BEAT RATE IMPLICATIONS ON THE FLUID DYNAMICS OF A 50 CC LEFT VENTRICULAR ASSIST DEVICE

A Thesis in
Bioengineering

By
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ABSTRACT

Although left ventricular assist devices (LVADs) have had success in assisting the failing heart, thrombus formation within these devices still limits their long term use. Research has shown that thrombosis in the Penn State pulsatile LVAD, on a polyurethane blood sac, is largely a function of the underlying fluid mechanics and may be correlated to wall shear rates below 500 s$^{-1}$. Given the variability in animal trial heart rates and systolic durations, it is useful to understand the fluid mechanics of pulsatile LVADs under these circumstances. Studies were performed on the Penn State pulsatile 50 cc LVAD to characterize shear rates in thrombolytic regions. Particle image velocimetry (PIV) was used to capture planar flow in the pump body for beat rates of 75-150 bpm and systolic durations of 38-50%. Shear rates were calculated along the lower device wall, with particular attention given to the uncertainty of the shear rate measurement at 12 and 35 µm/pixel magnifications. Spatial and temporal shear rate changes associated with data collection frequency were also investigated. The accuracy of the shear rate calculation increased by approximately 40% from 35 to 12 µm/pixel. In addition, data collection in 10 ms intervals was preferable over 50 ms to capture velocity fluctuations near the wall. Global flow shows little changes in flow pattern with increasing beat rate and systolic duration, with wall shear rates scaling by approximately the square of the average inlet velocity. These studies show that changes in in vivo operating conditions strongly influence wall shear rates within our device, and likely play a significant role in thrombus deposition. Refinement of PIV techniques at higher magnifications can be useful in moving towards better prediction of thrombosis in LVADs.
# TABLE OF CONTENTS

LIST OF FIGURES .................................................................................................................. vi

LIST OF TABLES ....................................................................................................................... x

ACKNOWLEDGEMENTS ........................................................................................................... xi

Chapter 1  Introduction .............................................................................................................. 1

1.1  Overview of the Penn State Artificial Heart Program ................................................. 4
1.2  Development of a Penn State 50 cc Device ................................................................. 6
1.3  Present Study ....................................................................................................................... 12

Chapter 2  Particle Image Velocimetry .................................................................................... 14

2.1  Particle Image Velocimetry System ............................................................................... 14
    2.1.1  Light Source .............................................................................................................. 15
    2.1.2  Optics .......................................................................................................................... 17
    2.1.3  Tracer Particles .......................................................................................................... 20
    2.1.4  Image Capture ............................................................................................................. 21

2.2  Image Processing .............................................................................................................. 24
    2.2.1  Pulse Separation ......................................................................................................... 24
    2.2.2  Cross Correlation ....................................................................................................... 25
    2.2.3  Vector Conditioning ................................................................................................... 27

Chapter 3  Methods ..................................................................................................................... 29

3.1  The Penn State 50 cc V-2 LVAD .................................................................................... 29
    3.1.1  Clinical and Experimental Devices .......................................................................... 30
    3.1.2  Pump Driver .............................................................................................................. 31
    3.1.3  Valves and Valve Orientation .................................................................................... 33

3.2  Mock Circulatory Loop .................................................................................................... 34
    3.2.1  Mock Circulatory Loop Components ....................................................................... 35
    3.2.2  Monitoring Systems .................................................................................................. 38
    3.2.3  Data Acquisition ....................................................................................................... 42

3.3  Blood Analog ...................................................................................................................... 43

3.4  PIV Techniques and Operating Conditions ..................................................................... 45
Chapter 4  Results and Discussion ................................................................. 49
  4.1 Wall Shear Rate Estimation ................................................................. 49
    4.1.1 Wall Identification and Zero Masking ........................................... 50
    4.1.2 Interrogation Region Velocity and Fluid Centroid Shift .................. 51
  4.2 Influence of PIV Magnification on Shear Rate Estimation ................. 55
  4.3 Temporal and Spatial Fluctuations with PIV Data Measurement .......... 61
  4.4 Beat Rate and Systolic Duration Global Flow Experiments .............. 72
    4.4.1 Early Diastolic Flow 7% into the Cardiac Cycle ......................... 73
    4.4.2 Mid Diastolic Flow 28% into the Cardiac Cycle ......................... 75
    4.4.3 Late Diastolic Flow 50% into the Cardiac Cycle ....................... 77
    4.4.4 Systolic Flow 78% into the Cardiac Cycle ................................... 79
  4.5 High Magnification Wall Shear Rate Calculation across Beat Rates and
    Systolic Durations .................................................................................. 81
    4.5.1 High Magnification Wall Shear Rate Calculation Along Wall B ....... 82
    4.5.2 High Magnification Wall Shear Rate Calculation Along Wall E........ 87
    4.5.3 High Magnification Wall Shear Rate Calculation Along Wall H ...... 91
    4.5.4 High Magnification Wall Shear Rate Calculation Along Wall K ...... 93
    4.5.5 High Magnification Wall Shear Rate Calculation Along Wall N ....... 96

Chapter 5  Conclusions .............................................................................. 100
  4.5.1 Summary of Findings ....................................................................... 100
  4.5.2 Future Work ..................................................................................... 102

Bibliography ............................................................................................... 104

Appendix A  Spatial Shear Rates at High Magnification .......................... 108

Appendix B  Beat Rate and Systolic Duration Flow Maps ....................... 116

Appendix C  High Magnification Wall Shear Rate Contour Maps ............. 129
LIST OF FIGURES

Figure 1-1: LionHeart left ventricular assist system (Mehta 2001) ........................................4
Figure 1-2: Original 50 cc V-0 design (Hochareon 2003b) ...........................................7
Figure 1-3: 3, 6, and 9mm planes studied with PIV (Hochareon 2003b) .........................8
Figure 1-4: Low flow regions of the 50 cc device 100 ms into diastole (Hochareon 2003b) .................................................................................................................................9
Figure 1-5: Mitral valve angles considered for the V-0 model (Kreider 2006b) ..............10
Figure 1-6: Five 50 cc design considerations (Wivholm 2008) ........................................11
Figure 1-7: Geometric changes of the three 50 cc device designs (Wivholm 2008) ...12
Figure 2-1: Diagram of a typical PIV setup (Raffel 1998) ...............................................15
Figure 2-2: Internal components of the laser head (New Wave Research 2000) .........16
Figure 2-3: Schematic of lightsheet optics (TSI 1999) ...................................................17
Figure 2-4: Schematic of the PIV laser, optics, and model configuration .....................18
Figure 2-5: SolidWorks sectional view of the acrylic model and PIV image at the 5 mm plane ..............................................................................................................................19
Figure 2-6: Inflow waveform with sample threshold and trigger delay .......................23
Figure 2-7: Peaks of the cross correlation function (Hochareon 2003b) .....................27
Figure 2-8: Insight 3G™ vector map and Tecplot 360 contour map ...........................28
Figure 3-1: Penn State 50 cc V-2 animal implant .........................................................30
Figure 3-2: Acrylic Penn State 50 cc V-2 model ...........................................................31
Figure 3-3: Relative CCD saturation of Teflon and PVC pusher plates ....................32
Figure 3-4: Inlet and outlet valve orientations (Kreider 2006a) ................................34
Figure 3-5: Mock circulatory loop ...............................................................................35
Figure 3-6: Compliance chamber ..............................................................................36
Figure 3-7: Resistance plates .................................................................37
Figure 3-8: Venous reservoir with mixing plate.................................38
Figure 3-9: Atrial and arterial pressure waveforms ..........................39
Figure 3-10: Inflow and outflow waveforms for 75 bpm (38% systolic duration).....41
Figure 3-11: LVDT waveform for low and high beat rates ..................42
Figure 3-12: Viscosity and elasticity curves for blood and blood analog .......45
Figure 3-13: 5 mm measurement plane ..................................................46
Figure 4-1: Insight 3G™ image illustrating the wall identification and zero masking techniques .................................................................51
Figure 4-2: Insight 3G™ image illustrating the considered velocities for the wall shear rate calculation .................................................................52
Figure 4-3: Insight 3G™ image illustrating the 10% interrogation region criteria...53
Figure 4-4: Insight 3G™ image illustrating the fluid centroid shift and vector transformation .................................................................54
Figure 4-5: Schematic of data collection sites for the mid and high PIV magnifications ..........................................................................................55
Figure 4-6: Flow maps 300 ms into the cardiac cycle for the mid and high PIV magnifications ..........................................................................................56
Figure 4-7: Wall shear rate plots for the mid and high PIV magnifications ........57
Figure 4-8: Shear rate calculations for 200, 350, and 500 ms of the cardiac cycle for the mid and high PIV magnifications ................................................60
Figure 4-9: Low and high shear zones for the temporal and spatial wall shear rate study ..........................................................................................62
Figure 4-10: Wall shear rate plots for the low wall shear zone .................63
Figure 4-11: Spatial wall shear rate plots 500-550 ms into the cardiac cycle for the low wall shear zone ........................................................................64
Figure 4-12: Spatial wall shear rate plots 300-350 ms into the cardiac cycle for the low wall shear zone ........................................................................65
Figure 4-13: Temporal wall shear rate plots for 10 ms data collection for the low wall shear zone ........................................................................66
Figure 4-14: Temporal wall shear rate plots for 50 ms data collection for the low wall shear zone .................................................................67

Figure 4-15: Wall shear rate plots for the high wall shear zone .......................68

Figure 4-16: Spatial wall shear rate plots for 50-100 ms into the cardiac cycle for the high wall shear zone .................................................................69

Figure 4-17: Spatial wall shear rate plots for 200-250 ms into the cardiac cycle for the high wall shear zone .................................................................69

Figure 4-18: Temporal wall shear rate plots for 10 ms data collection for the high wall shear zone ................................................................................70

Figure 4-19: Temporal wall shear rate plots for 50 ms data collection for the high wall shear zone ................................................................................71

Figure 4-20: Global flow maps 7% into the cardiac cycle for the beat rate and systolic duration study ........................................................................74

Figure 4-21: Global flow maps 28% into the cardiac cycle for the beat rate and systolic duration study ........................................................................76

Figure 4-22: Global flow maps 50% into the cardiac cycle for the beat rate and systolic duration study ........................................................................78

Figure 4-23: Global flow maps 78% into the cardiac cycle for the beat rate and systolic duration study ........................................................................80

Figure 4-24: Wall locations considered in the shear rate study along the lower LVAD wall at the 5 mm plane .................................................................81

Figure 4-25: Wall shear rates for 75, 115, and 150 bpm at a 1 mm location along wall B .........................................................................................83

Figure 4-26: Wall shear rates for 75, 115, and 150 bpm at a 4 mm location along wall B .........................................................................................84

Figure 4-27: Contour plots displaying wall shear rate calculations along wall B ......85

Figure 4-28: Normalized wall shear rates for 75, 115, and 150 bpm at a 1 mm location along wall B .........................................................................................86

Figure 4-29: Normalized wall shear rates for 75, 115, and 150 bpm at a 4 mm location along wall B .........................................................................................87

Figure 4-30: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall E .........................................................................................88
Figure 4-31: Contour plots displaying wall shear rate calculations along wall E ......89

Figure 4-32: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall E .................................................................90

Figure 4-33: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall H ..............................................................91

Figure 4-34: Contour plots displaying wall shear rate calculations along wall H .....92

Figure 4-35: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall H .................................................................93

Figure 4-36: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall K .................................................................94

Figure 4-37: Contour plots displaying wall shear rate calculations along wall K .....95

Figure 4-38: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall K .................................................................96

Figure 4-39: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall N .................................................................97

Figure 4-40: Contour plots displaying wall shear rate calculations along wall N ......98

Figure 4-41: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall N .................................................................99

Figure 5-1: Velocity line plot 10 mm along wall E for 64% of diastole at a 75 bpm heart rate and 38% systolic duration .........................................................103
LIST OF TABLES

Table 3-1: Geometric measurements of the V-2 design ...........................................29

Table 3-2: Average arterial and atrial pressure conditions with increasing beat rate and systolic duration.........................................................................................40

Table 4-1: Tangential velocity measurements for the mid and high PIV magnifications ..................................................................................................................59

Table 4-2: Vector distance from wall measurements for the mid and high PIV magnifications............................................................................................................59

Table 4-3: Average flow rates and inlet velocities for 75, 115, and 150 bpm heart rates.....................................................................................................................84
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Chapter 1

Introduction

Nearly 5.7 million Americans are afflicted with heart failure, with 670,000 new diagnoses being made each year (AHA 2010). The most common causes of heart failure are coronary artery disease, high blood pressure, and diabetes. While medication and dietary change can be solutions towards heart recovery, clinical interventions in the form of transplantation or circulatory support are sometimes necessary. Heart transplantation is a viable treatment for patients with end stage organ failure, although the availability of organs for transplant does not satisfy the current national demand. The number of total transplants performed in 2009 was approximately 2,200, a 2% increase from the previous year. The total number of donors was about 2,300. Despite the high rate of transplant success, an estimated 3,100 Americans remain on the waiting list. Of these, nearly 400 have been waitlisted for a period greater than 5 years (UNOS 2009).

Due to the lack of available heart donors, treatment in the form of ventricular assist devices (VADs) is desirable. VADs are circulatory support devices that reduce the overall workload of the heart by providing most of the pumping power, when the native heart’s cardiac output is insufficient. The left ventricle of the heart must work against larger systemic pressures than the right ventricle. Therefore, VAD replacement most often occurs on the left side of the heart in the form of left ventricular assist devices (LVADs). Typically, LVADs are used as bridge to transplant therapy while patients with advanced stage heart failure await a donor heart. More recently, however, these devices
have been used for bridge to recovery in conjunction with pharmacological therapy to recover myocardial function. Offsetting most of the pumping workload by the LVAD unloads the stress on the heart and, with proper drug delivery, may reverse pathological hypertrophy. Successful bridge to recovery weans a patient off of a LVAD and leads to full native heart function. This avoids the need for transplantation and as immunosuppression therapy is no longer a requirement, reduces the risk of failure. Bridge to recovery is becoming more realizable as evolving LVAD technology has led to decreased hemodynamic complications. Initial studies involving patients with cardiomyopathy showed survival rates of 78% five years after LVAD weaning and removal (Dandel 2005). Simon et al. further reported cardiac restoration in 8 of 10 patients 1 year after LVAD explantation (Simon 2005). While bridge to recovery has shown promise, clinical predictors of recovery and long-term success remain to be seen. Although the debate over therapy options is ongoing, early reports suggest equivalent survival rates of patients bridged to transplant versus those that recovered native heart function after LVAD use (Farrar 2001).

As LVAD engineering advances, their use for long term or permanent support becomes more likely. In treatment known as destination therapy, a VAD replaces the natural pumping function of the heart for patients with chronic heart failure that are either ineligible for heart transplantation or are severely compromised and cannot await transplantation. The REMATCH study involving 129 patients and 20 cardiac transplant centers reported one and two year survival rates of 52% and 23%, respectively, under destination therapy. The improved quality of life for patients with prolonged periods of
implantation justifies LVAD use as long term support, however, complications such as infection, thrombosis, hemolysis, thromboembolism, and mechanical failure still hinder their practicality (Birks 2010).

In moving towards a sensible solution for these problems, various pulsatile and continuous-flow LVAD designs have been proposed. As an implant, pulsatile volume displacement pumps provide appropriate hemodynamic support while mimicking the heart’s natural rhythmic beating, yet their size tends to preclude their use for small patients. High infection rates, limited long term durability, audible pump operation, and drivelines puncturing the skin furthermore reduce the use of pulsatile LVADs. However, a Penn State 70cc electric device (LionHeart) using transcutaneous energy transfer (TET) has shown success as a fully-implantable system and is shown in Figure 1-1. Axial flow devices are becoming more popular for their reduced size and less invasive surgical implantation. These devices do not require the use of prosthetic heart valves as do pulsatile LVADs, and their smaller drivelines may reduce incidences of infection. Despite this, outlet graft placement associated with axial pumps has led to issues with stasis and clot formation in the aorta (Haj-Yahia 2007). Lastly, continuous flow devices using hydrodynamic suspension or magnetic levitation are under development to reduce mechanical wear and contact forces leading to increased durability (Birks 2010). While minimizing blood-contacting forces has resulted in reduced levels of hemolysis, the long-term benefit of these devices remains to be seen.
1.1 Overview of the Penn State Artificial Heart Program

Considerable effort has gone into the development of a range of Penn State LVADs, from 100, 70, and 50 cc adult to 12cc pediatric devices, over the past 4 decades. Since the first Penn State LVAD implantation at Hershey Medical Center in 1976 (Gaines 1985), advances have been made in the development of pneumatic and pusher plate driven devices that assist or replace the function of the native heart. With the combined efforts of Penn State and Arrow, the 70cc LionHeart was in clinical trials by 2001 (Mehta 2001).

The LionHeart, shown in Figure 1-1, is a positive displacement blood pump composed of inlet and outlet cannulae, a motor controller, a compliance chamber, and an energy transmission system. Its unique transcutaneous power system allows for increased patient mobility and decreased infection rates as no drivelines break the skin.

Figure 1-1: LionHeart left ventricular assist system (Mehta 2001).
LionHeart is implanted by connecting the inlet cannula to the apex of the left ventricle, rerouting blood to the systemic circulation through an end-to-side anastomosis at the descending aorta. The 3.2 pound fully implantable system operates under passive filling conditions so as to not disrupt the natural homeostasis of the cardiovascular system. To account for physiologic demands, the motor controller adjusts the timing of the pusher plate as a function of the end diastolic volume. When complete filling occurs, the polyurethane blood sac contacts the pusher plate signaling the beginning of diastole. Changes in filling times from beat to beat are sensed by the pusher plate and the systolic/diastolic durations of the stroke adjust to keep up with cardiac requirements. A compliance chamber is included to adjust for changes in gas volume that occur during pusher plate movement (Mehta 2001).

While the LionHeart advanced to clinical trials, concerns over pump thrombogenicity and hemolysis were still important. The potential for thrombus formation and hemolysis has been associated with the blood material interface, the surface topography, and the fluid mechanics within the device (Deutsch 2006). The fluid mechanics suggest that thrombosis is likely to occur in areas of low wall shear stress. The most thorough of fluid mechanic investigations within the 70cc device was done by Baldwin et al., in which laser doppler anemometry measurements showed shear stresses within the body of the pump on the range of 300-500 dynes/cm² (Baldwin 1988). Previous studies by Hubbell and McIntire suggest that shear rates above 500 s⁻¹ (approximately 20 dynes/cm²) inhibit thrombus growth and platelet adhesion on polyurethane (Hubbel and McIntire 1986). Studies involving the LionHeart have shown
thrombus occurring within specific areas of the pump housing, suggesting that further fluid mechanic analyses may be relevant (Richenbacher 1986).

While maintaining sufficient wall washing within an LVAD is necessary to prevent thrombosis, high wall shear rates may result in cell lysis. It has been shown that the level of hemolysis within LVADs is a product of both the magnitude of shear stress and exposure time. Sallam and Hwang showed that exposure times on the order of 1 ms can damage red blood cells for turbulent stresses of 4,000 dynes/cm$^2$ (Sallam and Hwang 1984). On the other hand, prolonged exposure to laminar stresses around 1,500 dynes/cm$^2$ may cause red cell damage (Nevaril 1969). The development of an LVAD with an appropriate range of stresses is critical in all aspects of pump design.

1.2 Development of a Penn State 50 cc Device

While the 70cc device is suitable for patients with large circulation volume, particularly patients weighing between 60-100 kg, the device is too large to be implanted in those with limited chest space. In order to accommodate smaller patients in need of an LVAD, a 50 cc device was created. The original design of the 50 cc device (model V-0) can be seen in Figure 1-2. Extensive efforts have gone into characterizing the level of thrombus formation within the 70cc device, and relating these levels to the fluid dynamics of the device. While LionHeart clinical implants have shown little clot deposition, geometric scaling of this device to a 50 cc pump has not shown the same level of success.
Yamanaka et al. performed a thirty-day *in vivo* study of the 50 cc LVAD to quantify the level of clot deposition within the device (Yamanaka 2003). While thrombi formed along many regions of the polyurethane blood sac, the majority of clots were attached to the back of the diaphragm and along the bottom of the device. To more fully understand the reason for clot deposition at these sites, flow studies focused on areas within the pump that displayed recirculation, high blood residence time, and low wall shear rate, as these flow regimes are associated with both platelet aggregation and thrombus deposition (Turitto 1998). The first *in vitro* study of 50 cc thrombolytic regions was conducted by Hochareon et al. with the use of particle image velocimetry (PIV), the LVAD, and a mock circulatory loop simulating the native cardiovascular system (Hochareon 2004a). Planes 3, 6, and 9 mm from the front LVAD edge, as shown in Figure 1-3, were studied over the entire pump cycle.
These results showed low wall shear rates, on the order of 250 s\(^{-1}\), along the bottom portion of the diaphragm for over 300 ms of the cardiac cycle. In order to more accurately measure the wall shear rates within the 50 cc LVAD, a high magnification PIV approach at 10 µm/pixel was carried out. These results further supported the likelihood of clot deposition in the lower area of the device, by showing that low wall shear zones were present throughout most of the cycle in the regions of reported clot deposition by Yamanaka \textit{et al.} (Yamanaka 2003). In particular, the PIV data showed low flow at the lower device wall as shown in Figure 1-4.

Figure 1-3: 3, 6, and 9 mm planes studied with PIV (Hochareon 2003b).
Should blood reside in these regions for extended periods of time, protein adsorption may occur at the wall which is known to heavily influence platelet adhesion (Ryu and Kim 1993). In addition, platelets activated by high stresses in valve regions may accumulate in these low flow areas and further influence coagulation (Bluestein 2004).

Kreider et al. considered the effects of mitral valve orientation on the development of the flow, particularly the initial formation of the diastolic jet, within the 50 cc V-0 device (Kreider 2006a). Bjork-Shiley Monostrut (BSM) (Shiley, Inc., Irvine, CA) valves with pyrolytic carbon (PC) occluders were considered. The significance of the diastolic jet’s ability to wash the walls of the device throughout the cardiac cycle was of particular interest. Kreider et al. showed that rotating the mitral valve through four orientations (0°, 15°, 30°, and 45° [Figure 1-5]) in the housing altered the flow penetration to the bottom wall where thrombosis is thought to occur. Kreider et al.
concluded that the 30 and 45° rotations not only produced the highest velocities in thrombus-prone regions, but also increased the duration of wall washing compared to other valve angles (Kreider 2006a).

![Diagram showing mitral valve angles considered for the V-0 model](image)

**Figure 1-5**: Mitral valve angles considered for the V-0 model (Kreider 2006b).

While the higher valve angles produced better flow characteristics within the LVAD, the potential for clotting, based on the wall shear rate, was still possible. In order to minimize the level of thrombus formation within the device, the model was modified (version V-1, Figure 1-6) by rounding the back edge of the model, lengthening the chamber depth, and angling the inlet and outlet ports towards the perimeter walls of the chamber. These modifications were made with the intent of further directing flow toward the walls to wash regions of the pump previously susceptible to thrombosis. Wivholm provided an analysis of three further device iterations, all shown in Figures 1-6 and 1-7 (Wivholm 2008). These pumps, designated V-2, V-3, and V-4, were created to help understand the relationship between geometric changes to the pump and the fluid mechanics within the device. All three devices are geometrically similar with the
exception of the port angles and locations. V-2 has both ports located the same distance from the center of the device with no relative rotation to one another. V-3 has an outlet port that is rotated away from the inlet of the pump and is lower in the device housing. This modification was made to help force the fluid out of the device and minimize the amount of time the fluid has to circulate within the pump body. In V-4, the outlet port is shifted to the center of the device to improve rotational washing within the device.

Results of this work showed that the outlet flow for V-3 exited the VAD approximately 50 ms earlier than did flow in the V-2 and V-4 models, although low flow regions between the inlet and outlet ports were identified due to decreased rotational flow throughout the cardiac cycle. On the other hand, V-4 displayed an extended rotational flow, but diminished washing between chamber ports remained a concern for thrombosis. Due to the uniformity of rotational flow and extended wall washing in the V-2 model, this device was chosen as the best model to consider in moving towards further research (Wivholm 2008).

Figure 1-6: Five 50 cc design considerations (Wivholm 2008).
1.3 Present Study

While substantial effort has gone into characterizing flow and wall shear in the 50 cc device, most of this work has been performed under operating conditions that are physiologic for an adult patient. Animal (calf) studies, however, have shown large fluctuations in beat rate and systolic/diastolic duration over the course of the implant, with all adjustments were made by the artificial heart controller in order to maintain sufficient cardiac output to the animal. Since these animal trials are used as models in predicting thrombosis in human implants, fluid mechanic analyses of these operating conditions are important. Jarvis et al. showed that increases in heart rate had a positive correlation with blood damage in the 100cc device (Jarvis 1991). This was verified through the presence of increased levels of free hemoglobin, platelet count, and beta-thromboglobulin in the blood after device explantation, all factors commonly attributed to hemolysis.
Oley et al. explored the effects of off-design operation of the 50 cc V-0 model, primarily focusing on the fluid dynamic changes within the device under altered beat rate and the resulting potential for thrombus formation (Oley 2005). Studies were performed at beat rates of 60, 75, and 90 beats per minute (bpm) at 35% systolic duration and 75 bpm at 50% systolic duration. The higher heart rate (90 bpm) yielded higher velocities in the diastolic jet and further penetration towards the bottom chamber wall. Increased systolic durations had a similar effect as the decrease in pump filling time increased washing along the bottom wall of the device. While increasing heart rate and decreasing diastolic duration likely reduced the level of flow stasis and clot formation in the bottom region of the pump, separation along the inlet wall was of particular concern. Geometric changes within the 50 cc V-2 model were made to lessen this flow separation.

While previous investigations have observed flow changes within older 50 cc designs under varying operating situations, little has been done to explore these effects in the V-2 device. Animal testing of this pump has shown that animal heart rates range between 90 and 180 bpm with systolic durations of 38-50%. The objectives of this study are to mimic these conditions in an in vitro setting and characterize the overall flow patterns and wall shear rates with PIV. Particular attention is given to the accuracy of the shear rate calculation and the necessary frequency of data collection with high magnification PIV.
Chapter 2

Particle Image Velocimetry

2.1 Particle Image Velocimetry System

Particle image velocimetry (PIV) is a non-invasive flow visualization technique capable of accurately measuring fluid velocities. It is an attractive diagnostic for artificial heart and VAD experimentation as it allows for flow measurement within devices over a relatively large spatial domain with appropriate time resolution. Three-dimensional (stereo, 3D) and two-dimensional (2D) PIV diagnostics are commercially available. Our focus is on 2D PIV as this is the system used for this study. A typical PIV system is shown schematically in Figure 2-1. A laser head directs two consecutive light pulses, separated by a time delay, $\Delta T$, through a series of optics which convert the circular beams into light sheets. These light sheets are then reflected by a dichroic mirror and focused within the model to a plane of flow interest. The fluid flowing through the model is homogenously seeded with particles that faithfully follow the flow field. Illumination of these particles within the light plane allows for a charge-coupled (CCD) camera to capture two particle field images within a user-specified $\Delta T$. Post-processing techniques segment these images into smaller interrogation regions (IRs), and displacements of particle groups, obtained from correlation analysis, from one image to the next are measured. By dividing the displacement of these particle groups over the known time separation, fluid velocities are determined within the 2D flow field.
2.1.1 Light Source

The selection process for a PIV laser typically involves two laser types, neodymium-doped yttrium aluminum garnet (Nd:YAG) and argon-ion lasers. The main difference in laser operation is energy output. Nd:YAG lasers are capable of delivering very high-energy laser pulsations on the order of 120 mJ with a 5-10 ns pulse width. In contrast, argon-ion types are continuous wave lasers that are far-less energy efficient and require the added use of a modulator or optical chopper to facilitate beam separation. The process by which Nd:YAG lasers produce high pulse energies is known as Q-switching and is a result of pumping large amounts of energy into the laser medium prior to emission. Due to its high efficiency, a frequency-doubled, pulsed Nd:YAG laser, part
of a Gemini PIV 15 system (New Wave Research, Inc., Fremont, CA) is used here (Figure 2-2). This dual head system outputs two temporally-separated 1064 nm infrared laser beams that are directed to a polarizer assembly where their energies are combined into a single output. After passing through a second-harmonic generator (SHG), the coupled lasers are polarized at a 532 nm wavelength in the visible spectrum (green). The output of the SHG focuses the beam onto dichroic mirrors which redirect any remaining 1064 nm energy to metal absorbers, and transmit the 532 nm energy to an optical attenuator. This attenuator is user-controlled through a potentiometer to regulate the energy that exits the laser shutter.

Figure 2-2: Internal components of the laser head (New Wave Research 2000).
2.1.2 Optics

Upon emission from the laser head, the 6 mm circular laser beam is directed to cylindrical and spherical lenses to condition the light into a thin sheet. This procedure is illustrated in Figure 2-3.

Figure 2-3: Schematic of lighsheet optics (TSI 1999).

The focal length of each lens determines the height and thickness of the sheet and is selected to optimize PIV imaging for a particular geometry.

A spherical lens producing a thicker light sheet will illuminate particles moving through the depth of the light sheet volume. This introduces perspective projection errors that bias the 2D velocity measurement to lower values (Raffel 1998). While lenses producing thinner light sheets mitigate this, they also reduce light sheet intensity. Thinner light sheets are associated with larger cross-sectional areas in which light
intensity is spread throughout. If intensity is insufficient, light scattering from particles may be too low to be detected by the CCD camera. For this study, a balance between thickness and intensity is satisfied with a 25 mm cylindrical and 500 mm spherical lens producing a light sheet 200 µm thick. The acrylic model is positioned within the light sheet waist for the best PIV imaging. The laser, optics, and model arrangement are shown in Figure 2-4.

Figure 2-4: Schematic of PIV laser, optics, and model configuration.

Alignment of the light sheet is essential to collect PIV data accurately at a known location within the model. This is accomplished by mounting the optics on a Newport 443 Series Low-Profile, Ball Bearing Linear Stage (Newport Corporation, Irvine, CA).
The stage allows movement of the light sheet in 10 μm increments through the depth of the model. The light sheet is vertically aligned with the edge of the model, and in the remaining two directions by making sure its reflection from the acrylic overlaps on the spherical lens. Proper alignment is ensured by visually comparing SolidWorks (3D CAD Design Software, Concord, MA) section drawings of the acrylic model to PIV images at a given plane as shown in Figure 2-5.

Figure 2-5: (A) SolidWorks sectional view of acrylic model and (B) PIV image at the 5 mm plane.
2.1.3 Tracer Particles

The measurement of particle displacements in a fluid over time determines the PIV velocity calculation. Therefore, fluid velocities are indirectly calculated from particle velocities. In order for an accurate measurement, particle selection is based on three criteria. The first is to select particles small enough to follow the flow. By using the Stokes number, a dimensionless parameter corresponding to the behavior of particles suspended in a fluid, estimates on particle lagging may be made. The Stokes number is derived from the Navier-Stokes equations and is a function of particle diameter, \( d \), particle density, \( \rho \), dynamic viscosity of the fluid, \( \mu \), and the pulse separation for PIV, \( \Delta T \). It is defined as

\[
St = \frac{d^2 \rho \rho_{particle}}{18 \mu_{fluid} \Delta T_{PIV}}.
\]

To ensure that particles effectively follow fluid motion in PIV applications, Crowe showed that the Stokes number must be \( <<1 \) (Crowe 1998).

The largest reductions in the Stokes number are accomplished by minimizing particle diameter. In doing so, however, the second criteria \( i.e., \) the light scattering efficiency of particles, may be compromised. The CCD camera requires sufficient light scattering for a valid detection. Particles were selected to meet both of these requirements and are 10 \( \mu \)m hollow glass spheres (Potters Industries, Inc., Valley Forge, PA). These particles result in a Stokes number that is always less than 0.058 when
seeded in a sodium iodide solution with a pulse separation larger than 25 µs, the minimum ΔT used in this study.

One final particle criterion is concentration. Provided that in and out of plane particle loss is negligible, reliable velocity measurements require that at least 5 particles exist per IR (Raffel 1998). Keane and Adrian showed that at this particle number, valid detection probability exceeds 95% (Keane and Adrian 1992). Increasing particle numbers well above this may lead to laser attenuation and excessive scattering that saturates the CCD camera. Particle counts less than this increase the measurement uncertainty and decrease the signal strength. Efforts were made to maintain particle densities between 5-12 particles per IR at all magnifications.

2.1.4 Image Capture

A two megapixel CCD camera (Model 630057 PowerView Plus, TSI, Inc., Shoreview, MN) with a Nikon 50 mm F1.8 lens (Nikon Corporation, Tokyo, Japan) was used for image acquisition. The CCD is an array of semiconductor gates that collect, store, and transfer charge. Each individual gate, represented by a pixel, measures the level of optical brightness reflected from tracer particles for two temporally separated images. The CCD chip has a pixel resolution of 1600 x 1200 with a 7.4 µm/pixel square spacing. The gate intensities for each image undergo photoelectric conversion and are sent as an electrical signal to a frame grabber in the attached PC. The frame grabber digitizes this signal and produces an image pair viewable by a liquid-crystal display.
(LCD) screen. CCD cameras are capable of collecting data at frame rates of 32 frames per second while maintaining high resolution.

The camera is mounted on three traverses for positioning and the lens edge is aligned parallel to the light sheet. Laser pulsing and image capture are coordinated through a LaserPulse Synchronizer (Model 610035, TSI, Inc., Shoreview, MN). The synchronizer interfaces with a trigger and delay box built by the Applied Research Laboratory at Penn State. The trigger box allows the user to collect data at specific phases of the cardiac cycle by setting a delay based on the inflow waveform described in Section 3.2.2. A threshold level on the rising portion of the inflow waveform is set by a potentiometer. The trigger box then produces a second signal that may be delayed from this threshold in 0.1 ms increments. A specified number of image pairs are then captured at this trigger delay through coordination with the synchronizer. The threshold and trigger delays are displayed on an oscilloscope (Model TDS210, Tektronics, Inc., Beaverton, OR). A sample trace is displayed in Figure 2-6.
The synchronization of camera exposure and laser emission for a set of images is controlled through Insight™ 3G software (TSI, Inc., Shoreview, MN). A frame straddling mode is used to fire both laser pulses for consecutive image exposures. The first laser pulse occurs at the very end of the first camera exposure, and the second pulse at the onset of the second exposure. This technique allows short time intervals between pulses which increases the ability to measure higher fluid velocities. Images are calibrated by aligning the light sheet on an object of known dimensions and measuring the number of pixels occupying that geometry.

Figure 2-6: Inflow waveform with sample threshold and trigger delay.
2.2 Image Processing

After all images are collected, an Insight™ 3G processing algorithm measures the displacement of the tracer particles over the pulse separation to obtain fluid velocities. This velocity measurement has a spatial resolution dependent on the size of the IRs within the image. Each image pair (1600 x 1200 pixels) is divided into smaller IRs that are 32 x 32 pixels in size, for example. A spatially averaged velocity within each region is determined through a statistical cross correlation technique (described in detail in Section 2.2.2). The end result is a velocity vector applied to the center of each region within an image pair.

2.2.1 Pulse Separation

The laser pulse separation determines the time between consecutive laser pulses and is chosen on the basis of flow velocities. The $\Delta T$ must be long enough to allow for sufficient flow movement from one frame to the next to resolve particle displacements. Christensen reported that particle displacements should be more than one pixel to minimize the incidence of peak-locking in which sub-pixel particle displacements are biased toward zero velocity values (Christensen 2004). The $\Delta T$ should be controlled to produce displacements of at least two pixels when possible. Areas of probable peak-locking may be analyzed by plotting histograms of particle displacements. Several peak estimators exist that minimize the effects of peak locking with a convolution function specific for small particle sizes. While the $\Delta T$ must be high enough for sufficient displacements, it should also be small enough to minimize the number of particles
entering and exiting an IR. The appropriate pulse separation for a given region of the 50 cc V-2 device is not trivial. The pulsatile nature of the device inherently has regions of high and low flow that are visible in a single PIV image. This leads to areas requiring a range of $\Delta T$’s for accurate measurement. The three-dimensionality of the device further complicates the ability to assign an appropriate $\Delta T$ due to particles moving into and out of the light plane. Also, near wall measurements necessary for wall shear rate calculations must be conducted within the boundary layer. These regions of flow contain large velocity gradients requiring both high and low $\Delta T$’s to satisfy the variety of particle displacements. Standard rules for optimizing PIV data collection are to ensure that in-plane displacements are less than one-fourth the interrogation spot size, and that maximum out-of-plane displacements are less than one fourth of the light sheet thickness. Adhering to these rules minimizes the degree of prospective projection and results in accurate in-plane velocity measurement. Pulse separations between 25-1000 $\mu$s were used here to satisfy these conditions.

2.2.2 Cross Correlation

The general technique for cross correlation involves finding a velocity in each region through a convolution function. This function uses a pattern recognition method to observe changes in particle patterns from one frame to the next. The sum of the differences in particle location between frames determines the correlation peak. A high quality correlation is represented by minimal differences between two particle patterns and is observed as a single correlation peak as shown in Figure 2-7. False correlations
are represented by smaller correlation peaks as a result of fewer particle pairs being recognized in the convolution. A signal-to-noise ratio (SNR) compares the height of the highest peak to the average peak height. The SNR within each IR must be above a certain threshold for a valid vector to be applied to that region.

The Insight\textsuperscript{TM} 3G correlation method used here has a fast Fourier transform (FFT) correlation engine, with a Gaussian peak detection algorithm, on a recursive Nyquist grid. The correlation works by calculating a 2D FFT for each IR in both image frames. FFT’s for identical regions of separate frames are then multiplied together resulting in a FFT conjugate. The inverse FFT of this conjugate is computed to form the correlation plane in which valid correlation peaks are established and velocity calculations are made (Gilbert 2003). The recursive nature of the grid further divides each IR into smaller sub-regions and correlates them in the same manner. Velocities from the initial correlation are used as a guide in determining velocities in the smaller IRs. This iterative method for measuring velocities not only strengthens the overall correlation, but increases the spatial resolution of velocity vectors. Final vector density is also enhanced by a 50% overlap criteria in which each IR is shifted to the spatial domain of the four adjacent ones. Starting window sizes were 64 x 64 pixels with final dimensions of 32 x 32 pixels for the studies here.
2.2.3 Vector Conditioning

Once the correlation and velocity vectors are calculated, an Insight\textsuperscript{TM} 3G filter is applied to interpolate data in regions where false vectors are observed. This vector validation conditioner compares the median values of the U and V velocity components for a given IR with those of a surrounding 3x3 IR perimeter. If the velocities in these IRs are similar in magnitude and direction, invalid vectors are replaced by the median value of the neighboring velocities. The resulting image is a vector field with green arrows representing valid velocities, and red vectors indicating invalid velocities. These vector maps were converted into contour flow plots for better illustration with Tecplot 360 (Tecplot, Inc., Bellevue, WA) software (Figure 2-8).

Figure 2-7: Peaks of the cross correlation function. The high intensity multi-colored peak indicates a valid correlation (Hochareon 2003b).
Figure 2-8: (A) Insight™ 3G vector map with green arrows indicating valid counts and red arrows invalid counts. (B) Corresponding Tecplot 360 contour plot.
Chapter 3

Methods

3.1 The Penn State 50 cc V-2 LVAD

Comparisons of flow studies in the five models of the 50 cc LVAD, presented in Figure 1-6, showed that the V-2 design introduces a more favorable rotational flow, with less separation along the walls of the device. The geometry of the device is similar to V-1, with the port dimensions and pusher plate size being identical. The main geometric modification to the device is in the curvature of the front wall. V-2 preserves the cylindrical chamber and flat front wall, as in device V-0, in contrast to the curved wall of V-1 (Figure 1-6). The inlet and outlet ports of V-2 are parallel to one another as in V-1, and the connection between the ports and the blood sac is tapered to provide a smoother flow transition between the ports and body. Inlet and outlet ports of the device are placed proximal to the blood sac to set up the rotational flow pattern more quickly. The dimensions of V-2 are given in Table 3-1.

Table 3-1: Geometric measurements of the V-2 design.

<table>
<thead>
<tr>
<th>V-2 dimensions</th>
<th>Mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>chamber radius</td>
<td>33.5</td>
</tr>
<tr>
<td>pusher plate radius</td>
<td>31.75</td>
</tr>
<tr>
<td>chamber depth</td>
<td>23.24</td>
</tr>
<tr>
<td>end systole depth</td>
<td>3.8</td>
</tr>
<tr>
<td>inlet port diameter</td>
<td>19.5</td>
</tr>
<tr>
<td>inlet valve size</td>
<td>23</td>
</tr>
<tr>
<td>outlet port diameter</td>
<td>17.7</td>
</tr>
<tr>
<td>aortic valve size</td>
<td>21</td>
</tr>
</tbody>
</table>
3.1.1 Clinical and Experimental Devices

The clinical blood pump used in animal studies is constructed out of a titanium outer casing as shown in Figure 3-1. The pump houses an electric DC motor which powers a roller screw attached to a pusher plate. A micro-controller synchronizes the reciprocating motion of the pusher plate based on the end-diastolic volume. The controller’s timing algorithm ensures complete pump filling and ejection by altering the systolic duration with changes in the inlet pressure. The pusher plate contacts a polyurethane blood sac that lines the entire inside of the device and is the main blood-contacting surface. Two BSM valves at the inlet and outlet ports maintain unidirectional flow through the device.

Figure 3-1: Penn State 50 cc V-2 animal implant.

In order to study the fluid mechanics within the device in an *in vitro* setting, optical access within the model is necessary. For this reason, a model of the clinical
device was machined out of optically clear acrylic with an index of refraction of 1.49. The device houses a polyurethane diaphragm rather than a complete blood sac to allow optical measurements to be made. The diaphragm is not attached to the pusher plate to more closely approximate the sac motion in vivo (Hochareon 2003a). The complete acrylic device is shown in Figure 3-2.

3.1.2 Pump Driver

A Superpump, positive displacement piston system comprised of a head, amplifier, and ViViGen Waveform Generator (StarFish Medical, Victoria, B.C.) is used to set up the overall flow within the device. The pulsatile nature of flow is established through the reciprocating motion of a polyvinyl chloride (PVC) pusher plate attached to a piston shaft. The pusher plate is constructed out of dark PVC rather than the white
Teflon used in previous Penn State flow studies. This modification was made in order to reduce the saturation of the CCD chip during portions of the cardiac cycle. Any saturation at edges of the pusher plate may extend into the near wall fluid regions thus hindering the ability to make shear rate calculations. Figure 3-3 shows the reduction in CCD saturation when data is taken in the same location of the V-2 device with the two different pusher plate materials.

![Figure 3-3: Relative CCD saturation of (A) Teflon and (B) PVC pusher plates.](image)

To mimic the movement of the pusher plate in animal trials, the Superpump’s fully programmable operating system pulses the plate in a sinusoidal fashion, highly similar to that of the implant. The ViViGen software can accurately set beat rate, systolic duration, and stroke length in order to further simulate the settings observed *in vivo.*
The Superpump is positioned in line with the acrylic model and both are fixed to a breadboard to ensure a fixed relative position of the pusher plate to the model. A stroke length of 15 mm, allowing for complete filling and ejection of the pump, is accounted for through an adjustable amplitude control. At the end of a single stroke (end systole), the pusher plate comes to within 3.8 mm of the front wall of the device. Both the stroke length and distance of the pusher plate to the wall are maintained within the animal studies for consistency.

3.1.3 Valves and Valve Orientation

BSM tilting disk valves are used in this study. The valve housing is Stellite and two different occluder materials, PC and Delrin, were considered. The 23 mm inlet (mitral) and 21 mm outlet (aortic) valves were stripped of their suture rings to allow for easy mounting within the acrylic model. The valves were seated in Teflon casings and fixed within the pump ports to provide a smooth flow transition from the device body to the circulatory loop. Teflon rings placed around the valve housing prevent any backflow around the outer housing edge. Valve orientations, previously studied by Kreider, showed strong rotational flows at 30° and 0° for the inlet and outlet valves, respectively (Kreider 2006a). Valve orientations are shown in Figure 3-4. The inlet valve was rotated 30° from the horizontal axis of the device towards the front and outer wall of the inlet port to provide early onset of rotational flow that continues well through late diastole. The outlet valve is situated with the rear strut parallel to the front wall of the device and the major orifice opening towards the outer wall of the outlet port.
3.2 Mock Circulatory Loop

Efforts to match the experimental conditions of the animal studies are accomplished with a mock circulatory loop. Originally designed by Rosenberg, this system simulates the fundamental elements of the native cardiovascular system through a venous reservoir, atrial and arterial compliance chambers, and a resistance plate, all connected by Tygon tubing and incorporated with the acrylic model (Rosenberg 1972). Capable of holding approximately five liters, the mock vasculature, shown in Figure 3-5, mimics essential physiologic conditions needed to test and validate the pumping performance of the V-2 50 cc LVAD.
3.2.1 Mock Circulatory Loop Components

Two chambers, one shown in Figure 3-6, located upstream and downstream of the acrylic model, are integrated into the circulatory circuit to mimic the physiologic compliance of the native cardiovascular vessels. These structures, in their natural state, experience a wide range of pressures requiring them to stretch. The ability of the vessels to distend and increase their volume with increased pressure is known as compliance, and may be mathematically described as

\[ C = \frac{\Delta V}{\Delta P} \]

It is well known that at low pressures the venous compliance is much larger than the arterial compliance, but at increased pressures and volumes venous compliance and arterial compliance are similar. In attempts to mimic this response, the compliance
chambers in the mock loop are constructed out of variable volume cylinders with flexible rods attached to a piston-like shaft. The compliance can be altered by adjusting the fulcrum location of two vertical metallic blocks, or the thickness of the flexible rod. In general, a stiffer rod is used to account for the greater pressures of the arterial circulation. Both compliance chambers allow flow through one inch inlet and outlet tubing. Pressure taps, inserted into the chambers, measure the changes in fluid pressure throughout the cardiac cycle.

Figure 3-6: Compliance chamber.

Another factor associated with the distension of blood vessels is resistance to flow. Changes in vessel size are the main way the human body regulates blood flow. Quantitatively, the resistance of blood flow through the cardiovascular system is often modeled by Poiseuille’s equation

\[ R = \frac{8\mu L}{\pi r^4}. \]
Therefore, the three primary factors that contribute to flow resistance within the vessels are vessel radius, vessel length, and blood viscosity. Of the three, vessel radius is the most influential in producing changes in resistance. Physiologically, this is accomplished by contraction and relaxation of the smooth muscle in the wall of the vessel. Experimentally, changes in resistance are achieved through compressing tubing between two rigid plates (Figure 3-7) that are located between the arterial compliance and venous reservoir. While changes in compliance can be used to raise or lower arterial pressures within the circulatory loop, adjustments in plate resistance are the easiest way to achieve physiologic levels.

Figure 3-7: Resistance plates.

The venous reservoir (Figure 3-8), located just upstream of the atrial compliance, is the final component of the circulatory loop. This reservoir, designed specifically to promote mixing of particle seeding, supplies a hydrostatic pressure to the atrial
compliance while maintaining a consistent fluid level height. To provide a homogenous particle distribution within the fluid, the reservoir sits atop a mixing plate (Fisher Scientific, Vernon Hills, IL) that rotates a magnetic stir bar within the fluid. A user adjustable knob controls the stir bar’s rate of rotation.

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Figure 3-8: Venous reservoir with mixing plate.

---

3.2.2 Monitoring Systems

Pressure transducers (Argon Medical Devices, Athens, TX) were used to measure venous and arterial pressures during systole and diastole for all heart rates. Changes in pressure are sensed through the deformation of a diaphragm that is measured by a strain
A gauge element. Measurements were taken at the height of the compliance chambers through a pressure tap such that readings were representative of the inlet and outlet pressures of the LVAD. A calibration curve was established over physiological ranges using a pneumatic transducer tester (Model DPM 1B, Bio-Tek Instruments, Inc., Winooski, VT) and universal pressure meter (Model DPM-II, Bio-Tek Instruments, Inc., Winooski, VT). Arterial pressures were set at 120/80 mmHg and venous pressures at 30/5 mmHg at the lowest beat rate. Sample pressure waveforms are given in Figure 3-9.

![Atrial and arterial pressure waveforms](image.png)

Figure 3-9: Atrial and arterial pressure waveforms.

While pressures were maintained as close to physiologic as possible, limitations on the circulatory loop, mainly in the size of the compliance chamber, restricted our ability to maintain these conditions at the higher beat rates. Additionally, mean aortic
pressure is only measured within animal trials for 4-7 days post-operative and venous pressure is not recorded. Due to the limited availability of clinical pressure fluctuations with changing beat rate, *in vitro* pressures were reduced to the lowest possible level for all beat rates as shown in Table 3-2.

<table>
<thead>
<tr>
<th>Heart Rate (bpm)</th>
<th>Systolic Duration (%)</th>
<th>Arterial Pressure Systolic/Diastolic (mmHg)</th>
<th>Atrial Pressure Systolic/Diastolic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>38</td>
<td>120/80</td>
<td>30/5</td>
</tr>
<tr>
<td>90</td>
<td>41</td>
<td>120/80</td>
<td>37/8</td>
</tr>
<tr>
<td>105</td>
<td>43</td>
<td>140/80</td>
<td>39/9</td>
</tr>
<tr>
<td>120</td>
<td>46</td>
<td>170/100</td>
<td>39/10</td>
</tr>
<tr>
<td>135</td>
<td>49</td>
<td>180/120</td>
<td>47/11</td>
</tr>
<tr>
<td>150</td>
<td>50</td>
<td>220/140</td>
<td>47/11</td>
</tr>
</tbody>
</table>

Average flow rates through the inlet and outlet ports were monitored with ultrasonic probes (Model 20XL, Transonic Systems, Inc., Ithaca, NY) attached to Tygon tubing just upstream and downstream of the LVAD. The probes were calibrated for the appropriate blood analog and were connected to a flow meter (Model TS410, Transonic Systems, Inc., Ithaca, NY) with a digital readout displaying average flow rate. Flow waveforms for the LVAD with BSM PC valves are shown in Figure 3-10 for the lowest beat rate.
The motion of the pusher plate was tracked through a linear variable displacement transducer (LVDT) (MACH 1 Series, Solartron Metrology, West Sussex, UK). The LVDT was used to ensure the stroke length of 15 mm. A calibration curve was established by compressing the shaft in linear increments and recording the voltage output. Any adjustments to stroke length were made through the Superpump amplifier controller, and the same stroke length was matched to all beat rates to ensure consistency of operating conditions. Figure 3-11 shows the stroke profile for min, 75 bpm, and max, 150 bpm, beat rates.

Figure 3-10: Inflow and outflow waveforms for 75 bpm (38% systolic duration).
3.2.3 Data Acquisition

The flow waveforms, pressure readings, and LVDT traces were all continuously recorded through the use of a 1 MHz data acquisition board (Model WaveBook 512, IOtech, Inc., Norton, MA) connected to a PC. An in-house trigger box was used to coordinate the timing of data capture in the cycle, where a known time delay was applied relative to the start of diastole. Visualization of this trigger was simultaneously recorded with WaveBook and all signal traces were viewable through WaveView software (IOtech, Inc., Norton, MA).

Figure 3-11: LVDT waveform for low and high beat rates.
3.3 Blood Analog

Blood in its natural state is characterized by two main components, the formed elements, including erythrocytes, leukocytes, and platelets, and the suspending fluid, plasma. Blood functions primarily as a medium for gas transport, yet also plays key roles in waste removal, nutrient transport, and signal transduction. In fluid mechanic studies involving LVADs, the viscoelasticity of blood is important as changes in viscosity and elasticity affect flow properties (Long 2005). The viscosity describes the fluid’s resistance to motion, whereas the elasticity represents the blood’s ability to return to its initial state after deformation.

Blood is characterized as a non-Newtonian shear thinning fluid in which shear stress is not linearly proportional to shear rate. Hematocrit, or the proportion of packed red blood cells to total blood volume, can have a significant influence on the degree of blood viscoelasticity. For a healthy human adult, blood hematocrit is approximately 40%. At this hematocrit, blood responds with an exponential decrease in viscoelasticity with increasing shear rate. Under low shear conditions (<50 s\(^{-1}\)), such as those seen in the capillaries, blood tends to be less deformable and aggregates into stacks of erythrocytes known as rouleaux. As shear rate increases above 100 s\(^{-1}\), stresses between aggregated cells force them to separate and align with the direction of flow thus decreasing the viscoelasticity of blood. As shear rates increase to >1000 s\(^{-1}\), blood cells no longer have a tendency to aggregate and blood can be approximated as a constant viscosity fluid.
Although blood would be an ideal measurement fluid for PIV fluid dynamic analyses, its opacity does not allow for laser penetration and particle illumination. In order to maintain the properties of viscosity and elasticity in an optically clear fluid, a blood analog was developed (Long 2005). This analog, created out of a percentage by weight solution of 0.03% xantham gum, 16% glycerin, 33.97% water, and 50% NaI matches the viscoelastic nature of 40% Hct blood. Xantham gum supplies the elastic nature of the shear-thinning fluid, while the glycerin and water match the viscosity. The NaI is added to match the index of refraction (1.49) to that of the acrylic model. Blood viscosity and elasticity matched to 40% Hct blood is verified through measurements made over a range of shear rates (1-1000 s⁻¹) with a viscoelastic analyzer (Vilastic-3, Vilastic Scientific, Inc., Austin, TX). Sample measurement curves are shown in Figure 3-12.
3.4 PIV Techniques and Operating Conditions

The pulsatile nature of the 50 cc LVAD and large geometry relative to light sheet thickness make PIV data collection both an interesting and appropriate technique for characterizing flow fields within the device. In attempting to predict thrombosis within this model, our studies focus on the flow development at a cross body plane 5 mm from the front wall of the device as shown in Figure 3-13.

Figure 3-12: Viscosity and elasticity curves for blood and blood analog.
This plane was selected as prior 50 cc device investigations by Hochareon showed that areas of low wall shear rates at the base of the pump, in this plane, correlated well to \textit{in vivo} clot deposition (Hochareon 2004a). Flow in this plane was examined at low (65 $\mu$m/pixel), mid (35 $\mu$m/pixel), and high (12 $\mu$m/pixel) PIV magnifications. Global plane body flows were captured at the low magnification for BSM PC valves to observe overall changes in flow development with beat rate. This global analysis was performed over the entire cardiac cycle at heart rates ranging from 75-150 bpm in 15 bpm increments. The changes in beat rate were accompanied by systolic durations presented in Table 3-2 to mimic the animal study conditions. All velocity maps generated at the low magnification are for an ensemble average of 100 image pairs. Data was taken every 7\% of the cardiac cycle to garner an overall understanding of flow and beat rate scalability.
Mid and high magnification results were examined for consistency and repeatability of measurement. A specific concentration, at this magnification, focused on resolving shear rates at near wall locations. Data was collected at a heart rate of 86 bpm and 37% systolic duration for 200 image pairs. These images were averaged for statistical purposes and to minimize beat-to-beat variability. An increase in PIV magnification from 65, to 35 and 12 µm/pixel, allows closer wall velocity measurements to be made with improved spatial resolution. The error associated with these measurements is considered in the shear rate calculation for mid and high magnifications. BSM Delrin valves were used in all mid and high magnification studies.

Next, at high magnification, the amount of data required to characterize flow within V-2 increases substantially. Efforts to optimize the amount of data collection are desirable, and the unsteadiness of V-2 raises questions about the appropriate frequency of data collection. For this reason, data was collected at every 10 ms in the cycle at a heart rate of 86 bpm and 37% systolic duration for 200 image pairs. Shear rate comparisons for 10 and 50 ms intervals are made at two locations in the pump. Both low and high flow scenarios are examined; one along the base of the 5 mm plane and the other at the centerline of the inlet port. Spatial and temporal analyses were considered to resolve issues with the necessary intervals for data collection.

Finally, an extensive shear rate study is conducted at 12 µm/pixel to resolve flow features near the wall. Heart rates of 75, 115, and 150 bpm and corresponding systolic durations of 38, 45, and 50% are considered in this analysis. In order to directly compare
wall shear rate measurements at the same instant in the cardiac cycle for multiple heart rates, the data collection frequency was scaled on both diastolic and systolic cycle times. For all heart rates, 200 image pairs were collected every 7% of diastole and every 7% of systole. BSM PC valves were studied for these scenarios. Comparisons between this *in vitro* data and *in vivo* experiments will strengthen the prediction of thrombus formation in the 50 cc device.
Chapter 4

Results and Discussion

4.1 Wall Shear Rate Estimation

In order to calculate wall shear rates from PIV results, an algorithm was developed in MATLAB (The MathWorks, Inc., Natick, MA) by Hochareon (Hochareon 2003b). The application of this program to high magnification PIV has been previously considered and is given further attention here. The program uses near wall velocities from PIV measurements, along with wall identification techniques, to calculate wall shear rates according to the following equation:

\[
\frac{du}{dy} = \frac{u_t - u_w}{y_t - y_w}
\]

In our 2D calculations of wall shear rate, the shear rate is a function of the near wall tangential component of velocity, \( u_t \), the wall velocity, \( u_w \), the orthogonal distance of \( u_t \) to the wall, \( y_t \), and the wall location, \( y_w \). The no-slip boundary condition applies at the LVAD wall and \( u_w \) goes to zero. The wall at each measurement location is defined as the origin forcing \( y_w \) to go to zero as well. The resulting equation is dependent on the value of \( u_t \) and \( y_t \) only, thus any error associated with the wall shear rate calculation is based on the accuracy of these measurements.
4.1.1 Wall Identification and Zero Masking

The LVAD wall curvature is observed in Insight™ 3G images illustrating that the device wall cuts through IRs at arbitrary locations, as shown in Figure 4-1. Proper identification of the wall was necessary to avoid error propagating into the shear rate calculation. A technique developed by Hochareon et al. allowed the user to manually indicate the wall location and then applied a fifth order polynomial regression to reconstruct the wall geometry (Hochareon 2004b). The accuracy of this reconstruction was analyzed by observing changes in image intensity gradients orthogonal to the wall surface, from non-fluid regions, through the wall, and into fluid regions. We determined that the wall location may be identified to within a half a pixel as the sharpest intensity gradients occurred within this limit. Once the wall was defined, areas outside of the wall and in non-fluid regions were masked with zero background intensity. This eliminated any imperfections in the non-fluid regions of the model and pusher plate saturations that may have been identified as particles in the cross correlation. Stationary objects that may have biased IR velocity measurements to zero were thus removed. A sample PIV image after wall identification and zero-masking is shown in Figure 4-1.
4.1.2 IR Velocity and Fluid Centroid Shift

After the LVAD wall and non-fluid regions were appropriately identified, images were processed with Insight™ 3G according to the settings outlined in Section 2.2. Near wall velocity measurements considered in the shear rate calculation lied within IRs either encompassing or directly adjacent to the LVAD wall. IR sizes of 32 x 32 pixels were selected to improve particle counts within a particular window, while minimizing large displacement gradients near the wall. All considered vectors were applied to the center of the IRs as displayed in Figure 4-2, with valid and invalid vectors determined from the quality of the correlation peak. It is important to note that vectors based on the 50%
overlap criteria were not considered in the shear rate calculation, although future improvements may lead to shear rate calculations even closer to the wall due to increased vector density.

A 10% size criterion was set within the MATLAB program, such that any IRs with less than 10% fluid volume were dismissed. These limits were established due to insufficient particle counts (<5 particles per IR) existing in regions very near the wall. A region with insufficient particle density is highlighted in Figure 4-3. In cases such as these, fluid velocities from the adjacent IRs were used in the shear rate calculation. An example of this is shown in Figure 4-3.

Figure 4-2: Insight 3G™ image illustrating velocities considered in the wall shear rate calculation. The green and red arrows indicate valid and invalid velocities, respectively.
Velocity measurements at this point in the analysis were still applied to the center of each IR. However, this velocity represents particle displacements within the fluid volume only and should be moved to the centroid of the fluid region. A centroid shifting technique moved the location of the velocity vector to the centroid of the fluid volume. Tangential projections of velocity vectors were then calculated with respect to wall curvature within each IR, and the orthogonal distance of each vector to the wall was determined. The two remaining components required for the wall shear rate calculation, $u_t$ and $y_t$, were now defined for all IRs along the wall. The resulting image is shown in Figure 4-4.

Figure 4-3: Insight 3G™ image illustrating application of the 10% IR criteria. The yellow box indicates an IR with <10% fluid volume occupancy. The yellow arrow represents the velocity measurement in the adjacent IR. The green and red arrows indicate valid and invalid velocities, respectively.
$U_u$ and $y_u$ calculations were computed at all IRs for the total number of collected image pairs. Only IRs with 50-200 valid velocity counts were considered in the shear rate calculation and velocities for each region were averaged. Notice that the red vector of Figure 4-3 is now green in Figure 4-4, signifying enough valid counts within this fluid region. The vector density along the wall was dependent on the number of valid counts. IRs with insufficient vector counts were ignored and adjoining IRs were considered. The result was an average wall shear rate calculation for IRs along the wall at a spatial resolution dependent on PIV magnification and IR size.

Figure 4-4: Insight 3G™ image illustrating fluid centroid shift and vector transformations. The green arrows indicate valid tangential velocity components considered in the wall shear rate calculation. The dashed blue lines indicate the distance of the velocity vector to the wall.
4.2 Influence of PIV Magnification on Shear Rate Estimation

The wall shear rate calculation outcomes were observed at both mid and high magnifications for data collection at the 5 mm plane. Overlapping regions of the lower left side of the pump, near the outlet port, were considered and are shown in Figure 4-5. A 16 mm section along the lower outlet wall is highlighted and shear rate calculations at both magnifications are compared.

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Figure 4-5. Schematic of pump body displaying areas of PIV data collection. The (A) blue box indicates the mid PIV magnification and the (B) red and (C) green boxes the high PIV magnification areas of study. Wall shear rates are calculated along a 16 mm portion of the wall in the direction of the (D) orange line.

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Flow maps within these sections, illustrating average flow at a given time step in the cardiac cycle, are shown in Figure 4-6. Image pairs were collected from 150-500 ms into the cardiac cycle, as these were the times the inlet jet was dominant in the indicated regions. Flow magnitude is indicated by a contour map with arrows corresponding to the
direction of flow. The consistency of data at both magnifications is shown through highly similar flow characteristics and velocities throughout the entire cardiac cycle.

Figure 4-6. Flow maps corresponding to the locations defined in Figure 4-5. The mid PIV magnification results are represented by the (A) blue box, and the high PIV magnification results by the (B) red and (C) green boxes. Flow similarities at the two different PIV magnifications exist for flow 300 ms from the onset of diastole.

Wall shear rates were calculated along the 16 mm section of Figure 4-5 according to the procedure outlined in Section 4.1. The shear rates, calculated at 50 ms increments throughout the cardiac cycle, are presented as contour maps for both magnifications in Figure 4-7. Wall shear rates within the 50 ms intervals were interpolated between
neighboring time steps for visual clarity. The shear rate magnitude and direction are represented by the color legend. Positive shear is defined by flow in the clockwise direction and is shown as yellow to red hues on the color map. Negative shear is characterized by flow in the counter-clockwise direction and corresponds to the green and blue tones. As shear values are normalized by 500 s$^{-1}$, values between -1 and 1 are of concern because they have potential for thrombus formation. The x-axis indicates the position along the wall for a defined region, and the y-axis displays the cardiac cycle time.

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**Figure 4-7**: Contour plot displaying wall shear rate calculations along the (D) orange line of Figure 4-5 for the (A) mid and (B) high PIV magnifications. Positive shear is a result of flow in the clockwise direction, with negative shear caused by flow in the counter-clockwise direction. The shear rate was normalized over 500 s$^{-1}$ to observe areas between -1 and 1 that are prone to thrombus deposition.
The shear rate distributions at both magnifications appear similar in both magnitude and direction for most time steps. These shear rates, however, were calculated from $u_t$ and $y_t$ measurements that were dependent on PIV magnification and IR size. Because the spatial resolution of 32 x 32 pixels remains unchanged for both magnifications, only the effect of PIV magnification on the wall shear rate calculation is considered.

At the mid magnification, $u_t$ values used in the shear rate calculation were generally larger than those at the high magnification. This was a result of the IRs extending further into the fluid volume at the mid magnification resulting in fluid flow that was less influenced by the no slip boundary condition at the wall. Similarly, $y_t$ values were larger at the mid magnification due to fluid centroids being located further from the wall. Values of $u_t$ and $y_t$ can be seen in Tables 4-1 and 4-2, respectively, for 200, 350, and 500 ms time steps at both magnifications. These points in the cycle were chosen as they display low, mid, and high relative regions of shear. The corresponding shear rate calculations are displayed in Figure 4-8.
Table 4-1: $U_t$ measurements for the mid and high PIV magnifications.

<table>
<thead>
<tr>
<th>Magnification (µm/pixel)</th>
<th>35</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Cycle Time (ms)</td>
<td>200</td>
<td>350</td>
</tr>
<tr>
<td>$\text{Average } u_t$ (m/s)</td>
<td>0.094</td>
<td>0.362</td>
</tr>
<tr>
<td>$\text{Minimum } u_t$ (m/s)</td>
<td>0.026</td>
<td>0.142</td>
</tr>
<tr>
<td>$\text{Maximum } u_t$ (m/s)</td>
<td>0.175</td>
<td>0.518</td>
</tr>
</tbody>
</table>

Table 4-2: $Y_t$ measurements for the mid and high PIV magnifications.

<table>
<thead>
<tr>
<th>Magnification (µm/pixel)</th>
<th>35</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Cycle Time (ms)</td>
<td>200</td>
<td>350</td>
</tr>
<tr>
<td>$\text{Average } y_t$ (µm)</td>
<td>657.8</td>
<td></td>
</tr>
<tr>
<td>$\text{Minimum } y_t$ (µm)</td>
<td>285.8</td>
<td></td>
</tr>
<tr>
<td>$\text{Maximum } y_t$ (µm)</td>
<td>1181.8</td>
<td></td>
</tr>
</tbody>
</table>
The shear rates are similar in magnitude for all three time steps with deviations seen only at the peak shear rates occurring at 350 ms. While it may seem that the added collection time required by high magnification PIV has little benefit, the accuracy of the calculation must be considered. Raffel et al. have shown that for data that is not pixel locked, minimum velocities with PIV can be resolved to approximately 0.2 times the spatial resolution divided by the $\Delta T$ (Raffel 1998). Pixel locking was examined by plotting histograms of sub-pixel particle displacements. There were no indications of pixel locking in the regions of high flow considered. The minimum pulse separations at mid and high magnifications were 300 $\mu$s and 150 $\mu$s, respectively. This leads to velocity resolutions of 0.023 m/s at mid and 0.016 m/s at high magnifications. Average velocities, shown in Table 4-1, are greater than this implying accurate velocity measurement.

Figure 4-8: Shear rate calculations for 200, 350, and 500 ms of the cardiac cycle from Figure 4-7. Dashed and solid lines represent the mid and high PIV magnifications, respectively.
In order to directly compare the accuracy of the wall shear rate calculation at both magnifications, velocities measured 325 µm from the wall, satisfying the ranges shown in Table 4-2, were analyzed. At this distance, a velocity value of 0.163 m/s will produce a shear rate of approximately 500 s\(^{-1}\). The error associated with this velocity measurement is plus or minus the velocity resolution defined above. The ability to locate the wall to within a half a pixel has already been discussed in Section 4.1.1. From this, the error in the \(y_t\) measurement is ± 17.5 µm at the mid magnification, and ± 6 µm at the high magnification. As such, the error in the wall shear rate calculation is approximately 100 s\(^{-1}\) at the mid magnification, and 60 s\(^{-1}\) at the high magnification. Thus, increasing the magnification by about a factor of 3 leads to a 40% reduction in the shear rate error. This improved confidence at higher magnifications was used as a basis for the remaining shear rate studies.

### 4.3 Temporal and Spatial Fluctuations with PIV Data Measurement

While increases in magnification led to improved shear rate accuracy, additional data collection was required as smaller sections of the 50 cc wall were analyzed. Furthermore, efforts to resolve shear rates closer to the wall exposed large ranges of velocity gradients within the boundary layer. Rapidly changing flow in these regions caused by pump pulsatility led to questions about the necessary frequency of data collection. To test this, images were acquired at 10 and 50 ms intervals in areas of low flow at the bottom wall of the 5 mm body plane and high flow at the centerline inlet port, as shown in Figure 4-9.
Data was collected from 50-600 ms of the cardiac cycle for image B of Figure 4-9. The orange arrow, representing a 16 mm section of the wall, was sequenced in the clockwise direction resulting in negative shear rates being calculated. Shear rate plots at 10 and 50 ms data collection times for this phase are displayed in Figure 4-10.
The contour map, as a whole, displays shear rates with highly similar magnitude and direction for both 10 and 50 ms incremented data. A substantial portion of this region displays shear rates along the bottom wall that are less than 500 s\(^{-1}\). These results are consistent with those observed by Hochareon at neighboring planes (Hochareon 2004a) in the 50 cc V-0 device. Raw shear values were plotted along the wall in 10 ms increments for 50 ms blocks of relative low and high negative shear. The low shear region is shown in Figure 4-11 for 500-550 ms of the cardiac cycle and the high shear region in Figure 4-12 for 300-350 ms. These areas were explored to observe differences in spatial shear rate changes for both low and high shear zones.

Figure 4-10: Contour plot displaying wall shear rate calculations along the orange line in B of Figure 4-8 at the high PIV magnification. Data was collected every 10 ms in (A), and every 50 ms in (B).
The shear rates increase in a stepwise manner from 500-550 ms of the cycle for 10 ms increments, although cross over is present at multiple locations for several time bands. The 520 ms interval intersects 3 of the 5 neighboring line plots. Flow maps at this interval show no evidence of rapid changes in velocity vector magnitude and direction, nor do they show the low vector counts in these regions that could lead to fluctuations in $y_i$ values. Lines with such oscillations are suggestive of beat to beat variability. The overall shear rate for this portion of the cycle is well under 500 s$^{-1}$, suggesting that this section of the wall is susceptible to thrombosis.

Figure 4-11: Spatial plots of shear rates from Figure 4-9, region S1, corresponding to regions of relative low flow 500-550 ms into the cardiac cycle.
Shear rate plots at the higher flow time steps were more sensitive to data collection intervals. Several cross over points exist between adjacent time bands. The 320 ms plot lies completely below that of all other bands for about 12 mm of the wall. The 300 and 350 ms intervals are closer in magnitude than all neighboring time steps at a distance of about 4.5 mm. Perhaps more importantly, locations further along the wall (~7.5-9.5 mm) reach 500 s\(^{-1}\) thresholds that would be missed by data interpolation over 50 ms. These regions lie on the edge of shear rate values that may be sufficient for thrombus washing. Spatial plots within this portion of the cardiac cycle suggest that 50 ms time increments are not sufficient for data collection in higher shear regions. Temporal plots at 3, 6, 9, 12, and 15 mm locations along the wall further examine shear rate variability.

**Figure 4-12:** Spatial plots of shear rates from Figure 4-9, region S1, corresponding to regions of relative high flow 300-350 ms into the cardiac cycle.
Figure 4-13 examines temporal shear rates in 10 ms increments, while Figure 4-14 does the same for 50 ms increments. These plots once again show similarities in shear rate patterns as a whole, although fluctuations in shear magnitude exist in 10 ms periods. Fifty ms contour plots tend to smooth out these resolvable gradients, missing time steps where flow may have an impact on thrombosis. For example, the 320 ms cycle time of Figure 4-13 gives three locations along the wall where shear rates exceed 500 s⁻¹. Figure 4-14 only shows two time steps reaching this level.

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**Figure 4-13:** Temporal plots of shear rates from Figure 4-9, region S1, corresponding to data collection in 10 ms intervals.
Further examination of wall shear distributions for the high shear region (image D of Figure 4-9) are shown in Figure 4-15 for comparison. A 13 mm segment of the wall was analyzed for similar shear rate fluctuations. High shear regions of the inlet port have shear rates between ~100 and 1600 s\(^{-1}\) over 250 ms of the cardiac cycle. Initial inspection of the 10 and 50 ms contour plots show both the presence and absence of a distinct band of low shear between 50 and 100 ms. This time frame is shown in Figure 4-16, with peak shear regions shown in Figure 4-17.

Figure 4-14: Temporal plots of shear rates from Figure 4-9, region S1, corresponding to data collection in 50 ms intervals.
Figure 4-16 illustrates the importance of fine incremental data collection. From ~9-13 mm, all four time steps between lower (50 ms) and upper (100 ms) bands would be over-predicted by collecting data every 50 ms. This is contrary to the results of Figure 4-12, in which shear rates were under-predicted with 50 ms increments. Figure 4-17 further strengthens the argument for 10 ms data, displaying all bands lying outside the 50 ms extrema at a location 6 mm along the wall.

Figure 4-15: Contour plot displaying wall shear rate calculations along the orange line in D of Figure 4-9 at the high magnification. Data was collected every 10 ms in (A), and every 50 ms in (B).
Figure 4-16: Spatial plots of shear rates from Figure 4-9, region S2, corresponding to regions of relative low flow 50-100 ms into the cardiac cycle.

Figure 4-17: Spatial plots of shear rates from Figure 4-9, region S2, corresponding to regions of relative high flow 200-250 ms into the cardiac cycle.
Temporal plots for Figure 4-15 are shown in Figures 4-18 and 4-19 every 2.33 mm along the wall to 11.66 mm. Shear rates over- and under-predicted from one collection interval to the next occurs again. Time steps 60-90 ms into the cycle for all locations of Figure 4-19 are, on average, approximately twice the expected shear rate values of Figure 4-18.

Figure 4-18: Temporal plots of shear rates from Figure 4-9, region S2, corresponding to data collection in 10 ms intervals.
The remaining spatial plots for high and low shear zones can be found in Appendix A. These results show significant variations in wall shear rates, irrespective of cycle time, between 10 and 50 ms data collection times. Periods of over- and under-prediction are frequent, and occur at both the high and low shear zones of Figure 4-9. From these results we recommend that data be collected in 10 ms intervals so as not to miss important shear information. It is useful to note, however, that the 10 ms data collection interval concentrated only on a heart rate of 86 bpm with a systolic duration of 37%. Different operating conditions will alter total diastolic and systolic cycle lengths, requiring the 10 ms interval to be considered as a percentage of both diastole and systole for direct comparison. A 10 ms interval corresponds to data collection every 2.3 and 3.9% of diastole and systole, respectively, for 86 bpm and 37% systolic duration, while a 50 ms interval results in image capture every 11.4% of diastole and 19.4% of systole.

Figure 4-19: Temporal plots of shear rates from Figure 4-9, region S2, corresponding to data collection in 10 ms intervals.
Compromises on these percentages to reduce data collection time are further examined in the high magnification wall shear rate study of Section 4.5.

4.4 Beat Rate and Systolic Duration Global Flow Experiments

Global plane flows were studied at the conditions outlined in Table 3-2. The objective of this study was to determine how variations in operating conditions affect the overall 5 mm plane flow profiles. As mentioned in Section 1.3, Oley et al. performed similar studies, but they were limited to a maximum heart rate of 90 bpm with a systolic duration of 35% for V-0. These studies showed unwanted inlet side flow separation with improved jet penetration at the bottom wall attributed to increased heart rates. Higher beat rates up to 150 bpm with peak systolic durations of 50% are routine in V-2 animal studies. It is suspected that increasing the beat rate and systolic duration to this magnitude would lead to similar, yet more drastic changes in planar flow compared to V-0. Data was collected every 7% of the cardiac cycle for all beat rates. This scaling does not consider the effects of changes in systolic duration, so the same portion of the cycle cannot be directly compared between beat rates. Regardless, relative flow comparisons are useful in displaying overall flow development. A complete collection of flow maps is compiled in Appendix B, with planes in early diastole, mid diastole, late diastole, and systole shown in Figures 4-20, 4-21, 4-22, and 4-23, respectively.
4.4.1 Early Diastolic Flow 7% into the Cardiac Cycle

The cardiac cycle begins with the mitral valve opening and flow entering through its major and minor orifices. High 3D flow in these areas, circled in red, leads to low vector density near the valve. The inlet jet begins to develop at this point, following the inlet wall with little flow separation, for all beat rates. A clockwise flow leads to a rotational flow pattern forming later in the cardiac cycle. Instances of counter-clockwise flow are apparent along the upper wall between the inlet and outlet ports. At this point in the cycle, flow patterns show little difference in direction, with increases in magnitude for each beat rate. Peak velocities for successively increasing beat rates are 0.28 m/s, 0.39 m/s, 0.47 m/s, 0.57 m/s, 0.73 m/s, and 0.89 m/s.
Figure 4-20: Flow maps, at the 5 mm plane, 7% into the cardiac cycle displaying beat rates (bpm)/systolic durations (%) of (A) 75/38, (B) 90/41, (C) 105/43, (D) 120/46, (E) 135/49, and (F) 150/50. Red circles show areas of low planar flow caused by 3D flow through the mitral valve orifices. All data was collected at the 5 mm plane.
4.4.2 Mid Diastolic Flow 28% into the Cardiac Cycle

The flow exhibits a strong rotational pattern for all beat rates as the inlet jet extends further into the outlet side of the pump in mid diastole. The diastolic jet continues to follow the inlet wall, although flow separation, highlighted in red, is clear at beat rates of 75, 90, 105, and 120 bpm. This region of detached flow is consistent with results by Oley et al. for V-0 at beat rates to 90 bpm. On the other hand, beat rates of 135 and 150 bpm appear to promote strong washing on the inlet wall with little observable flow separation. However, because systolic durations increase with beat rate, it is to be expected that the flow maps for these upper beat rates are further into the cycle. Analyzing previous time steps confirms that this is true, and that the flow is still separated. The degree of separation is difficult to quantify, but qualitatively appears to be less at beat rates of 135 and 150 bpm. Flow at this time of the cycle is completely clockwise for all beat rates. The region along the outlet wall that appears as flow separation is not physical, but is caused by diaphragm reflections.
Figure 4-21: Flow maps, at the 5 mm plane, 28% into the cardiac cycle displaying beat rates (bpm)/systolic durations (%) of (A) 75/38, (B) 90/41, (C) 105/43, (D) 120/46, (E) 135/49, and (F) 150/50. Red circles show areas of flow separation for maps A-D, with minimal separation observed in maps E and F.
4.4.3 Late Diastolic Flow 50\% into the Cardiac Cycle

Flow in late diastole perhaps shows the greatest differences between the 75-120 and 135-150 heart rates. Once again, these differences may be attributed to varying systolic durations. Flow maps at 42\% for 135 and 150 bpm show similar overall patterns to those of lower beat rates at 50\%, with the only difference being increased velocity with increased beat rate. The inlet jet has penetrated into the outlet side of the device just prior to systole. The jet has established good rotational flow which will continue into early systole.
Figure 4-22: Flow maps, at the 5 mm plane, 50% into the cardiac cycle displaying beat rates (bpm)/systolic durations (%) of (A) 75/38, (B) 90/41, (C) 105/43, (D) 120/46, (E) 135/49, and (F) 150/50.
4.4.4 Systolic Flow 78% into the Cardiac Cycle

Nearing the end of the cycle, flow at all beat rates moves through the aortic valve leaving behind a small circulating flow. The wake of the exiting jet forms a recirculation zone, highlighted in red, near the mid to upper inlet wall of the device. Flow has primarily exited the pump at this point in preparation for the mitral valve to open again and restart the cardiac cycle.

This beat rate study, at all locations within the cardiac cycle, demonstrates that flow patterns in V-2 are similar and roughly independent of beat rate and systolic durations. On the other hand, the flow magnitude appears to scale with beat rate. This scaling is discussed in the following section by looking at changes in wall shear rate with increasing beat rate and systolic duration.
Figure 4-23: Flow maps, at the 5 mm plane, 78% into the cardiac cycle displaying beat rates (bpm)/systolic durations (%) of (A) 75/38, (B) 90/41, (C) 105/43, (D) 120/46, (E) 135/49, and (F) 150/50. Red circles show areas of recirculation.
4.5 High Magnification Wall Shear Rate Calculation across Beat Rates and Systolic Durations

The effects of beat rate and systolic duration on the flow within the 50 cc LVAD were presented in Section 4.4. The relationship between these parameters and flow changes was investigated by calculating shear rates along the lower device wall, in regions of known thrombus deposition, at the 5 mm plane. A 91 mm section, beginning 7.5 mm (inlet) and ending 6.8 mm (outlet) from the body midline, as shown in Figure 4-24, was considered. This section was divided into 15 wall segments and wall shear rates were calculated at the high (12 µm/pixel) magnification for each segment. Walls were sequenced in a counter-clockwise direction primarily against the direction of flow. Here the results of walls B, E, H, K, and N are explored in more detail, with shear rate contour plots for all remaining sections given in Appendix C.

Figure 4-24: Wall locations considered in the shear rate study along the lower LVAD wall at the 5 mm plane. The (B, E, H, K, and N) red arrows indicate walls that are given detailed attention in Sections 4.5.1-5. The remaining orange walls have shear rate contour plots shown in Appendix C. Blue boxes (18.36 x 13.32 mm) indicate the size of a CCD window at the high magnification. The green line is the pump body midline.
The overall similarity in flow observed in Section 4.4 led to beat rates of 75, 115, and 150 bpm being studied here with corresponding systolic durations of 38, 45, and 50%. In seeking direct wall shear rate comparisons for all beat rates and systolic durations, at multiple instances of the cardiac cycle, images were acquired in 7% increments for both diastole and systole. This percentage was chosen as a compromise between data collection time and temporal and spatial shear rate resolution.

4.5.1 High Magnification Wall Shear Rate Calculation along Wall B

The results of the shear rate calculation for wall B are illustrated by line plots, shown in Figures 4-25 and 4-26, at locations 1 and 4 mm along the wall. These plots show shear rates largely above the 500 s\(^{-1}\) threshold for thrombosis, throughout most of diastole, for heart rates of 115 and 150 bpm. At 75 bpm, shear rates reach this value for only 50-78% of diastole at the 1 mm position and 57-71% of diastole at the 4 mm position. The majority of systole for all beat rates at these locations is likely susceptible to clot deposition as low shear rates exist throughout. Peak negative shear rates of approximately 1400 (75 bpm), 3300 (115 bpm), and 4500 s\(^{-1}\) (150 bpm) are present at the 1 mm location.

Regions of positive wall shear at the 4 mm position suggest flow reversal from 28-42% of diastole at 75 bpm. The results of Section 4.4.2 showed areas of flow separation in close proximity to this region during these time steps. Further examination shows that recirculating flow is present at the separation region, forcing the fluid to turn
towards the inlet. Furthermore, the lower beat rates showed larger regions of separation compared to the higher ones. This is the most probable explanation for positive shear being present during diastole at the lowest beat rate only.

Figure 4-25: Wall shear rates for 75, 115, and 150 bpm at a 1 mm location along wall B of Figure 4-24.
The shear rate distributions for all beat rates are similar throughout the cycle. The scalability of these parameters was investigated with changes in the average inlet velocities. These velocities were calculated for all beat rates by dividing the average volumetric flow rates by the device inlet area (5.38 x 10^{-4} m^2). The results of this calculation are given in Table 4-3.

Table 4-3: Average flow rates and inlet velocities for 75, 115, and 150 bpm heart rates.

<table>
<thead>
<tr>
<th>Heart Rate (bpm)</th>
<th>Flow Rate (L/min)</th>
<th>Average Inlet Velocity (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>3.44</td>
<td>0.11</td>
</tr>
<tr>
<td>115</td>
<td>5.22</td>
<td>0.16</td>
</tr>
<tr>
<td>150</td>
<td>6.83</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Figure 4-26: Wall shear rates for 75, 115, and 150 bpm at a 4 mm location along wall B of Figure 4-24.
Shear contour plots along the wall length show that increases in beat rate approximately scale with the square of the average inlet velocity, as shown in Figure 4-27. There is an overall similar pattern of shear rate for most of the cardiac cycle. The region of flow reversal at 75 bpm is made apparent by the yellow band of positive wall shear toward the end of the wall. This recirculating flow extends into wall C, and is completely absent thereafter for all locations along the inlet side of the pump.

Figure 4-27: Contour plots displaying wall shear rate calculations along wall B of Figure 4-24 at the high magnification and the 5 mm plane. (A), (B), and (C) display shear rate distributions for 75, 115, and 150 bpm, respectively. All images are of wall shear rates normalized over the square of the average inlet velocity. Dashed lines correspond to the shear rate plots of Figures 4-28 and 4-29 at locations 1 and 4 mm along the wall.
Normalized shear rates at the 1 and 4 mm locations are plotted over time, along the dashed lines of Figure 4-27, in Figures 4-28 and 4-29. The scaling by average inlet velocity squared holds well for all of systole, with early diastolic differences attributed to the previously mentioned flow reversal. Two particular points, both at 71% of diastole, show outlying data for 150 bpm, although normalized shear rates realign within about two time steps.

Figure 4-28: Normalized wall shear rates for 75, 115, and 150 bpm at a 1 mm location along wall B of Figure 4-24.
4.5.2 High Magnification Wall Shear Rate Calculation along Wall E

Shear rates along section E exhibit similar trends to those of wall B at a 3 mm location, as shown in Figure 4-30. Shear rates at this position reach very similar maximum values, with identical regions of diastole being exposed to sub 500 s\(^{-1}\) shear rates at 75 bpm. The consistency of data collection, for all beat rates, is demonstrated by the fact that end systole shear rates are within ~150 s\(^{-1}\) of those at the onset of diastole.

Figure 4-29: Normalized wall shear rates for 75, 115, and 150 bpm at a 4 mm location along wall B of Figure 4-24.
Figure 4-30: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall E of Figure 4-24.

Contour plots (Figure 4-31) strengthen the arguments for the selected scaling, showing sections of high and low shear occurring in the same time span for all heart rates. Interestingly enough, peak shear rates occur earlier in the cycle along this section compared to wall B. Peak shear appears around 57% of diastole for 75 and 150 bpm, and as early as 50% of diastole at 115 bpm. As this section is further downstream from the inlet valve, we suspect that the same portion of the inflow jet is not necessarily responsible for the highest shear rates from one wall to the next. Furthermore, the inflow jet appears to have both intensified and grown by the time it reaches sections of this wall compared to wall B. At 75 bpm, light blue regions of shear seen as late as 42% into diastole for wall B appear around 28% of diastole for wall E. Similarly, these regions
tend to vanish around 85% of diastole for wall B and are sustained until the end of diastole for wall E.

Figure 4-31: Contour plots displaying wall shear rate calculations along wall E of Figure 4-24 at the high magnification and the 5 mm plane. (A), (B), and (C) display shear rate distributions for 75, 115, and 150 bpm, respectively. All images are of wall shear rates normalized over the square of the average inlet velocity. Dashed lines correspond to the shear rate plots of Figure 4-32 at a location 3 mm along the wall.

Shear rate line plots, displayed in Figure 4-32, are extracted along the 3 mm line of Figure 4-31 to again evaluate the effects of the normalization. These plots reveal the usefulness of the scaling by showing near identical patterns of shear rate. Notable
differences are present for all heart rates at the larger shear rate magnitudes. In general, regions of highest shear rates tend to deviate further from the normalization when contrasted with lower shear rates. The beginning of these differences occurs around 42% of diastole, with the largest difference at 50% of diastole. Percent differences for these locations are 25.1 and 32.3%, respectively. While the reason behind these discrepancies is not known, shear rates at the higher beat rates are substantially above 500 s\(^{-1}\) for more of the cardiac cycle compared to 75 bpm. As the 50 cc pump has been shown to experience all 3 studied beat rates during animal trials, we suspect that any regions reaching 500 s\(^{-1}\), at any point during the implant, will not show thrombosis.

Figure 4-32: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall E of Figure 4-24.
4.5.3 High Magnification Wall Shear Rate Calculation along Wall H

The highest shear rates occur along segment H. A location 3 mm from the beginning of wall H is chosen to illustrate this (Figure 4-33). Maximum shear rates of 7200 s\(^{-1}\) are realized around 64% of diastole at 150 bpm. Shear rates under 500 s\(^{-1}\) occur the least at this wall compared to walls N, K, E, and B.

![Shear rate plots](image)

Figure 4-33: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall H of Figure 4-24.

Shear rate plots, shown in Figure 4-34, illustrate the effectiveness of flow normalization once again. At this location in the pump, shear rates tend to be higher throughout systole when compared to earlier wall locations. A region of high shear is introduced for all beat rates at a distance of 3-5 mm along the wall. Wall H shows that substantial fluctuations in negative shear, from \(~700\) s\(^{-1}\) to \(~1400\) s\(^{-1}\) at 64% of diastole
and 75 bpm, occur over the wall. This suggests that the flow is changing strength as it changes direction and moves toward the device outlet. Velocity profiles in these regions would be useful in identifying these interesting flow characteristics, and they are alluded to as a reason for future work in Chapter 5.

Figure 4-34: Contour plots displaying wall shear rate calculations along wall H of Figure 4-24 at the high magnification and the 5 mm plane. (A), (B), and (C) display shear rate distributions for 75, 115, and 150 bpm, respectively. All images are of wall shear rates normalized over the square of the average inlet velocity. Dashed lines correspond to the shear rate plots of Figure 4-35 at a location 3 mm along the wall.
Normalization of data at the 3 mm line of Figure 4-34 is shown in Figure 4-35. Once again this scaling is appropriate for most of the cardiac cycle, although it is not as effective in high shear regions as evidenced by the spread of data around 57-85% of diastole. These results are consistent with those of wall E, signifying that higher shear rates may require a different scaling approach.

Figure 4-35: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall H of Figure 4-24.

4.5.4 High Magnification Wall Shear Rate Calculation along Wall K

Shear rates along wall K at the 3 mm location, shown in Figure 4-36, show wall shear rates between 0 and -500 s\(^{-1}\) for almost the entire cycle at 75 bpm. Shear rates reaching magnitudes of 3900 s\(^{-1}\) occur at 150 bpm. The negative shear rate regions extend into
systole for all beat rates at this wall. This is expected as the strongest portion of flow progresses through these regions between 64% of diastole and 14% of systole. Shear rates at 75 bpm only exceed 500 s\(^{-1}\) at 64% of diastole by about 40 s\(^{-1}\). However, this lies within our error of 60 s\(^{-1}\) as discussed in Section 4.2. Thus, thrombus formation may or may not be likely throughout the entire cardiac cycle for 75 bpm. Shear rates remain above 500 s\(^{-1}\) until 64% of systole at 115 bpm and 71% of systole at 150 bpm. This site is an area of possible thrombus deposition.

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Figure 4-36: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall K of Figure 4-24.

Shear plots (Figure 4-37) and a data line at 3 mm (Figure 4-38) display the same incidences of high scaled shear rates varying with beat rate, while lower shear rates tend to match more closely. Both 75 and 115 bpm exhibit similar overall contours compared
to 150 bpm, although systole normalization appears to be more appropriate between 75 and 150 bpm.

Figure 4-37: Contour plots displaying wall shear rate calculations along wall K of Figure 4-24 at the high magnification and the 5 mm plane. (A), (B), and (C) display shear rate distributions for 75, 115, and 150 bpm, respectively. All images are of wall shear rates normalized over the square of the average inlet velocity. Dashed lines correspond to the shear rate plots of Figure 4-38 at a location 3 mm along the wall.
4.5.5 High Magnification Wall Shear Rate Calculation along Wall N

The results of the shear rate calculation for wall N are shown in Figure 4-39, at a location 3 mm along the wall. Peak negative shear rates, as low as 3200 s\(^{-1}\) at 150 bpm, occur 71% into diastole, with maximum positive shear, reaching near 500 s\(^{-1}\) for 115 bpm, observed 92% into systole. Shear rates above 500 s\(^{-1}\) are observed for approximately 72% of the cardiac cycle for 115 and 150 bpm heart rates. On the other hand, the 75 bpm shear rates fall within the -500 to 500 s\(^{-1}\) range for nearly the entire cardiac cycle. These results are similar to those of wall K.

Figure 4-38: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall K of Figure 4-24.
The shear rate scales well for diastole for all beat rates, and for systole at beat rates of 115 and 150 bpm, as shown in Figure 4-40. Regions during systole at 75 bpm illustrate increased shear relative to other heart rates. Contour plots for subsequent regions (Appendix C) show that these differences decrease near the base of the pump body and are essentially absent by wall K of Figure 4-24. Brief periods of positive wall shear are evidenced by the yellow tones late in systole. This flow reversal is likely caused by the pusher plate disrupting the rotational flow between the pusher plate edge and the device wall.

Figure 4-39: Wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall N of Figure 4-24.
At the 3 mm section of Figure 4-40, shown in Figure 4-41, the largest difference in normalized shear rate occurs 57% into systole between 75 and 150 bpm. The minimum and maximum percent difference in normalized shear rate between 2 beat rates are 1.2% (21% into diastole) and 72.5% (57% into systole), respectively. Beat rate normalization yet again appears to be less effective at the higher beat rates.

**Figure 4-40**: Contour plots displaying wall shear rate calculations along wall N of Figure 4-24 at the high magnification and the 5 mm plane. (A), (B), and (C) display shear rate distributions for 75, 115, and 150 bpm, respectively. All images are of wall shear rates normalized over the square of the average inlet velocity. Dashed lines correspond to the shear rate plots of Figure 4-41 at a location 3 mm along the wall.
Overall, changes in beat rate and systolic duration normalize fairly well with the average inlet velocity squared. These results agree with the flow maps of Section 4.4 which show that changes in operating conditions primarily strengthen the flow field, leaving flow patterns nearly unchanged.

Figure 4-41: Normalized wall shear rates for 75, 115, and 150 bpm at a 3 mm location along wall N of Figure 4-24.
Chapter 5

Conclusions

5.1 Summary of Findings

Extensive effort has gone into the development of a pulsatile Penn State 50 cc LVAD for cardiac support of patients with limited chest cavity size. In moving towards human trials, 30 day animal studies were used to test the performance of the device \textit{in vivo}. Results of this work, by researchers at Hershey Medical Center, showed thrombus formation in several sections of the pump, with deposition favoring regions of the lower wall, a result not seen in larger devices. An important aspect of thrombogenicity is the local fluid flow. Animal experiments are characterized by large variations in pump beat rate and systolic duration. These variations are not easy to model in the laboratory. To better understand this relationship, particle image velocimetry (PIV) was used to characterize flow within the device for beat rates of 75, 90, 105, 120, 135, and 150 bpm and corresponding systolic durations of 38, 41, 43, 46, 49, and 50%. Specific attention was given to measuring wall shear rates in regions of known thrombus deposition, as studies have shown that thrombi forming on the device blood sac are likely for shear rates below 500 s\(^{-1}\).

Global flow, at a 5 mm plane from the front wall of the device, was examined at a PIV resolution of 65 µm/pixel. Beat rate and systolic duration changes induced little alteration in flow patterns in the pump body, with the magnitude of flow intensifying with both increased beat rate and systolic duration. To better study wall shear rates, we
explored shear rates calculated at the 12 and 35 µm/pixel PIV resolutions. Increasing the magnification from 35 to 12 µm/pixel resulted in better resolution of near wall velocities and improved confidence in wall identification, both of which improve the shear rate calculation. From these experiments, the error associated with a first order shear rate approximation decreased by approximately 40% from the mid to high magnification.

We then explored the frequency of PIV data collection along regions of the lower device wall. Data was collected in both 10 and 50 ms intervals for a beat rate of 86 bpm and systolic duration of 37%. Ten ms intervals showed significant shear rate variability in near wall locations that a 50 ms collection time missed. For areas along the wall, 50 ms increments both over- and under-predicted shear rates around the 500 s⁻¹ threshold. We concluded that data collection should ideally be done in 10 ms intervals for this heart rate and systolic duration.

Finally, shear rates were calculated along a 91 mm section of the lower device wall at the 12 µm/pixel PIV magnification. Data was collected in 7% increments for all beat rates and systolic durations to permit comparisons at the same points in the cardiac cycle. Shear line plots showed substantial regions of low shear rates, under 500 s⁻¹, present for a large percentage of diastole at 75 bpm, and for several time steps for all beat rates in systole. Changes in flow magnitude, seen in earlier global studies, were examined through normalized shear contour plots. Shear rates were shown to reasonably scale with the square of the average inlet velocity. This normalization was appropriate for lower shear ranges, with larger deviations in higher shear regions present for some
locations within the pump. This normalization can be useful when predicting the potential for thrombus formation for differing operating conditions. It is important to note, however, that the amount of thrombus observed on explanted animal trial blood sacs is likely a function of the range of beat rates and systolic durations seen in vivo. While lower beat rates may result in pump regions exposed to shear rates less than 500 s\(^{-1}\), minor increases will produce shear rates well above this threshold at the same locations. These changes may have consequential effects on thrombosis within our pulsatile device, although this effect is difficult to understand with the beat rate variability that is present during animal trials. Regardless, we feel that if the shear exceeds 500 s\(^{-1}\) at some time point during the cardiac cycle, this is sufficient to prevent thrombus deposition from developing. Operating the pump at a single beat rate and systolic duration, regardless of inlet pressure, may provide more insight into this relationship.

### 5.2 Future Work

In characterizing shear rate distributions along the lower 50 cc pump wall, it becomes clear that changes in flow within the boundary layer could be important. We briefly investigate the effects of beat rate and systolic duration on boundary layer flow here. A typical plot, at a location 10 mm along wall E of Figure 4-24, is shown in Figure 5-1. The plot corresponds to 64% of diastole for 75 bpm and 38% systolic duration. No effort has been made here to resolve the velocities into tangential and normal components. Evidence of a turbulent boundary layer however, is present. Future work to
measure and decompose these vectors might provide insight into the influence of operating conditions on velocity profiles near the wall as a function of time and space.

Figure 5-1: Velocity line plot 10 mm along wall E of Figure 4-24. Velocity values correspond to 64% of diastole for the 75 bpm heart rate and 38% systolic duration.
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Appendix A

Spatial Shear Rates at High Magnification
Appendix B

Beat Rate and Systolic Duration Flow Maps
Appendix C

High Magnification Wall Shear Rate Contour Maps

Wall A

75 bpm, 38% systolic duration
115 bpm, 45% systolic duration

150 bpm, 50% systolic duration
Wall B

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall C

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall D

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall E

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall F

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall G

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall H

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall I

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall J

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall K

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall L

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall M

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall N

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration
Wall O

75 bpm, 38% systolic duration

115 bpm, 45% systolic duration
150 bpm, 50% systolic duration