SHEAR RATES DERIVED FROM ULTRASOUND IMAGERY AND PARTICLE IMAGE VELOCIMETRY (PIV)

[1,2]Andrew Walker, [1]Kogan Lee, [1]Melissa Lui, [2]Gary Dobson, [1]Clifton Johnston
[1]*Department of Mechanical and Manufacturing Engineering, University of Calgary, Calgary, Alberta, Canada*
[2]*Department of Anesthesia, University of Calgary, Calgary, Alberta, Canada*

INTRODUCTION

Numerous flow environments exist within the cardiovascular system including turbulent flow at arterial bifurcations, vortex flow patterns distal to implanted stents and jet flow through an arterial stenosis. These flow environments can lead to sites of low shear stress on the endothelial lining of the arterial wall leading to endothelial cell inflammation and the inability to maintain vascular homeostasis [1-3]. Therefore, accurate measurement of arterial blood flow and wall shear stress in vivo is important given their relationship to the onset of atherosclerotic disease and their association to the development of plaques, arterial hyperplasia and hemolysis.

Several technologies are currently available for *in vivo* blood flow measurement including magnetic resonance imaging (MRI) and pulse wave Doppler. MRI is capable of measuring flow in multiple spatial directions with good resolution; however, several scans at a high cost are required to reconstruct the flow, while the process is cumbersome and may require long breath holds for the patient under investigation [4]. Pulse wave Doppler improves upon the temporal resolution of MRI; however, this approach is limited by its dependence on the angle of incidence between the ultrasound beam and flow in question and an inability to measure flow in multiple directions [4].

An alternative to these approaches is the use of particle image velocimetry (PIV) that uses a field mapping technique with optical imaging to measure blood flow and shear stress [5]. However, optical imaging is not possible when investigating an opaque flow environment such as arterial blood flow [6]. To combat this, the use of ultrasound brightness (B)-mode imagery and echo-contrast containing microbubbles allows for the acquisition of images that are amenable to PIV analysis [7]. This method is termed ePIV. Given that this approach uses ultrasound imagery, it improves upon the temporal and cost concerns associated with MRI while generating velocity profiles in multiple spatial directions that are not reliant on the angle between the beam and the flow as in the case of Doppler.

Currently, an ePIV system is under development at the University of Calgary. This investigation represents our initial feasibility studies comparing ePIV derived velocity profiles in steady and pulsatile flow environments to analytical models based on Poiseuille's Law using normal saline and five dilutions of pentaspan and voluven. Furthermore, shear stress values based on our steady state ePIV derived velocity profiles were compared to theoretical values. Our ePIV steady state velocity and shear stress models displayed a close fit to the analytical models. Similar results were noted for our pulsatile velocity models at the midline; however, larger discrepancies in velocity were noted at the tube wall. This suggests that Poiseuille's Law is not ideal to model pulsatile flow.

METHODS

Ultrasound Imaging

ePIV measurements were made with a Vivid i (GE) ultrasound system using a linear probe (5-13 MHz) and vascular application software. The B-mode was used for this investigation. B-mode ultrasound sweeps a focused beam across the area of interest that encounters scattering particles generating echoes that are transmitted back to the ultrasound transducer. The vertical position of the scattering particles is determined by the time delay from pulse transmittance from the ultrasound transducer to reception of the return echo. Horizontal location is determined by the location of the firing linear transducers. Ultrasound images for this investigation were acquired with a linear probe at 10 MHz at a frame rate of 78 frames per second.

Flow Generation

Steady and pulsatile flows of 1 mL/s and 2 mL/s were generated by a Shelley Biomedical Compuflo 1000 cardiovascular mimicking pump. Latex tubing (0.3 cm radius) to simulate the brachial artery was suspended in a 45 cm long custom-made plexiglass flow chamber with an acoustic window to allow for ultrasound interrogation. Dilutions of normal saline, and 12.5%, 25%, 50%, 75% and 100% pentaspan and voluven were driven by the cardiovascular mimicking pump through the flow loop. Voluven and pentaspan (pentastarch) are hydroxyl-ethyl starches that are used for blood substitution or volume expansion. There are attractive as replacement fluids due to increased availability and decreased costs compared to packed red blood cells. Reynolds numbers varied from 192 for normal saline (lowest viscosity) to 35.1 for 100% pentaspan (highest viscosity).

Echo Contrast

Echo-contrast in the form of microbubbles was added to the dilutions until images appropriate for analysis with PIV were obtained. The acoustic impedance disparity between our dilutions and the microbubbles allowed for the generation of reflected signals that produced clear echo images (Figure 1). Echo-contrast agents are of common use in echo-cardiography as the highly reflective properties of the microbubbles allows for the effective tracking of blood flow through the heart [4]. The microbubbles often survive several cardiac cycles upon which they are destroyed by the ultrasound signal [4]. We used Definity microbubbles that consist of a lipid shell encapsulating octafluoropropane gas with a mean diameter of 1.1 ~ 3.3 μm [8].

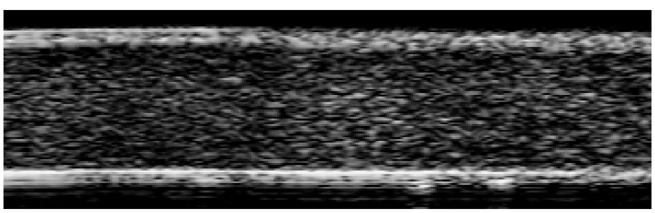


Figure 1. Reflected echoes from injected Definity microbubbles in a 100% normal saline solution flowing through a 0.3 cm radius latex tube.

ePIV Analysis

Recordings were made in steady state and pulsatile flow environments. Seventy-eight images were captured per second and were downloaded for PIV analysis using MATLAB 7.4 software. PIV allows for the investigation of flow by tracking particle (microbubble) movement between two consecutive images. The images were divided into 32 pixel x 32 pixel size interrogation windows. A cross-correlation algorithm was then applied to the interrogation window that is based on the displacement of tracer particles in the second image relative to their position in the first divided by time delay between image acquisition [9]. This calculates the local displacement of microbubbles between the two images. Application of the cross-correlation algorithm across all interrogation windows allows for the creation of a velocity field map that displays velocity vectors of magnitude and direction across the flow under investigation (Figure 2).

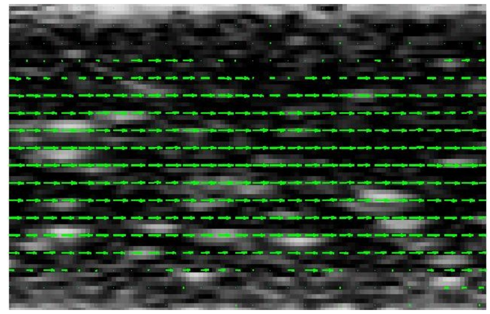


Figure 2. ePIV derived image of 100% normal saline flow through a latex tube of 0.3 cm radius

Cross-correlation between two image pairs was completed for all captured frames of our pulsatile flow data that was subsequently averaged to give average velocity determined by ePIV across all image frames. Averaged values were used to generate pulsatile ePIV velocity profiles. A total of 15 velocity vectors were produced across the diameter of the tube equating to a spatial resolution of 0.4 mm. Cross-correlation was not completed for all frames of steady flow data given that flow was held constant throughout this portion of the investigation.

Model Comparison

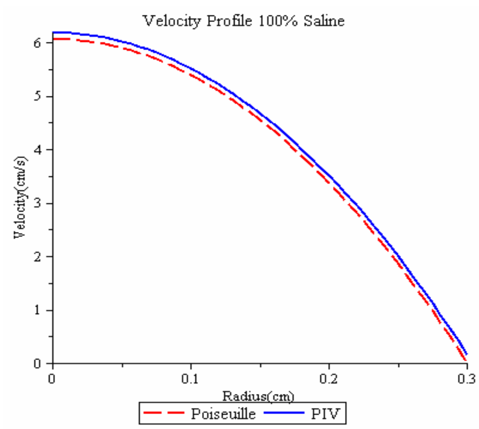
Steady and pulsatile ePIV derived velocity profiles were modeled using nonlinear fits and compared to theoretical velocity profiles based on Poiseuille's Law that assumed a fully developed laminar flow. Theoretical models were generated from peak ePIV velocities using a Poiseuille model program developed in Maplesoft 12.0 software. A single theoretical model was developed for our steady flow condition while individual theoretical profiles were created for each frame of our pulsatile data. This allowed for the creation of 3-dimesional models that compared velocity profiles derived from ePIV velocities and theoretical values across each frame of a single pulse. Shear stress values for our steady flow data were based on ePIV and theoretical based velocity profiles. Values were calculated in Maplesoft 12.0.

RESULTS

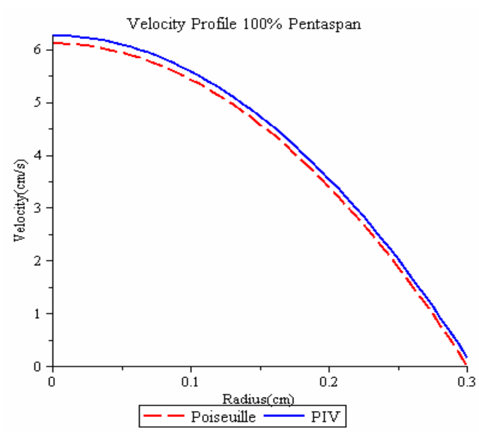
Steady State

Peak steady state velocities derived from ePIV ranged from 6.53 cm/s for 25% voluven to 5.90 cm/s for 100% voluven. A good fit was achieved between our ePIV derived velocity profiles and theoretical models based on Poiseuille's Law. Closest fit occurred at the tube midline and decreased towards the tube wall. A less than 4% difference in predicted velocities between the ePIV and theoretical model was noted for 100% saline (Figure 3a).

a.



b.



c.

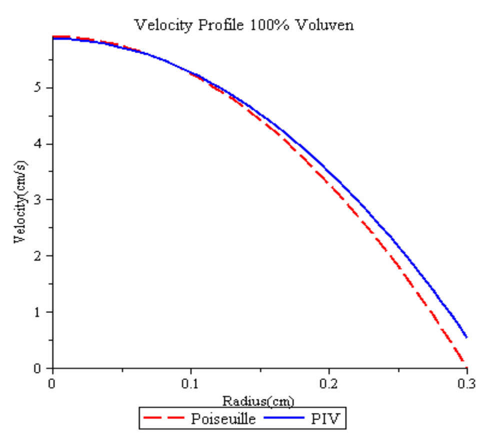
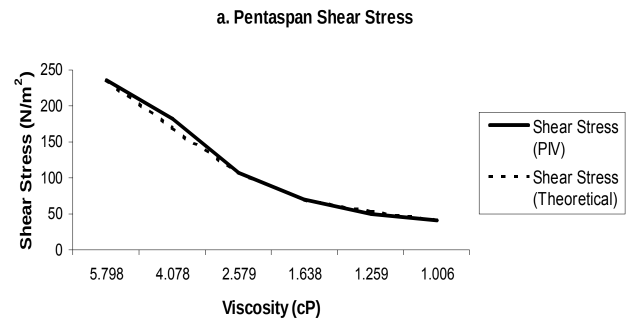


Figure 3. ePIV and theoretical derived velocity profiles at steady state for (a) normal saline, (b) 100% pentaspan and (c) 100% voluven.

ePIV derived shear stress models of pentaspan at 25°C at all concentrations resulted in a close fit to the theoretical models (Figure 4a). A 12.54 N/m^2 difference was noted for 75% pentaspan. For all other concentrations, discrepancies between the ePIV and theoretical model ranged from 0.10 to 2.66 N/m^2. Maximum difference for voluven (10.03 N/m^2) occurred at 75% dilution (Figure 4b). Differences at remaining dilutions ranged from 0.10 to 8.73 N/m^2.



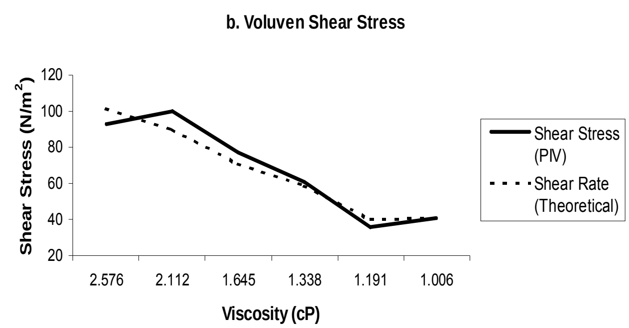


Figure 4. ePIV and theoretical derived shear stress values for steady state (a) pentaspan and (b) voluven at all concentrations at 25°C.

<u>Pulsatile</u>

Peak velocities for our pulsatile data measured by ePIV ranged from 3.84 cm/s for 100% pentaspan (5.79 cP) to 4.95 cm/s for 25% voluven (1.34 cP). Similar to steady state results, ePIV velocity models displayed closest fit to theoretical models at midline and decreased towards tube wall. Specifically, the theoretical model overestimated velocities for normal saline near the distal wall by 21.5% and 16.9% for 100% voluven at the proximal wall. For 100% pentaspan, the theoretical model assuming Poiseuille flow overestimated velocity near the proximal wall by 11.7% and underestimated velocity by 17.4% near the distal wall.

The range between low and high midline velocities through the duration of a pulse was noticeably lower for 100% pentaspan compared to normal saline and 100% voluven. Difference between low and high midline velocity for normal saline and 100% voluven were 2.18 cm/s 1.65 cm/s respectively compared to 1.12 cm/s for 100% pentaspan (Figure 5).

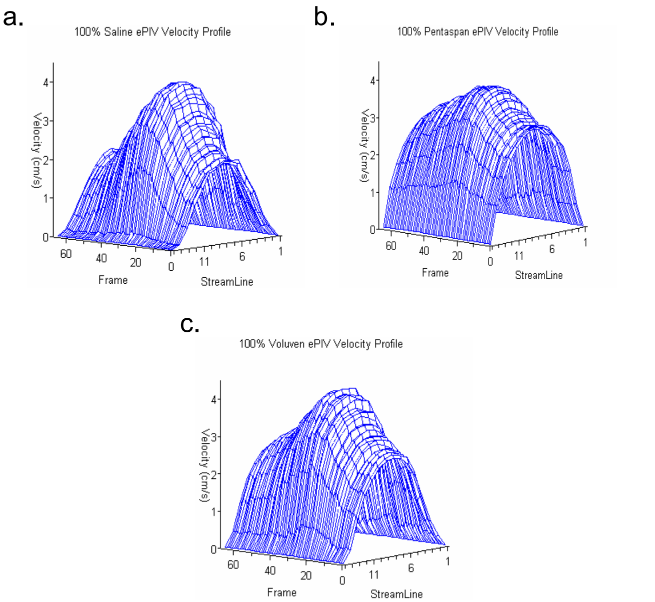


Figure 5. Pulsatile ePIV derived velocity profiles of (a) normal saline, (b) 100% pentaspan and (c) 100% voluven.

DISCUSSION

Steady state ePIV velocity profiles displayed a good fit to the theoretical models based on Poiseuille's Law. In general, the closest fit occurred at the midline and decreased towards the tube wall. The discrepancies observed at the wall may be the result of ultrasound reverberation causing the ultrasound signal to bounce back and forth between two interfaces with a large acoustic impedance disparity, in this instance the latex tubing and fluid containing microbubbles. Furthermore, because our spatial resolution was 0.4 mm, our predicted ePIV wall velocity measurements may in fact be displaced this distance from the actual tube wall. This was confirmed by our velocity profile comparisons where ePIV velocity fit was generally closest at the midline and decreased towards the tube wall.

Our predicted shear stress values displayed a close fit to theoretical values at all concentrations of pentaspan. Our predicted ePIV shear stress values from dilutions of 100% to 12.5% voluven displayed a fit that was consistent with the theoretical fit assuming Poiseuille's Law. Variations were found to occur about the theoretical curve with a maximum error of 10%. ePIV velocity measurements at all concentrations of voluven displayed larger discrepancies with the theoretical model at the tube wall in comparison to pentaspan as can be seen in figure 3c. Clearly, there was difficulty in obtaining accurate wall velocity measurements when using dilutions of voluven. Further velocity measurement in both steady and pulsatile flow environments at all concentrations of voluven warrants investigation.

The errors observed between our pulsatile ePIV and theoretical profiles assuming Poiseuille's Law were not surprising and confirmed our initial expectations that Poiseuille's Law was not an ideal model for pulsatile flow environments. We are currently completing computational fluid dynamics models (CFD) of our dilutions that will permit us to investigate the physics of our flow environment, allowing for an improved means of modelling our pulsatile data. Initial results appear promising when compared to the CFD models with close fits of pulsatile velocity profiles achieved for normal saline and 100% dilutions of voluven and pentaspan.

CONCLUSION

The use of ultrasound imaging and PIV represents a non-invasive approach to quantifying arterial shear stress while providing an alternative to MRI and pulse wave Doppler techniques. This is of particular importance to measuring flow characteristics in the cardiovascular system as this technology would allow for the investigation of *in vivo* blood flow measurements through implanted devices in the heart including heart valves and stents with conveniently and readily available technology.

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