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A Thrombus Susceptibility Comparison of Two Pulsatile Penn State 50cc Left Ventricular Assist Device Designs

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Abstract

Left ventricular assist devices (LVADs) have proven successful as bridge to transplant devices for patients awaiting donor organs. While survival rates continue to increase, destination therapy remains hindered by thrombus formation within the device. Research has shown that thrombosis is correlated to the fluid dynamics within the device and may be a result of sustained shear rates below 500 s^{-1} on the polyurethane blood sac used in the Penn State pulsatile LVAD. Particle image velocimetry is used to compare flow within two 50 cc LVAD designs to assess fluid patterns and quantify wall shear rates in regions known from *in vivo* studies to be susceptible to thrombus formation. The two designs differ in their front face geometry. The V-1 model has an outward facing “dome” whereas the face of the V-2 model is flat. A thrombus susceptibility metric, which uses measured wall shear rates and exposure times, was applied to objectively compare pump designs over the entire cardiac cycle. For each design, there are regions where wall shear rates remained below 500 s^{-1} for the entire cardiac cycle resulting in high thrombus susceptibility potential. Results of this study indicate that the V-2 device had an overall lower propensity for thrombus formation in the current region of interest.

Keywords

ventricular assist device; particle image velocimetry; fluid mechanics; thrombosis

Introduction

Approximately 5.7 million Americans are afflicted with heart failure (HF), with a reported 670,000 newly diagnosed patients each year.¹⁵ Additionally, HF contributed to 300,000 deaths and 2.4–3.5 million hospitalizations per year. Those with advanced stage HF constitute between 1–10% of the afflicted population. While heart transplantation remains the preferred treatment method, the number of donor organs remains constant and limited. The relative contribution of left ventricular assist devices (LVADs) is increasing, both as a bridge to transplant and as a destination therapy.² Along with pharmacological intervention; LVADs help reverse pathological hypertrophy and recover normal myocardial function.³

In 2001, the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) demonstrated the success of LVADs as a means of mechanical circulatory support.¹⁴ The study, conducted by Columbia University, the National Heart, Lung, and Blood Institute, and Thoratec Corporation, concluded that LVADs can significantly extend and improve the lives of end stage HF patients who are

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ineligible for transplantation. The study randomized 129 patients ineligible for transplant into either a LVAD supported group, or a group receiving medical therapy. Those implanted with the HeartMate™ XVE LVAD reported 52% one year survival rates compared to 25% for patients in the control group. Currently, the one year survival rates for the HeartMate™ II device are approximately 85% and therefore are reaching similar outcomes as heart transplantation.⁷

While survival rates continue to improve, several serious side effects continue to limit LVAD usage. In addition to bleeding and infection, thrombosis remains perhaps the most significant long-term complication. The reduction of thrombus formation within the device is clinically relevant due to the consequences of embolization and vascular blockage. Thrombus formation within the LVAD is related to the surface material, topography, and the local fluid mechanics within the device.⁸ Pulsatile LVADs ranging in size from 10–100 cubic centimeters (cc) have been studied by The Pennsylvania State University since the 1970's to help address such complications.

The first Penn State pneumatic ventricular assist pump was implanted at Hershey Medical center in 1976. The Division of Artificial Organs has since been working to reduce the size of the device for adult patients with lower circulation volumes and for pediatric patients. The 70 cc LionHeart™ reached clinical trials in 2001 and showed little clot deposition; however, it was too large for most patients.¹⁸ The 50 cc V-0 device was developed in 2000. This pusher plate driven design is suitable for adult patients with limited chest cavity size and benefits a larger patient population.⁹

Extensive effort has been given to the characterization of thrombosis within the 50 cc device. Thirty day bovine studies were used to test the performance of the device *in vivo*. In 2003, Yamanaka *et al.* performed an *in vivo* study of three such 50 cc implants. Explanted blood sacs were examined for locations where thrombus formation was present.²⁵ In parallel, a particle image velocimetry (PIV) study by Hochareon *et al.* found a strong correlation between *in vivo* clot deposition and corresponding wall locations where flow remained static.¹⁰ Particular interest was given to regions where wall shear rates remained below 500 s^{-1} across the cardiac cycle, as this has been shown to promote platelet adhesion and thrombus stability on polyurethane, the blood contacting material in the Penn State VADs.¹²

Platelet activation has been shown to occur during mechanical heart valve closure.⁴ Upon activation, platelets release the contents of stored granules which in turn activate additional platelets. These activated platelets clump together forming a precursor for thrombus formation. Therefore, regions experiencing long residence times are susceptible to platelet deposition. Baldwin *et al.* previously noted that a strong diastolic jet is necessary to produce the rotational flow pattern which leads to washing across the device.¹ As such, Kreider *et al.* considered the effects of altering the orientation of the mitral valve to study the effects that this would have on the formation of the diastolic jet within the V-0 device. Rotation of the mitral valve 30° toward the fluid region and away from the pusher plate was found to increase the duration of wall washing in thrombus-prone regions.¹³

Although the ideal valve orientation resulted in improved flow characteristics, there were still regions exposed to sustained shear rates below 500 s^{-1} . The V-2 model was developed to reduce flow separation within the original V-0 model as observed by Oley *et al.* in 2005.²¹ Alternative design modifications were then considered for the 50 cc device. These changes were made with the intent of further directing flow toward the walls to promote extended washing. The three designs, (V-2, V-3, and V-4) were identical except for the location and orientation of their outlet ports. Flow characteristics were largely similar,

however poorer wall washing and rotational flow were observed for V-3 and V-4. The V-2 model, with its parallel ports, displayed the most desirable flow characteristics and was chosen as the design to pursue further.²⁰

Most recently, Nanna *et al.* explored the flow changes resulting from altered operating conditions for the V-2 model.¹⁹ Shear rates were found to reasonably scale with the kinematic viscosity over the square of the average inlet velocity for beat rates ranging from 75–150 bpm and systolic durations of 38–50%. Results of this work also helped to quantify the resolution dependent accuracy of PIV. In addition, the necessary frequency of PIV data collection was determined to best capture the pulsatile flow field within the 50 cc LVAD.

While previous studies have focused on modifications to the port regions and valve orientation, little has been done to investigate how geometric changes to the front wall of the device may alter thrombus potential. In this study, we seek to identify the best design (V-1 and V-2) to move forward. Near wall measurements have never been investigated for either device; nor have PIV planes normal to the diaphragm of the 50 cc LVAD ever been examined to study a secondary aspect of flow within these devices. The aim of this study is to compare the thrombus potential of these designs under low flow conditions in an *in vitro* setting using PIV.

Materials and Methods

To study the fluid mechanics of the two LVAD geometries, optically clear models were machined from an acrylic block with an index of refraction of 1.49. Both V-1 and V-2, shown in Figure 1a, each have an identical stroke volume of 50 cc. Each have their inlet and outlet ports parallel to the body of the device. The designs differ in the front face, where V-1 has an outward-facing “dome” beginning at the base whereas the face of V-2 is flat. The dome extends 8 mm outward at its greatest depth orthogonal to the front face of V-2. Each model accurately represents the physical dimensions of the pumps used in animal trials. A smooth polyurethane urea (PUU) diaphragm seals the fluid facing side of the acrylic. A polyvinyl chloride pusher plate in turn contacts this diaphragm (Figure 1a). Pulsatile flow is driven by moving the pusher plate into and out of the model by a positive displacement piston system (StarFish Medical, Victoria, B.C.). The waveform has a peak to peak amplitude of 23 mm to ensure that the pusher plate fully detaches from the diaphragm at the end of diastole. A rate of 75 bpm with 38% systolic duration was maintained for all experiments. Full detachment of the diaphragm to the pusher plate was verified by high speed video. This condition is necessary to limit fatigue of the blood sac material *in vivo* and is a good representation of the *in vivo* operation of the pump.

Bjork–Shiley Monostrut tilting disk valves were placed at both the inlet and outlet ports to maintain unidirectional flow through the device. The inlet valve has an outer diameter of 23 mm while the outlet valve has an outer diameter of 21 mm. The inlet valve strut is rotated 30° from the horizontal axis of the pump while the outlet valve strut is positioned parallel to the horizontal axis (Figure 1c). These angles were chosen based upon the filling characteristics observed by Kreider *et al.*¹³

The models were independently incorporated into a mock circulatory flow loop (Figure 1d) developed by Rosenberg *et al.*²³ The loop contained atrial and arterial compliance chambers. The atrial chamber, located upstream of the LVAD, maintained systolic/diastolic pressures of 30/5 mmHg. The arterial chamber maintained pressures of 120/80 mmHg approximately 254 mm downstream of the LVAD. These pressures were monitored by pressure transducers (Argon Medical Devices, Athens, TX) at a tap in each compliance chamber. The flow loop also included two parallel plates to adjust the Tygon tubing diameter downstream of the

arterial compliance chamber and in turn alter systemic resistance. A fluid reservoir represents the venous blood volume and also serves to mix PIV seed particles. Ultrasonic flow probes (Transonic Systems, Inc., Ithaca, NY) were located at the inlet and outlet ports of the LVAD. All pressure and flow waveforms were monitored by a 1 MHz data acquisition board (IOtech, Inc., Norton, MA) connected to a PC.

A shear thinning, 40% hematocrit blood analog composed of water, glycerin, xanthan gum, and sodium iodide was used in the flow loop.¹⁶ The viscoelastic properties of the fluid were measured over a shear range of 0–1000 s⁻¹ using a Vilastic-3 viscoelasticity analyzer (Vilastic, Austin, TX). The fluid matches the refractive index of the acrylic model and was seeded with 10 µm hollow glass spheres (Potters Industries, Inc., Valley Forge, PA) for PIV measurement. The particles effectively follow fluid motion within the device as the Stokes number is $\ll 1$ for all measurement conditions.⁶

To study the fluid mechanics as a function of the LVAD geometry, a 2D particle image velocimetry system was used. The system incorporated a Nd:YAG laser as part of a Gemini PIV 15 system (New Wave Research, Inc., Fremont, CA). The system directed two 532 nm polarized laser beams through spherical and cylindrical lenses to produce a light sheet that is 250 µm thick at the lens focal length of 500 mm. A two megapixel CCD camera (TSI, Inc., Shoreview, MN) with a 50 mm F1.8 lens (Nikon Corporation, Tokyo, Japan) was used for image capture. Laser pulsing and image capture were coordinated through a LaserPulse Synchronizer (TSI, Inc., Shoreview, MN). The synchronization of camera exposure and laser pulses for each set of images was controlled through InsightTM 3G software (TSI, Inc., Shoreview, MN).

Two imaging orientations were used to measure wall shear rates across the lower front wall of each LVAD (Figure 1). The box in Figure 1a contains the portion of the pump's flow field imaged during normal plane analysis at nine distinct planes at a resolution of 30 µm/pixel. The box in Figure 1b contains the region imaged for global flow visualization at the 1 mm parallel plane at a resolution of 45 µm/pixel. Figure 1b also contains the locations of the nine normal planes. For the normal planes, all distances (mm) are measured from the outer edge of the inlet port. The plane labeled 34.25 mm is the center of the pump body. The 9.75 mm plane is the center of the inlet port while the 59.6 mm plane is the center of the outlet port. The 4.87 mm plane is located midway between the center and outer edge of the inlet port. The 19.5 mm plane is the inner edge of the inlet port. The 50.8 mm plane is the inner edge of the outlet port, and the 64 mm plane is midway between the center and outer edge of the outlet port.

For all planes of interest, data was collected in 7% intervals for each of diastole and systole. This interval was a compromise between temporal accuracy and data collection time.¹⁹ Synchronization of laser pulse and image capture was triggered by a set delay from the voltage rise of the inflow waveform during each cardiac cycle. Two hundred image pairs were collected for every interval for statistical accuracy.²² Following data collection, all images were masked to block background pixels unrelated to flow.

An InsightTM 3G processing algorithm divided each image pair into small interrogation regions (IR) of 32 × 32 pixels. The displacement of the glass spheres, within each IR, was analyzed with a cross correlation method to observe changes in particle location from one image to the next. Using a fast Fourier transform correlation engine, Gaussian peak detection algorithm, and a recursive Nyquist grid, displacement vectors were determined. For the recursive Nyquist grid, the first processing pass computes the vector field at the starting IR dimension which is 64×64 pixels with a Nyquist grid engine at 50 % overlap grid spacing. Results of the first pass are used to optimize the spot offsets for the second

processing pass. The offset is equal to the integer pixel displacement measured in the first processing pass so that subsequent processing passes would have a peak location within a half pixel of the correlation center.

For each IR, displacement vectors were divided by the laser pulse separation time to produce velocity vectors for the entire flow field. An Insight™ 3G vector conditioning method was used to replace invalid vectors with the median of neighboring valid vector velocities. These invalid counts could result from a number of factors including out of plane flow, low particle displacement, or large flow gradients.²² To further limit invalid IR vectors, laser pulse separation was varied from 100–1000 μ s to best fit the changing pulsatile flow field throughout the cardiac cycle. Pulse separation was optimized until average particle motion between frames is half an IR to ensure peak locking does not occur.²² The flow field is then processed for a single image captured at this pulse separation to ensure that greater than 80% of vectors are valid.

The velocity vectors for all 200 image pairs were averaged to obtain a velocity flow field for each region. The averaged flow field is then put into a first-order wall shear rate algorithm, previously described by Hochareon *et al.*¹¹ This algorithm divides the near wall tangential component of velocity by the normal distance to the wall for each IR centroid. The no-slip boundary condition was applied along the wall.

Error Analysis

Cooper *et al.* determined that we can locate the wall to roughly a half pixel using image intensity gradients.⁵ At the resolutions of 30 μ m/pixel and 45 μ m/pixel, the nearest point to the wall in which we can calculate wall shear rate is 96 μ m and 144 μ m, respectively.¹⁹ The wall shear rate calculation is resolution dependent, as velocities and wall location can be more accurately resolved at higher magnifications.¹⁹ Therefore, measured wall shear rates were verified with high magnification PIV measurements of 12 μ m/pixel.

For data that are not pixel locked, we can estimate the minimum velocity resolution to 0.1–0.2 times the spatial resolution divided by the laser pulse delay.²² Pulse delays were varied by plane and location within the cardiac cycle in order to optimize particle displacements. Therefore, for the PIV resolution of 30 μ m/pixel, the maximum velocity resolution achievable is 0.003 m/s to 0.006 m/s. At a resolution of 45 μ m/pixel, maximum velocity resolution is 0.0045 m/s to 0.009 m/s; assuming a low velocity, planar flow, where a maximum pulse separation of 1000 μ s is used. Histograms of velocity magnitudes were plotted using Tecplot 360 (Tecplot, Inc., Bellevue, WA) to verify that peak locking did not occur. Peak locking (velocity gradients biased towards 0 m/s) results when estimating particle displacements to sub-pixel accuracy.

PIV error analysis has shown that measurements are sub pixel accurate up to 10–20% of the spatial resolution. As such, the bias error with the wall shear calculation is $\pm 20\%$.^(5,22) The precision error was calculated to gain an estimate of our repeatability. To calculate this, an array of velocity values corresponding to a distinct point within the flow field were extracted (one for each of the 200 images acquired for a given time step). This was done for 10 distinct points within three different time steps containing 200 images each. A student t-distribution at a 95% confidence interval was then performed to assess the difference in velocity between 200 images in a given time step for each distinct point chosen. The average precision error was found to be 1.8%. Using the bias error (20%) along with the average precision error (1.8%), we estimate our overall uncertainty to be approximately 20.1% (as the Euclidean norm, rounded to one decimal place). This suggests that repeatability is not a dominant source of error in our measurements.⁵

Data was also checked for sample loss which could occur due to strong three dimensional flow. This was done through Tecplot 360 by reviewing plots of vector counts and looking for dropout in the 200 samples at each acquired point. This was limited experimentally by altering the pulse separation until greater than 80 percent of valid vector counts were obtained prior to data collection at every temporal interval. Sample loss was not an issue for this data.

Results and Discussion

In order to investigate the thrombus susceptibility of the two pump designs, near wall velocity measurements were made for planes both normal and parallel to the diaphragm of the device (Figure 1). A parallel plane, 1 mm from the front face of the LVAD was used to visualize near wall flow patterns. Normal planes spaced throughout the device were then used to calculate wall shear rates from near wall velocity vectors along these lines. In Figure 3, there is a comparison at four times in diastole, 1 mm into the flow field, as shown by the box in Figure 1b. The times are, from left to right, 7, 35, 64, and 92 % of diastole, respectively (Figure 2). Flow visualization for V-1 is shown in Figure 3a while the same time points for V-2 are given in Figure 3b. At the 1 mm plane, the inlet jet for each model is blocked from reaching the base of the pump by a secondary jet moving perpendicular to the downward jet, as is visible at 35% diastole. This secondary jet moves right to left across the lower front face of the pump and originates from a plane further from the front wall. The secondary jet, thought to be caused by the 30° rotation of the inlet valve, reached a maximum velocity of 0.85 m/s for the V-1 model and 1.08 m/s for the V-2 model, both at 50% of diastole.

Baldwin *et al.* noted that a strong diastolic jet is necessary to produce the rotational flow pattern which leads to washing of the body of the device.¹ The V-2 design had a tighter, more centrally located center of rotation throughout diastole compared to the V-1 model (Figure 3). The center of rotation for the V-1 model wanders throughout the pump body over the course of diastole. The tighter center results in a stronger rotational flow pattern for the V-2 model. The tapering of the left side of the V-1 jet may be due to a stagnant flow region within the dome of the V-1 model. The inlet jet for the V-1 model reached a peak velocity of 1.44 m/s while that of the V-2 model reached a peak velocity of 1.35 m/s, both at 42% of diastole.

Figure 4 displays a comparison of 7, 35, 64, and 92% of systole (Figure 2) for each pump for V-1 in Figure 4a and V-2 in Figure 4b. During systole, flow intensifies within the outlet port region as the pusher plate forces the diaphragm into the fluid chamber. Here, V-1 reached a maximum velocity of 0.73 m/s while V-2 peaked at 0.74 m/s, both at 50% of systole (not shown). There are less noticeable differences in flow patterns between the two pumps during the systolic cycle at the 1 mm parallel plane.

Nine planes normal to the front face of the LVAD were used to compare wall shear rates between the two pump designs (Figure 1b). Three planes were located within each port with an additional three planes between the ports. Contour plots were created to gain an overall perspective of wall shear for both diastole and systole. Comparison between the two pumps was performed by plotting raw wall shear values as a function of time in 5 mm wall location increments along each plane. These 5 mm increments for comparison were chosen to provide a field of measurements across the entire lower region of the pump. The origin of the wall shear calculation begins along the base of the pump at a plane 10.16 mm from the front face (indicated by the dark circle in Figure 1a). This plane marks the location where the diaphragm seals the acrylic chamber.

The V-1 model surpassed the 500 s^{-1} threshold for thrombus stability and platelet adhesion¹² for 31 of 45 measured spatial locations during diastole and 19 of 45 for systole. The V-2 model surpassed the threshold for 42 of 45 spatial locations during diastole and 24 of 45 for systole. Overall, V-2 experienced higher peak shear magnitudes, compared to V-1, for 29 of the 45 measured spatial locations during diastole and 35 of the 45 for systole.

Figure 5a displays a cross-sectional view of the LVAD at the 9.75 mm plane (the center of the inlet port). The lightened region indicates the flow field examined at a PIV resolution of $30 \mu\text{m}/\text{pixel}$. The black line indicates the region of the wall where the wall shear calculation was performed. In Figure 5b, there is a comparison of wall shear rate contour plots for the inlet region of each pump for the extent of diastole. Results are displayed as a percentage of the diastolic cycle from 0 to 496 ms. In these plots, the raw shear values are normalized by 500 s^{-1} : a value of 1 corresponds to 500 s^{-1} . The blue hues indicate shear resulting from a downward moving flow. The yellow to red hues indicate shear resulting from an upward moving flow. In Figure 5b (along with Figure 7b and Figure 9) each normal plane is separated into three regions. A technique detailed in reference [11] allows the user to manually indicate the wall location and apply a fifth order polynomial regression to reconstruct the wall geometry. Due to the complex geometry of the LVAD face, reconstruction becomes less challenging computationally if one large complex wall is broken into three consecutive walls; each having a less complex geometry than the original wall.

The sudden reduction in shear rate (approximately 1/3 of the wall from the base at the 4.87 and 9.75 mm planes in Figure 5b) is the result of the horizontal jet, seen in Figure 3, blocking the downward vertical jet. A positive shear can be seen for both pumps (Figure 5b) caused by the upward component of the horizontal jet visible at 35% diastole in Figure 3. This positive shear intensifies for measurement planes close to the inner edge of the inlet port. This is the result of the orientation of the inlet valve and curved geometry of the pump base. In comparison, the V-2 pump exhibits higher wall shear rates toward the upper wall region of the 19.5 mm plane compared to the V-1 model. This is a reflection of the inlet jet profile seen in Figure 3b. The measured shear rates are similar for both models at the 4.87 and 9.75 mm planes.

Figure 6 displays a comparison of several locations of interest in the inlet regions of both pumps over the entire cardiac cycle. Figure 6a shows a comparison of the 5 mm wall location along the 4.87 mm plane (Figure 1b). At this location, the V-2 pump surpasses the 500 s^{-1} indicator whereas the V-1 reaches a maximum shear rate magnitude of only 439 s^{-1} over the entire cardiac cycle. For each pump, flow reverses direction along the wall for a brief time starting at 28% of diastole. The highest shear rate measured for either pump was found at the 30 mm wall location of the 9.75 mm plane, as seen in Figure 6b. At this location, V-1 reached a peak shear magnitude of 5595 s^{-1} which surpassed the peak shear of 4184 s^{-1} measured at this location for the V-2 design.

During systole, there is little washing within the inlet port region for either pump design. Over the 5 mm increments measured, there was only one instance for either pump where shear rates exceeded 500 s^{-1} for more than two consecutive time points. Each occurred along the 4.87 mm plane. Neither pump surpassed a shear rate of 500 s^{-1} during systole at the 19.5 mm plane.

Figure 7a displays a cross sectional view of the 34.25 mm plane which corresponds to the center of both LVAD designs. Figure 7b displays a comparison of wall shear rates for each design over the course of diastole. While shear rates are similar over the 26.9 mm plane, there are significant differences along the 34.25 and 42.5 mm planes. Along these lines, the

V-2 pump experiences significantly higher shear rates in the middle to upper imaging region of the lower front wall. This can be observed at 35% diastole in Figure 3b where velocity vectors are moving upward more strongly along the front face within the body of the pump compared to the same region for V-1 (Figure 3a).

The V-2 design also has higher shear rates over the course of systole for both the 34.25 and 42.5 mm planes compared to the V-1 design (Figure 1b). Figure 8 displays raw wall shear rates plotted over the entire cardiac cycle for both designs 15 mm from the base of the pump for the a) 34.25 and b) 42.5 mm plane. At this location, V-2 showed 131 % higher peak shear values over V-1 in Figure 8a and 41% higher values in Figure 8b.

Figure 9 displays the wall shear contour plots for the outlet port region over the entire cardiac cycle. Wall shear rates measured during diastole are plotted in Figure 9a (0–496 ms) and systole in Figure 9b (496–800 ms). The outlet port is the only region, for either pump, where significant washing occurs during systole. Flow patterns are similar for both pump designs in this region, with higher overall shear rates measured for the V-2 design.

While the wall shear contour maps can be useful for identifying areas of high or low shear rates, comparisons between the two LVAD models in relation to thrombus potential are subjective. A more objective method of quantifying thrombus susceptibility was developed by Medvitz through a computational fluid mechanics study of an adult size VAD.¹⁷ This method was recently employed by Roszelle to quantify weaning and valve orientation studies of the Penn State pediatric ventricular assist device.²⁴ The thrombus susceptibility potential (TSP) relates several variables to calculated wall shear rates to produce a value between 0 and 1; where 1 designates a very high potential, and 0 a very low potential. The TSP equation is given by:

$$TSP = 1 - \sum_0^N \frac{\Delta t \gamma_w}{\gamma_{cutoff} t_{crit}} \cdot \frac{e^{((\gamma_w - \gamma_{peak})/(\lambda_{cutoff} - \lambda_{peak}))} - 1}{e^1 - 1} \quad (1)$$

For application to PIV measurements, N is the number of time steps taken through the cardiac cycle and Δt is the amount of time between acquisitions. The calculated wall shear rate is indicated by γ_w . The γ_{peak} was set to 500 s^{-1} as this has been established as a threshold value for thrombus deposition on materials similar to that used in the Penn State LVAD [10]. The γ_{cutoff} value was set to 1000 s^{-1} as it is an established experimental value for inhibition of platelet deposition by Balasubramanian.² The t_{crit} value was chosen to be twice the length of the PIV Δt to reduce the effect of a high shear value at a single time-step. Equation 1 was applied to all wall locations measured by normal plane analysis for both pump designs. The TSP at each location is summed over the entire cardiac cycle and then plotted to determine which areas along the surface have high thrombus susceptibility. An assumption of the TSP is that platelet activation occurs upon entry into the device through the mitral valve. Low shear regions within the device are considered to be accumulating zones for deposition.

Results of the TSP are given in Figure 10 for the inlet port, Figure 11 for the body, and Figure 12 for the outlet port region. At the 4.87 mm (Figure 10a) and 9.75 mm (Figure 10b) planes, the steep rise in TSP near the base (for both pumps) can be traced to the abrupt decrease in shear rate seen in Figure 5b at these locations during diastole. This is the result of the inlet jet being blocked from penetrating to the device base. At these planes, there is minimal washing during systole with γ_w less than γ_{peak} . Systolic flow therefore had little effect on the decreasing TSP near the base of the pump at these locations. At the 19.5 mm plane (Figure 10c), V-2 has a reduced TSP at both 5 to 10 mm and 25 to 30 mm from the

base compared to V-1. The reduced TSP near the upper limits of the measurement area is the result of the diastolic jet reaching further into the pump body. The lowered TSP 5 to 10 mm from the base is the result of the stronger secondary jet moving upwards along this plane. Both of these characteristics are clear from the flow visualization at 35% diastole in Figure 3b.

Within the body region (Figure 11), the V-2 model showed an overall reduced TSP across all three planes of interest (with the exception of two small regions within the 34.25 (Figure 11b) and 42.5 mm (Figure 11c) planes). Aside from several singularities, both pumps measured γ_w less than γ_{peak} for the extent of systole. As a result, the TSP within the body region is largely a function of diastolic washing, as it is in the inlet port. The greatest discrepancy between the designs occurred at the 42.5mm plane beginning approximately 10 mm from the base. Here, the V-2 model had a TSP of 0 compared with a TSP of 1 for V-1 extending to the top of the measurement plane. The difference in TSP between both designs is reflected in the diastolic contour plots of Figure 7b.

The outlet port region (Figure 12) is the first to exhibit the effect of measured γ_w during systole as a major influence on calculated TSP. This is evident from the measured γ_w contour plots in Figure 9 for both pumps over the entire cardiac cycle. At the bottom of 50.8 mm plane (Figure 12a), significant flow separation exists γ_w less than γ_{peak} for both designs resulting in over the entire cardiac cycle. This is translated into a very high calculated TSP for both designs over the first 5–10 mm from the base. Past this location, TSP is reduced for both pumps, but to a much greater extent for V-2. Overall, at the 59.6 (Figure 12b) and 64 mm (Figure 12c) planes, the TSP is near 0 for both pumps over the majority of the imaging field aside from a brief spike at the base of the pump.

The TSP calculation was also applied to wall shear rates calculated along the perimeter of the wall for the 1 mm parallel plane. The results of this calculation are displayed in Figure 13. The origin begins at the upper right corner of the interrogation region as shown by the black curve in Figure 1b. The calculation progresses clockwise around the wall, ending at the upper left corner of the outlet side. Over the region measured, the V-1 model has a much higher TSP. This can be attributed to the “dome-like” front wall creating flow separation. Both pumps exhibit elevated TSP near the upper corner of the inlet port where the diastolic jet does not maintain close contact with the wall. Rotational flow reattaches past this region for each pump. For V-1, the rotational field detaches once again approximately 40 mm circumferentially from the origin and remains detached. Upon reattachment, the V-2 model maintains strong washing characteristics until approximately 80 mm circumferentially from the origin. Here, there is a separation of rotational flow persisting nearly 10 mm until it reattaches once again. The remainder of the outlet wall is the sufficiently washed. The high TSP (for V-2) seen in this 80–90 mm location corresponds to the same detachment region near the base of the 50.8 mm normal plane (Figure 12a). This indicates a highly susceptible region for the V-2 model as the wall is minimally washed for both measured components of flow.

Conclusions

Two LVAD model geometries were extensively studied using PIV. A wall shear rate calculation and thrombus susceptibility model were applied for two measured components of flow along the base and lower front wall of each model. Overall, V-2 showed improved washing characteristics when compared to the dome-like front face of the V-1 model. The effects of altered geometry were most noticeable during diastole where V2 exhibited a tighter center of rotational flow. While peak inflow was nearly identical in terms of velocity magnitude, the front face of V2 led to stronger shearing conditions. The TSP calculation

provided a means to objectively compare both models. Although the V-2 model showed improved characteristics, susceptible areas were identified; specifically along the base between the 42.5 and 50.8 mm planes. The body region, between the ports, was proven to be by far the most susceptible, along with the base of the pump for all normal planes analyzed. The base of the pump does however experience the majority of its washing from the component of flow parallel to the front face of the device. This parallel component of washing was markedly reduced for the V-1 design.

While useful, the TSP calculation is not an ideal indicator of thrombus potential for a given device. Based upon Virchow's triad, risk factors include: the local fluid mechanics, properties of the blood, and properties of the blood contacting surface. The TSP is a reasonable means of analysis as the blood contacting sac material is the same for all Penn State LVADs. Additionally, patients are typically administered similar anti-coagulants. This leaves local fluid mechanics as the variable. Variables used for the TSP calculation, such as γ_{peak} , γ_{cutoff} and t_{crit} , are currently being studied through platelet adhesion studies to more accurately define them for use with the sac material.

Bovine experiments are characterized by beat rates ranging from 75–150 bpm (systolic durations 38–50%). The TSP values within this work were generated based upon wall shear rates calculated from flow conditions within each device operating steadily at 75 bpm. The TSP found within this study should be viewed as a worse case scenario for the LVAD operating under low flow conditions. A primary assumption for the TSP metric is that platelet activation occurs upon entry into the device through the mitral valve⁴ and that low shear regions within the device are accumulating zones for deposition. Regions along the LVAD wall where the TSP transitions from a very low probability to a very high probability could prove to be most susceptible. This point would be indicative of a location where a transition of high shear to low shear occurs. Platelets activated in the high shear regions may be most likely to adhere in nearby low shear regions. More complete thrombosis models, with stronger theoretical grounding, are being developed concurrently. At the present time, the V-2 model has been shown to be less susceptible to thrombi and platelet adhesion. As such, this model should continue to move forward.

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References

1. Baldwin JT, Deutsch S, Geselowitz DB, Tarbell JM. LDA measurements of mean velocity and reynolds stress fields within an artificial heart ventricle. *ASME J Biomech Eng.* 1994; 116:190–200.
2. Balsasubramanian V, Slack SM. The effect of fluid shear and co-absorbed proteins on the stability of immobilized fibrinogen and subsequent platelet interactions. *J Biomater Sci Polymer.* 2002; 13:543–561.
3. Birks EJ. Left ventricular assist device and drug therapy for the reversal of heart failure. *The New England J of Medicine.* 2006; 355:1873.
4. Bluestein D, Yin W, Affeld K, Jesty J. Flow-induced platelet activation in mechanical heart valves. *J Heart Valve Dis.* 2004; 13:501–508. [PubMed: 15222299]
5. Cooper BT, Roszelle BN, Long TC, Deutsch S, Manning KB. The 12 cc Penn State pulsatile pediatric ventricular assist device: fluid dynamics associated with valve selection. *J of Biomechanical Engineering.* 2008; 130:041019.
6. Crowe, CT.; Sommerfeld, M.; Tsuji, Y. *Multiphase flows with droplets and particles.* CRC Press; Boca Raton, FL: 1998.

7. Deng MC, Ardehali A, Shemin R. Relative roles of heart transplantation and long-term mechanical circulatory support in contemporary management of advanced heart failure. *European J of Cardio-Thoracic Surgery*. 2011; 40:781–782.
8. Deutsch S, Tarbell JM, Manning KB, Rosenberg G, Fontaine AA. Experimental fluid mechanics of pulsatile artificial blood pumps. *Annual review fluid mechanics*. 2006; 38:65–86.
9. Hochareon P, Manning KB, Fontaine AA, Tarbell JM, Deutsch S. Fluid dynamic analysis of the 50cc Penn State artificial heart under physiological operating conditions using particle image velocimetry. *J of Biomechanical Engineering*. 2004; 126:585–593.
10. Hochareon P, Manning KB, Fontaine AA, Tarbell JM, Deutsch S. Correlation of *in vivo* clot deposition with the flow characteristics in the 50 cc Penn State artificial heart: a preliminary study. *ASAIO J*. 2004; 50:537–542. [PubMed: 15672785]
11. Hochareon P, Manning KB, Fontaine AA, Deutsch S, Tarbell JM. Wall shear-rate estimation within the 50cc Penn State artificial heart using particle image velocimetry. *J of Biomechanical Engineering*. 2004; 126:430–437.
12. Hubbell J, McIntire L. Visualization and analysis of mural thrombogenesis on collagen, polyurethane and nylon. *Biomaterials*. 1986; 7:354–363. [PubMed: 3778995]
13. Kreider J, Manning KB, Oley LA, Fontaine AA, Deutsch S. The 50cc Penn State LVAD: a parametric study of valve orientation flow dynamics. *ASAIO J*. 2006; 52:123–131. [PubMed: 16557096]
14. Lietz K, Long J, Kfoury A, Slaughter M, Silver M, Milano C, Rogers J, Naka Y, Mancini D, Miller L. Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era. *Circulation*. 2007; 116:497–505. [PubMed: 17638928]
15. Lloyd-Jones D, Adams R, Carnethon M. A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009; 119:21–181.
16. Long JA, Undar A, Manning KB, Deutsch S. Viscoelasticity of pediatric blood and its implications of the testing of a pulsatile pediatric blood pump. *ASAIO J*. 2005; 51:63–66.
17. Medvitz, RB. PhD Thesis. The Pennsylvania State University; 2008. Development and validation of a computational fluid dynamic methodology for pulsatile blood pump design and prediction of thrombus potential.
18. Mehta S, Pae W, Rosenberg G, Snyder A, Weiss W, Lewis J, Frank D, Thompson J, Pierce W. The LionHeart LVD-2000: a completely implanted left ventricular assist device for chronic circulatory support. *The Annals of Thoracic Surgery*. 2001; 71:156–161.
19. Nanna JC, Navitsky MA, Topper SR, Deutsch S, Manning KB. A fluid dynamics study in a 50 cc pulsatile ventricular assist device: influence of heart rate variability. *J of Biomechanical Engineering*. 2011; 133:10–17.
20. Nanna JC, Wivholm JA, Deutsch S, Manning KB. Flow field study comparing design iterations of a 50 cc left ventricular assist device. *ASAIO J*. 2011; 57:349–357. [PubMed: 21734560]
21. Oley LA, Manning KB, Fontaine AA, Deutsch S. Off-design considerations of the 50cc Penn State ventricular assist device. *Artificial Organs*. 2005; 29:378–386. [PubMed: 15854213]
22. Raffel, M.; Willert, CE.; Wereley, ST.; Kompenhans, J. Particle image velocimetry: a practical guide. Springer; 1998.
23. Rosenberg G, Phillips WM, Landis DL, Pierce WS. Design and evaluation of the Pennsylvania State University mock circulatory system. *ASAIO J*. 1981; 4:41–49.
24. Roszelle, B. PhD Thesis. The Pennsylvania State University; 2010. The 12 cc Penn State pediatric ventricular assist device: a flow visualization study of bridge-to-recovery and weaning.
25. Yamanaka H, Rosenberg G, Weiss WJ. A multiscale surface evaluation of thrombosis in left ventricular assist systems. *ASAIO J*. 2003; 49:222.

Figure 1.

a) Comparison of V-1 and V-2 model geometries and location of pusher-plate. The V-1 model has a curved, outward facing dome beginning near the base of the front wall. The box represents the region of the flow field examined during normal plane analysis. b) Front view of the LVAD face illustrating PIV normal planes of interest along with imaging region for global parallel plane flow visualization (boxed). Colored dots are referenced in Figures 6 and 8 while the curved black line is referenced in Figure 11. c) Valve orientations.¹³ d) Schematic of mock circulatory loop.²⁴

Figure 2. LVAD inflow and outflow waveforms for 75 bpm, 38% systolic duration. Percentages of diastole shown in Figure 3 and for systole in Figure 4.

Figure 3.

Comparison of diastolic flow for a) V-1 and b) V-2 models. Intervals shown, from left to right, are 7, 35, 64, and 92% of diastole. At 75 bpm, the diastolic portion of the cardiac cycle is 496 ms in duration.

Figure 4.

Comparison of systolic flow for a) V-1 and b) V-2 models. Time points shown, from left to right, are 7, 35, 64, and 92% of systole. At 75 bpm, the systolic portion of the cardiac cycle is 304 ms in duration.

Figure 5.

Comparison of wall shear rates normalized by 500 s^{-1} during diastole (100% corresponds to 496 ms) in the inlet region of the pump (the right hand side of Figure 1b). a) A cross sectional view of the 9.75 mm normal plane (lightened region) and wall region (black line) where the shear rate calculation is performed, similarly for the 4.87 and 19.5 mm planes. b) Comparison of wall shear contour plots for both pumps.

Figure 6.

Raw wall shear values measured over the cardiac cycle for a) the 5 mm wall location of the 4.87 mm plane (red dot on Figure 1b) and b) the 30 mm wall location of the 9.75 mm plane (blue dot on Figure 1b).

Figure 7.

Comparison of wall shear rates normalized by 500 s^{-1} during diastole (100% corresponds to 496 ms) in the body region of the pump (the middle of Figure 1b). a) A cross sectional view of the 34.25 mm normal plane (lightened region) and wall region (black line) where the shear rate calculation is performed, similarly for the 26.9 and 42.5 mm planes. b) Comparison of wall shear contour plots for both pumps in the body region.

Figure 8. Raw wall shear values measured 15 mm from the base along the wall over the cardiac cycle for a) 34.25 mm plane (orange dot on Figure 1b) and b) the 42.5 mm plane (green dot on Figure 1b). Peak shear was elevated 131% in a) and 41% in b).

Figure 9.

Comparison of wall shear rates normalized by 500 s^{-1} in the outlet region of the pump (the left hand side of Figure 1b) for a) the diastolic portion of the cardiac cycle (0 to 496 ms) and b) the systolic portion (496–800 ms). Overall, shear rates were elevated for the V-2 design.

Figure 10.

TSP calculation for V-1 (blue) and V-2 (red) within the inlet region for a) 4.87 mm, b) 9.75 mm, and c) 19.5 mm. Location 0 mm corresponds to the base of the pump. A TSP of 1 corresponds to a very high thrombus potential and 0 a very low potential.

Figure 11.
TSP calculation for V-1 (blue) and V-2 (red) within the body region for a) 26.9 mm, b) 34.25 mm, and c) 42.5 mm.

Figure 12.

TSP calculation for V-1 (blue) and V-2 (red) within the outlet region for a) 50.8 mm, b) 59.6 mm, and c) 64 mm.

Figure 13.

The 1 mm parallel plane TSP calculation for V-1 (circle) and V-2 (diamond) calculated for the wall region identified by the black line in Figure 1b. The origin begins at the upper right side of the interrogation region and progresses clockwise to end at the upper left corner of the outlet side.