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VISCOSITY MATCHING POSITIVELY AFFECTS THE CORRELATION OF PRESSURE-VOLUME LOOPS BETWEEN IN-VIVO AND EX-VIVO MODELS

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ABSTRACT

Using Visible Heart® methodologies, swine hearts were reanimated and implanted with a left ventricular assist device (LVAD). System components were modified to better understand the relationships between the data collected and system conditions. The viscosity of the blood-replacement buffer was increased to a more physiologic value (~3 cP). Pressure-Volume (PV) loop recordings from each heart on the ex-vivo perfusion system more closely mimic loops recorded from the heart in-vivo. This indicates that any system aiming to characterize or examine LVAD performance must include a buffer which mimics blood viscosity or data must be adjusted for the relative viscosity of the buffer.

Keywords: LVAD, ex-vivo heart perfusion, PV loops

1. INTRODUCTION

Left ventricular assist devices (LVADs) are systems implanted in end-stage heart failure patients. Though intended as a bridge-to-transplant therapy, many LVAD patients often live the remainder of their lives with these devices. Due to the improvements of this therapy coupled with the shortage of suitable heart donations and the strict criteria for heart recipients, the number of patients who receive LVADs as a destination therapy is increasing. It is estimated that for every one patient who receives an LVAD as a bridge-to-transplant therapy, there are two patients who receive an LVAD as destination therapy [1]. LVAD implantation and long-term usage is often accompanied with adverse events such as strokes, tissue suctioning, gastro-intestinal bleeding, and/or infection [2]. Furthermore, the current LVAD devices contains a complex system of components that all require further consideration and improvement. Figure 1 illustrates the use of an LVAD.

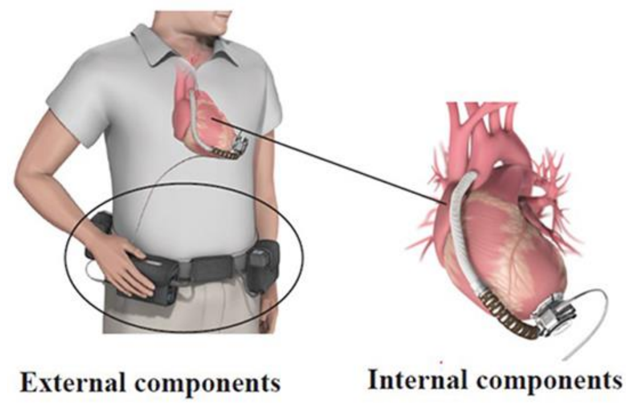

FIGURE 1: Medtronic's HeartWare HVAD system consists of multiple connected components, including: the pump, the outflow graft, the strain support, the controller, and batteries.

With more patients using LVADs for longer periods of time and thus an increase in the numbers of associated adverse events, device improvements are needed. However, effectively testing LVAD algorithms or component updates has been notoriously difficult, due to the complexity of the human cardio-vascular system. The Visible Heart® laboratories has developed a system to perfuse large mammalian hearts with a modified Krebs-Henseleit buffer [3]. This setup allows many complexities of the cardio-vascular system to be preserved for study without compromising the access and ability to implant complex devices and readily adjust system characteristics such as pre-loads and afterloads. However, the LVAD pump is designed to be compatible with blood and so the buffer on the Visible Heart® apparatus should mimic the fluid properties of blood. Therefore. The buffer was further modified with Hydroxyethyl Cellulose (HyC) to alter relative viscosity.

This paper examines the effects of this buffer modification on both the effective buffer clarity and the PV loops data collection from hearts reanimated on the Visible Heart® setup.

2. METHODS

The viscosities of the employed buffers were incrementally modified and examined so to achieve the desired viscosity (~3 cP). Next, swine hearts were reanimated using typical Visible Heart® methodologies [4]. After reanimation, a conductance catheter was inserted into the left ventricle to measure pressures and volumes to create PV loops.

2.1 Viscosity Modification

Several compounds were tested to modify the relative buffer viscosity. However, after further feasibility research HyC was determined to be most efficient for viscosity modifications and, more importantly, without affecting either the visibility of endoscopes within the hearts nor the ability of the buffer to deliver nutrients to the heart tissue (i.e. maintain viabilities).

2.2 Device Implant

During arrest, the sewing rings and outflow grafts were sewn onto each swine heart. After each reanimation, the HeartWare HVAD pump was implanted. Figure 3 shows the device implanted on a swine heart on the Visible Heart® apparatus.

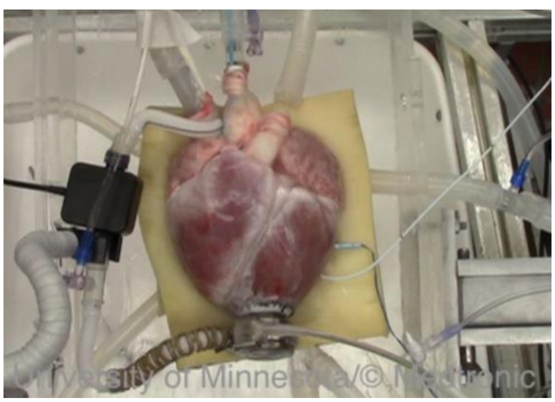

FIGURE 2: Medtronic's HeartWare HVAD consists of multiple connected components including the pump, outflow graft, strain relief, controller, and batteries.

2.3 Data Collection

Pressures and volumes were recorded throughout the cardiac cycle using the conductance catheter and data acquisition system from CD Leycom. This system is and has been used clinically to record PV loops from human patients. Figure 3 shows CD Leycom's software display used to collect and display data from a given heart.

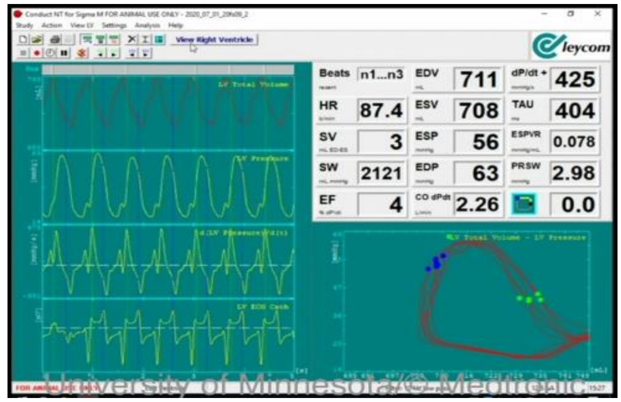

FIGURE 3: Different concentrations of Hydroxyethyl cellulose (HyC) were tested to match blood viscosity as closely as possible..

Each heart was initially reanimated using the commonly employed lower viscosity buffer and PV loops were collected at three different pump speeds; 2400, 2800, and 3200 rpm. Two different afterload conditions were also tested to obtain a trend from the data; 80 mmHg and 100 mmHg. The buffer was then switched to the high viscosity modification and the same data was collected for comparison.

3. RESULTS AND DISCUSSION

Accepted trends in the relationship of pump speed to PV loops were replicated. Significant variations were observed in the collected data when the buffer viscosity was increased. Volume shifts were observed in the PV loops and suction events occurred at conditions not observed with the lower viscosity buffer.

3.1 Viscosity Modification

Figure 4 shows the deduced curve of percentage concentration of HyC related to assessed buffer viscosity. As the viscosity increases exponentially, it was most efficient to use this additive and not impair overall heart function.

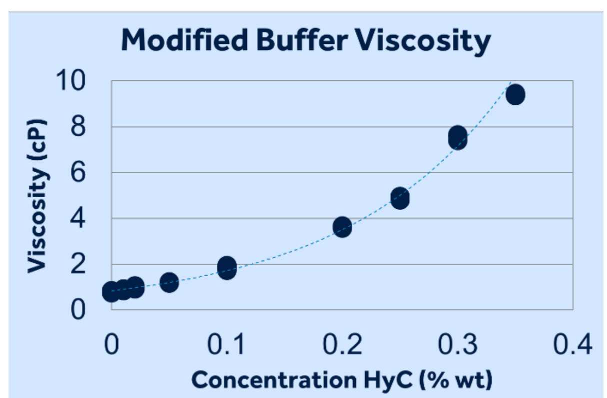

FIGURE 4: Different concentrations of Hydroxyethyl cellulose (HyC) were tested to match the viscosity of blood as closely as possible.

The heart was observed to decrease its functional abilities at viscosities higher than 3 cP due to limiting coronary flow. This is most likely due to the buffer's inability to carry oxygen as efficiently as red blood cells and so decreased fluid flow through the coronary arteries causes decreased oxygen delivery and therefore decreased function of the myocardium.

The clarity of the buffer was not significantly affected by the addition of HyC to increase viscosity; i.e. endoscopic camera views remained unobstructed.

3.2 PV Loops

Trends observed on the Visible Heart® apparatus were in line with those accepted clinically. Figure 5 shows the accepted trend for PV loops with an increase in LVAD speed [5]. Pressures, volumes, and morphologic data trends were replicated.

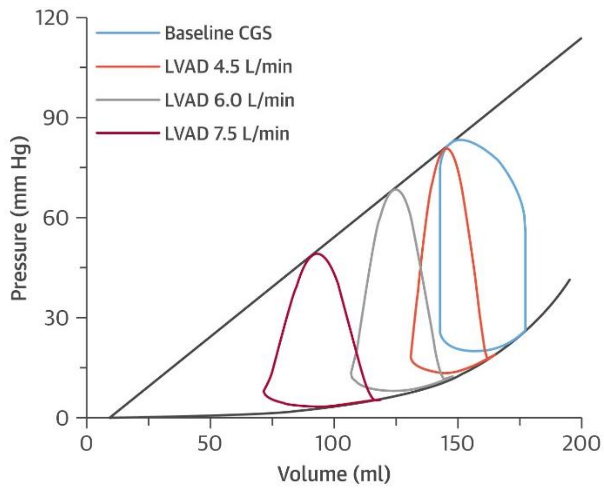

FIGURE 5: As LVAD speed increases, volume and pressure changes decrease.

Figure 6 shows the trend observed using data collected on the Visible Heart® apparatus.

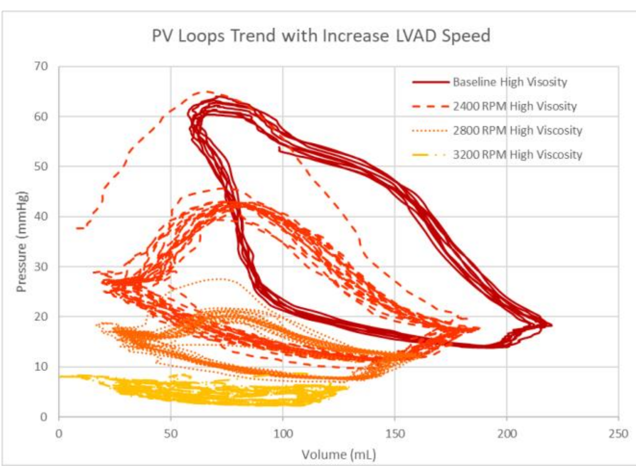

FIGURE 6: As LVAD speed increases, volume and pressure changes decrease as expected.

With an increase of the perfusate's viscosity, a leftward volume shift was observed for all conditions. Figure 7 illustrates this concept using baseline data.

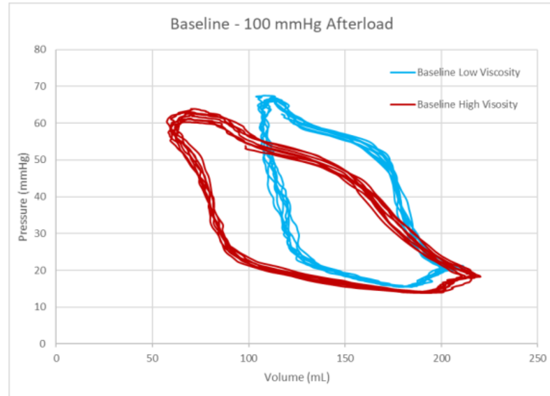

FIGURE 7: As buffer viscosity increases, the loops shifts left with a greater volume difference between systole and diastole.

These reanimated hearts were also observed to elicit tissue suction events at lower pump speeds. Figure 8 shows suction events occurring at the same pump speed and afterload with relatively increased buffer viscosity.

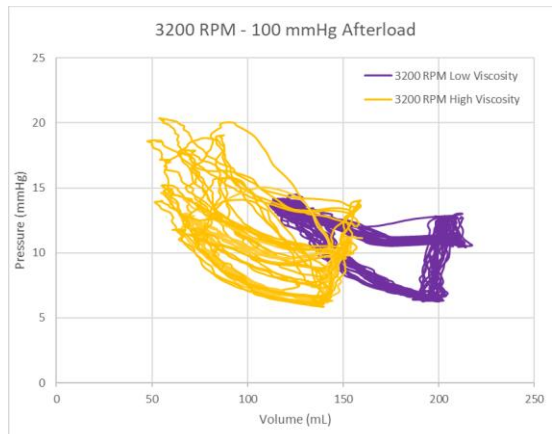

FIGURE 8: With an increase in the viscosity of the buffer, suction events were achieved at the same pump speed and afterload.

4. CONCLUSION

Overall, the use of HyC to increase the viscosity of the buffer on the Visible Heart® apparatus causes significant changes to the hemodynamic measurements taken from a given beating heart. These changes need to be considered when evaluating changes to an LVAD component design or algorithm modifications.

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