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A CORRELATIVE STUDY OF FLUID MECHANICS AND EVIDENCE OF THROMBUS FORMATION WITHIN THE PENN STATE 50 CC LEFT VENTRICULAR ASSIST DEVICE

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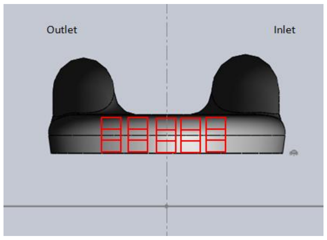
INTRODUCTION

An estimated 82.6 million American adults live with one or more forms of cardiovascular disease and in past years, it was the cause of over 55% of all deaths in the United States, more than any other type of major disease [1]. With a limited number of available donors, heart transplants are seldom an option. As a result, ventricular assist devices (VADs) have become a viable alternative to immediate transplant. Today, VADs are widely used as bridge-to-recovery, bridge-to-transplant and destination therapy devices. Despite past improvements in VAD design, a major complication that continues to arise is thrombus formation within the pump.

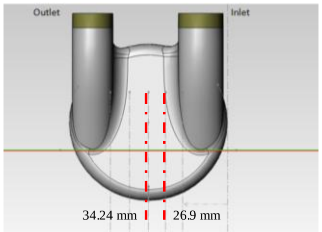
Thrombus formation within VADs is both a fluid mechanics and a biomaterials phenomenon. Previous work by Hubbell and McIntire have shown that thrombus formation is shear dependent and that thrombus formation on polyurethane is more likely in areas experiencing shear rates below 500 s^{-1} [2]. In previous left ventricular assist device (LVAD) models, Hochareon et al. measured low shear in PIV studies that corresponded to areas where macroscopic thrombi were found *in vivo* [3]. While improvements in LVAD design have largely eliminated macroscopic thrombi, precursors to thrombus formation, such as platelets and fibrin, can lead to eventual thrombus formation. The objective of this study is to correlate and quantify areas of similar low shear within a pulsatile V-2 LVAD found *in vitro* with evidence of platelet and fibrin deposition on blood sacs from animal studies.

METHODS AND MATERIALS

The fluid mechanics within an acrylic model of a Penn State 50cc V-2 LVAD were analyzed using particle image velocimetry. Flow of a viscoelastic blood analog was visualized along the front and bottom of the device. Dual-pulsed Nd:YAG lasers (New Wave Research Inc, Fremont, CA) illuminate 10 µm diameter glass particles as a synchronized high speed digital CCD camera (TSI, Inc., Shoreview, MN) acquired images, allowing the tracking of particle displacement over time during systole and diastole. With Insight™ software and post-processing, shear maps were produced for areas on the front and bottom surfaces of the device throughout the entire cardiac cycle. A beat rate of 75 beats per minute (bpm) was used for this study and data was acquired from both the front and bottom surfaces as indicated in Figure 1a.



(a)



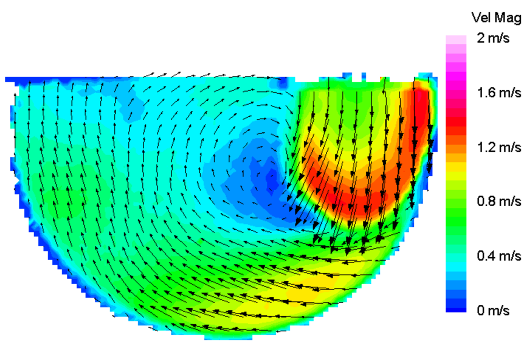
(b)

Figure 1. (a) Regions of the sac removed from the bottom for microscopic evaluation. (b) Front view of the V-2 LVAD indicating planes where PIV data was collected.

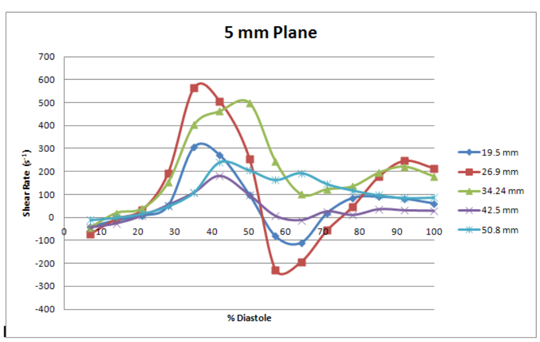
A microscopic surface evaluation, similar to that conducted by Yamanaka et al. [5], was then conducted on the polyurethane blood sac lining a V-2 LVAD explanted after a 30-day bovine study at the Hershey Medical Center. Throughout the study, the device was maintained at a constant beat rate of 75 bpm. At the end of the study, the device was explanted and areas identified as thrombus-prone regions along the front and bottom surfaces were examined for evidence of platelet and fibrin deposition. Samples approximately 5mm by 10mm were removed from the sac at locations corresponding to areas examined with PIV and then were further divided into four sub-sections. Two sub-sections were labeled with primary antibodies specific to surface proteins found on platelets and fibrin. After treatment with fluorescent secondary antibodies, samples were imaged using an Olympus FV1000 confocal microscope at a magnification of 600x. The remaining sub-samples were dehydrated using an alcohol dehydration series, placed in a critical point dryer, sputter coated with gold/palladium and examined using a JEOL 5400 scanning electron microscope (SEM) at a magnification of 500x.

RESULTS AND DISCUSSION

The current inlet valve orientation produces a substantial jet that allows for high shear due to washing along the bottom wall, particularly on the inlet side [4]. This inlet jet is seen below in Figure 2a. As a result, the shear rates observed in those areas of the pump tend to be higher throughout diastole. More specifically, the shear rates at the intersections of the 5mm parallel plane and the 26.9 mm and 34.24 mm normal planes (Figure 1b) are over the 500 s^{-1} threshold (Figure 2b).



(a)

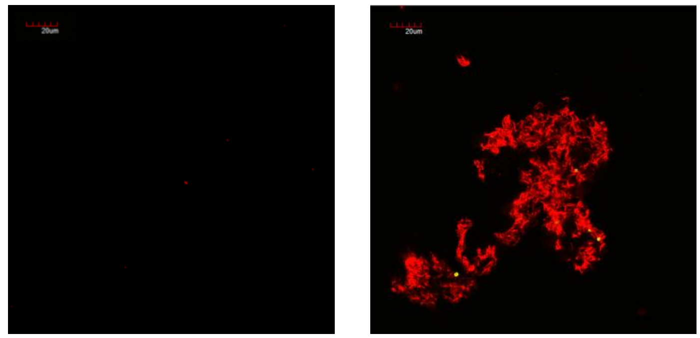


(b)

Figure 2. (a) Flow visualization of the inlet jet during diastole. (b) Shear rates at each normal plane along the 5 mm parallel plane during diastole.

The outlet side of the pump tends to experience lower shears because of jet detachment near the extreme bottom of the pump and subsequent recirculation in the center of the pump as the cycle progresses to systole (Figure 2a). On the same 5 mm parallel plane but at intersections with the 42.5 mm and 50.8 mm normal planes, the shear rate remains below 250 s^{-1} (Figure 2b).

Correspondingly, microscopic surface evaluation supports the hypothesis that more deposition occurs in areas of low shear. In high shear areas near the inlet, low fluorescence activity confirms little platelet and fibrin deposition (Figure 3a). However, the bottom surface on the outlet side shows substantially more evidence of platelet and fibrin deposition. In many randomly selected areas, fibrin clots (red) with occasionally embedded platelets (green) were found on the sac surface (Figure 3b). This demonstrates that this area of the device remains a concern.



(a) **(b)**

Figure 3. (a) An image acquired at the 19.5 mm normal plane and 5 mm parallel plane intersection. (b) An image acquired at the 50.8 mm normal plane and 5 mm parallel plane intersection.

CONCLUSIONS

The study of thrombus formation is multidisciplinary and complicated. The research to date has led to vast improvements in thrombosis from both fluid mechanics and material evaluation perspectives. This data and previous data indicate a strong correlation between regions of low shear and evidence of thrombosis such as platelet and fibrin deposition. In order to continue the progression towards clinical success of these devices, computational fluid dynamics may lead to models that serve as strong thrombosis predictors.

ACKNOWLEDGEMENT

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