);
    double P1 = pow((Tn/0.303),1.32);
    double P2 = 1 + pow((Tn/0.303),1.32);
    double P3 = 1 + pow((Tn/0.508),21.9);
    double P1dt = pow((Tndt/0.303),1.32);
    double P2dt = 1 + pow((Tndt/0.303),1.32);
    double P3dt = 1 + pow((Tndt/0.508),21.9);
    double En = P1/(P2*P3);
    double Endt = P1dt/(P2dt*P3dt);
    Erv = (EMAX_RV - EMIN_RV)*En + EMIN_RV;
    double Ervdt = (EMAX_RV - EMIN_RV)*Endt + EMIN_RV;
    
    CC = 1/Erv;
    double Crvdt = 1/Ervdt;
    CD = (Crvdt - CC)/dt;

    if (TT>dt){
        Tn = (TT-dt)/Tmax;
        P1 = pow((Tn/0.303),1.32);
        P2 = 1 + pow((Tn/0.303),1.32);
        P3 = 1 + pow((Tn/0.508),21.9);
        En = P1/(P2*P3);
        double CW = 1/((EMAX_RV - EMIN_RV)*En + EMIN_RV);
        CD = (Crvdt - CW)/(2*dt);
    }

    return 0;
}
```
Define Runge-Kutta Adaptive function

```c
int RK4()
{
    //SOLVE
    DT = DTS/NSS;
    TS = TI;

    for (i=0;i<NDOF;i++)
        YN[i] = YC[i];

    for (NTS=0;NTS<NSS;NTS++){
        for (i=0;i<NDOF;i++)
            YK[i] = YN[i];

        for (KR=0;KR<4;KR++){
            TT = TS + DT*RT[KR];
            Assemble();

            for (i=0;i<NDOF;i++)
                RK[KR][i] = BC[i];

        }

        for (i=0;i<NDOF;i++)
            YK[i] = YN[i] + DT*RY[KR]*RK[KR][i];
    }

    for (i=0;i<NDOF;i++)
        for (KR=0;KR<4;KR++){
            YN[i] = YN[i] + DT*RM[KR]*RK[KR][i];
            if (NSS==1)
                Y1[i] = YW[i];
            if (NSS==2)
                Y2[i] = YW[i];
        }

    TS = TS + DT;
}
return 0;
}```
main(void){
    //Start of Execution
    printf("Vascular Circuit Simulator\n");
    printf("Computational Mechanics Lab (CML)\n");
    printf("Cardiovascular Engineering Research Team (CERT)\n");
    printf("University of Central Florida\n");

    //Input Cardiovascular Parameters
    printf("Reading Input Parameters\n");
    Input();
    //Modify Cardiovascular Parameters if needed
    ResetInput();

    //loop over coupled iteration cycles
    int coupled_iter = 10; coupled_iter = coupled_iter++;
    while (coupled_iter) {
        //check to see if simulation is done writing files
        printf("Back to top of loop\n");
        FILE *t_file;
        do {
            t_file = fopen("C_ready.txt", "r");
            printf("Should have attempted to read C_ready.txt\n");
            if (t_file) {
                printf("Unable to read C_ready.txt\n");
                t_file = NULL;
            }
        } while (!t_file);
        sleep(30);
        printf("File C_ready.txt read\n");
        fclose(t_file);
        //Post-processing of CSV files from Starcon

        if (file_count > 1) {
            Input_CIV();
            Resistance();
            Inductance();

            //Adjusting bed resistance and inductance values
            R_MA_adj = (-1.0)*(R_MA_clean_ave - R_MA);
            R_SA_adj = (-1.0)*(R_SA_clean_ave - R_SA);
            R_LSA_adj = (-1.0)*(R_LSA_clean_ave - R_LSA);
            R_LPA_adj = (-1.0)*(R_LPA_clean_ave - R_LPA);
            R_LA_adj = (-1.0)*(R_LA_clean_ave - R_LA);
            R_CORA_adj = (-1.0)*(R_CORA_clean_ave - R_CORA);
            R_RPA_adj = (-1.0)*(R_RPA_clean_ave - R_RPA);
            R_RCA_adj = (-1.0)*(R_RCA_clean_ave - R_RCA);
            R_CORC_adj = (-1.0)*(R_CORC_clean_ave - R_CORC);
            R_IA_adj = (-1.0)*(R_IA_clean_ave - R_IA);

            //Adjusting Bed Resistance
            L_VLSB = L_VLSB_adj;
            L_VLSB = L_VLSB_adj;
            L_VLSB = L_VLSB_adj;
            L_VLSB = L_VLSB_adj;
            L_VLSB = L_VLSB_adj;
            L_VLSB = L_VLSB_adj;
            L_VLSB = L_VLSB_adj;
            L_VLSB = L_VLSB_adj;
    }
}
// Redefining Resistances and Inductances
R_DA = R_DA_clean_ave;
R_SA = R_SA_clean_ave;
R_LA = R_LA_clean_ave;
R_PA = R_PA_clean_ave;
R_LA = R_LA_clean_ave;
R_CORA = R_CORA_clean_ave;
R_RPA = R_RPA_clean_ave;
R_LA = R_LA_clean_ave;
R_RLA = R_RLA_clean_ave;
R_RIA = R_RIA_clean_ave;
R_LA = R_LA_clean_ave;
L_DUCTUS = L_DUCTUS_clean_ave;
L_DA = L_DA_clean_ave;
L_SA = L_SA_clean_ave;
L_LA = L_LA_clean_ave;
L_CORA = L_CORA_clean_ave;
L_RPA = L_RPA_clean_ave;
L_RLA = L_RLA_clean_ave;
L_RIA = L_RIA_clean_ave;
L_LA = L_LA_clean_ave;
L_CORA = L_CORA_clean_ave;
L_RLA = L_RLA_clean_ave;
L_RIA = L_RIA_clean_ave;
}

// Initialize System Matrices
for (i = 0; i < NODE; i++) {
    for (j = 0; j < NODE; j++) {
        A[i][j] = 0.0;
    }
}

// Open Solution File and Write Initial Solution

FILE *star_out_file; 
FILE *out_file;
out_file = fopen("File Location\NwwoodOut.dat","w");
if (out_file) 
    return 1;
fprintf(out_file,"%d %lf ", CNN, TE);
for (i = 0; i < NODE; i++)
    fprintf(out_file,"%s %s ", Y[i]);
fprintf(out_file,""
");

printf("Solving System of ODE's\n");

// Define parameters
TC = 60.0/1HR;
DTS = TC/NS;

// Define Variables for Star Input
double OA_OUT, RSA_OUT, LSA_OUT, RPA_OUT, LPA_OUT, LCA_OUT;
double K5_ratio = 1000.0/(1500.0*10000.0);
double R_PA_MIG = 0.000000000093;
double R_PA_MIG = 0.000000000093;
double Tot_Press_in;

// Star Start Only
//Loop Over Cardiac Cycles
for(n=1; n<Nc-4; n++){
    TI = 0.0;
}

//Loop Over Time Samples in Cycle
for(k=1;k<NS+1;k++){
    WU = (n+1)*WS + k;
    //Approximate Solution Using One Full Time Step
    NSS = 1;
    RRA();

    //Approximate Solution Using Two Half Time Steps
    NSS = 2;
    RRA();

    //Evaluate Approximation Errors to Adjust Time Step
    DTNIN = DTS;
    for(i=0;i<REDOF;i++){
        UN = (0.613*0.0)*fabs(Y2[i]-Y1[i]);
        DT = DTS*pow(ERAW/ER),0.2);
        if (DT<DTNIN)
            DTNIN = DT;
    }

    //Approximate Solution Using Adjusted Time Steps
    if (DTNIN < 0.8*DTS){
        NSS = 2*DTS/DTNIN + 1;
        RRA();
    }
}

//Advance Output Solution
TI = TI + DTS;
for (i=0; i<REDOF; i++)
    YC[i] = Y1[i];

//Write input tables for Starcan
if (n == Nc){
    star_out_file = fopen("File Location\Star_In_Arteries.csv","w");
    if (star_out_file == NULL) return 1;
    fprintf(star_out_file,"M1F,M2F,M3F,M4F,M5F,M6F,M7F,M8F,M9F,M10F\n",
            T1,OA_OUT,LSA_OUT,RCA_OUT,LCA_OUT,RPA_OUT,LPA_OUT,ACEA_OUT,LCPN_OUT,Te_Press_in);
    fclose(star_out_file);
}

    TE = TE + TC;
}
fclose(star_file);

//Copy Star_In_Arteries.csv to root directory in simulation
char command[255];
int result;
printf(command,\"copy %s %s\","File Location\Star_In_Arteries.csv","Remote File Location\Star_In_Arteries.csv");
result = system(command);
if ( result == 0 )
    puts(\"File Star_In_Arteries.csv successfully moved\n");
else
    perror(\"Error moving Star_In_Arteries.csv file\n");
printf("Sleeping for 10 secs to allow program to copy Star_In_Arteries file");
//Remove DirDone file
remove("File Location\DirDone.txt");

//Remove the C file
remove("File Location\C_ready.txt");

//Signal Starcom it is ready to begin simulation
printf("..........................Done\n");
file *StarReady_file;
StarReady_file=fopen("File Location\Star_Ready.txt","w");
if (!StarReady_file){
    printf("Cannot write StarReady file");
    getchar();
}
printf("StarReady_file","1");
fclose(StarReady_file);
REFERENCES


