In-vitro particle image velocimetry assessment of the endovascular haemodynamic features distal of stent-grafts that are associated with development of limb occlusion

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Abstract: Aneurysms are common vascular diseases which affect normal hemodynamics in the aorta. Endovascular aortic repair (EVAR) using stent-grafts is a common treatment that excludes the aneurysm from the circulation, preventing further growth and eventual rupture. However, complications such as endoleak, dislocation, or limb occlusion have been reported after EVAR. This study hypothesized that the compliance mismatch between the graft and parent artery causes hemodynamic disturbances at the distal edge of the graft. Therefore, the potential for the graft to cause limb occlusion was assessed. A compliant phantom was fabricated . A circulatory loop was developed to run the fluid and generate a physiological flow waveform. Particle Image Velocimetry was utilized to capture fluid dynamics in the replica. The result showed a low velocity region at the graft trailing edge wall. The low velocity boundary layer thickness decreased downstream of the graft. A flow recirculation was initiated and increased in size during the mid-acceleration at the low velocity region. Shear stresses fluctuated at the trailing edge of the graft which is a risk factor for intimal thickening followed by graft or limb occlusion. It was concluded that this hemodynamic behaviour was due to the graft and parent artery compliance mismatch.

Keywords: Particle image velocimetry, silicone phantom, haemodynamics, compliance, grafts, limb occlusion, recirculation

Introduction

Cardiovascular diseases (CVD) incur abnormal hemodynamics and are the leading cause of death globally (Lyons et al. 2016). Aneurysm is a common arterial disease which is enlargement of a localized segment of the artery. If left untreated, the artery diameter increases can lead rupture and fatal blood loss (Waite and Fine, 2007). A common arterial region for aneurysm is abdominal aorta. Aggarwal et al. (2011) reported that abdominal aortic aneurysm (AAA) can be diagnosed when a 50 % enlargement of original artery diameter is detected. Endovascular aortic repair (EVAR) surgery is a common treatment for the infrarenal abdominal aortic aneurysm. During EVAR surgery, a graft is inserted from the femoral artery and delivered via a sheath to the lesion area (Lindblad et al. 2015). In some aortic surgeries, fenestrated grafts and distal bifurcation to iliac branches are used to completely seal the aneurysm sac and facilitate flow to visceral vessels and iliac branches, respectively. The grafts commonly consist of a series of metal struts which are covered and stitched to either woven polyester or expanded polytetrafluorethylene (ePTFE) fabric (Voûte et al. 2012). The metal struts cannot extend beyond the fabric cover distally or proximally (Chuter et al. 2003). The metal structure plus the covering fabric imposes semi-rigidity to the lumen of the grafted area.

In this study, it was hypothesised that the compliance difference between the artery and the graft influence downstream hemodynamics. Rhee and Tarbell (1994) reported that such a compliance mismatch caused a 12-23% lower mean wall shear rate distal of a graft in a compliant lumen than observed proximally. Computational modelling of the arterial compliance mismatch has implied the difference in wall stress between the compliant and rigid regions may cause intimal thickening (He et al. 2015). It was reported that low or oscillatory wall shear stress (WSS) is a risk factor for thrombosis (Ku et al. 1985; Wootton and Ku 1999).

Various experimental and numerical studies have been conducted to explore the effect of grafts on hemodynamics after EVAR (Casciaro Mariano Ezequiel et al. 2016; Swaelens et al. 2016; Raptis et al. 2018; Van Noort et al. 2018). Most of them focused on the flow structure proximal to the graft and its influence on graft migration, renal flow, or endoleak (Segalova et al. 2011; Segalova et al. 2012; Argani et al. 2017; van de Velde et al. 2018). However, the risk of limb occlusion and stenosis due to graft extension to iliac branches has not been addressed in experimental or numerical studies. Maleux et al. (2008) assessed 288 patients after endovascular treatment and reported that 8 patients whom were treated with aorto-uni-iliac grafts experienced limb occlusion. It was concluded that the occlusion can be related to kinking of the metallic structure or graft migration. (Rödel et al. 2019) investigated the incidence of limb occlusion due to the Anaconda endograft. They studied 317 patients who underwent EVAR treatment with the second and third generation of the device. It was reported that 9.8% of the study group experienced limb occlusion. A post-EVAR review by Cochennec et al. (2007) showed that limb occlusion occurred in 7% of the patients. The objective of the study was to evaluate the hemodynamic effects of the EVAR graft to provide clearer insight for design optimization.

Methodology

This study used an idealised 1.33:1 scale, straight, compliant phantom of the iliac artery. The goal of this research was to observe the haemodynamics distal of the stent-graft in the iliac artery. Since haemodynamics in the intra-graft region were of minimal interest to this research, only the flow parameters, and mechanical properties of the iliac artery were matched. The bifurcation and tortuosity were ignored. This enabled more accurate phantom fabrication to ensure uniform deflection of the phantom walls under pulsatile flow, and mitigation of transverse motion caused by oscillating centrifugal forces.

Major artery walls have noticeable anisotropy at high strain with increased higher axial stiffness (Zhang et al. 2005). Hence, a longitudinal pattern was applied to the exterior wall of the phantom to mimic higher stiffness in axial direction (Figure 1). The relative axial and circumferential and longitudinal stiffness of an element (Figure 2) was determined using Equation.1.

$$k = \frac{AE}{L} \tag{1}$$

$$k_{eq-Circum.} = \left(\frac{1}{k_1} + \frac{1}{k_2}\right)^{-1} = \left(\frac{0.5\times1}{0.5} + \frac{1\times1}{0.5}\right)^{-1} = \frac{2}{3}$$

$$k_{eq-Long.} = k_3 + k_4 = \frac{0.25\times1}{1} + \frac{0.5\times1}{1} = \frac{3}{4}$$

Hence: $k_{eq-Long.} = \frac{9}{8} k_{eq-Circum.}$

Where *A* is the unit area, *E* is the unit Young's modulus, *L* is the unit length, and *k* is the unit spring constant. Hence, the phantom is stiffer in longitudinal direction.

The phantom was fabricated from transparent silicone (Sylgard 184 Dow Corning) using a lost core casting method (Geoghegan P et al. 2012; Yazdi et al. 2018). Male and female moulds were produced using additive manufacturing method. An UP Box (Tiertime, Beijing, China) FDM (fused deposition modeling) 3D printer with layer thickness of 0.2 mm was used for mould fabrication. To remove the surface ripples due to 3D printing layer extrusion, all mould pieces were lightly sand papered followed by acetone painting. Silicone and cross linking agent with 10:1 ratio were mixed and degassed in a vacuum chamber. The moulds were axially assembled and the silicone mixture was injected using a custom designed plunger and cured for 48 hours. The female moulds were mechanically removed from the phantom, and the male mould was dissolved in an acetone bath. The phantom had nominal constant a wall thickness of 2mm, internal diameter of 25mm, and elastic modulus of 1.32 MPa (Figure 1.a). A complete review of transparent silicone phantom fabrication for Particle Image Velocimetry (PIV) studies can be found in review done by Yazdi et al. (2018). Finally, an endovascular graft 35 mm in length and 25 mm in diameter provided by department of cardiology, Christchurch hospital, New Zealand, was placed at the middle of the silicone phantom (Figure 1.b).

A circulatory mimicking loop was developed to drive the working fluid through the phantom. The fluid circuit consisted of electromagnetic flowmeter, flow straightener (150 mm long honeycomb pipe), piston pump, header tank, and reservoir (Figure 3). The IFC 300 (KROHNE Ltd, UK) flowmeter was a non-intrusive device that did not disturb flow. An bespoke reciprocating piston pump was utilized to generate a physiological pulsatile flow waveform. The pump incorporated a high resolution stepper motor (200 steps per revolution), ball screw, piston, and cylinder. The piston rod was connected to a ball screw supported by bearings at the free and motorized ends. The stepper motor was controlled using a Labview program via a National Instruments 9401 digital module and 9172 CompactDAQ chassis using feedback control. The reciprocating piston pump was utilized to generate a physiological pulsatile flow wavefrom. The increased dimensions of the phantom allowed greater relative precision in the fabrication of the phantom wall thickness, and thus more uniform compliance. However, this change necessitated Reynolds and Womersley Number matching to ensure that the experiment retained physiological relevance. Reynolds number (Re) is a dimensionless parameter which defines the ratio of the inertial forces to viscous forces (Equation. 2). Womersley number (α) is a dimensionless parameter in biofluid mechanics which express the frequency of the ratio of the pulsation frequency to viscosity (Equation 3)

$$Re = \frac{VD}{\nu} \tag{2}$$

where *V* is the mean velocity, *D* is the inlet diameter and *ν* is the kinematic viscosity.

$$\alpha = r\sqrt{\frac{\omega}{\nu}} \tag{3}$$

where *r* is the internal lumen radius and *ω* is the angular frequency.

The flow waveform was adopted from Geoghegan P et al. (2013); (Docherty et al. 2017) and scaled to match the *in-vivo* Reynolds and Womersley numbers. Maximum Reynolds and Womersley numbers were 958 and 4.48, respectively. The flow rate was captured at eight points on the cardiac cycle (Figure 4). It was assumed that the haemodynamic outcomes of the reducing jet stream momentum during the first half of the deceleration phase of systole would be clinically interesting. Hence, the rest of the deceleration phase of flow was not captured. To eliminate optical distortion during the PIV experimentation, the circulatory loop was filled with a 39:61 aqueous glycerol solution, which has the same refractive index as the silicone phantom (1.413). The refractive index matched solution was prepared by titrating glycerine to water with continuous visual inspection of reductions in distortions in a checkerboard pattern placed behind the model (Yousif et al. 2011). The refractive index was verified with a NAR-3T Abbe benchtop refractometer (ATAGO CO., LTD, Tokyo, Japan). The working fluid had a density of 1140 kg/m3 and dynamic viscosity of 1.06×10-2 Pas which was measured experimentally using Cannon–Fenske viscometer and validated with published data (Geoghegan et al. 2012, Yazdi et al. 2018). The phantom was placed in a pressure box manufactured from acrylic sheet and filled with working fluid. This eliminated optical distortion, mimicked the surrounding tissue pressure, and also allowed control of transmural pressure and compliance. The phantom outlet was connected to a header tank with a constant head pressure, provided by 400 mm column of working fluid measured vertically above the centre of the phantom, to mimic the impedance of the circulatory system.

Planar PIV was used to capture and quantify the fluid dynamics in the phantom symmetry plane. Image acquisition was carried out using a TSI 4MP-LS camera (TSI Inc., Shoreview, MN, USA) which is a progressive scan interline CCD camera with 16Hz frame rate. The camera had resolution of 2360 × 1776 pixels. The PIV camera was equipped with a 50 mm Nikon AF Micro-Nikkor lens and the images captured with f8 aperture size. The working fluid was seeded with neutrally buoyant silver coated hollow glass spheres (Dantec Dynamics S-HGS-10) with 10 µm nominal diameter. A double pulse Nd-YAG laser (New Wave Solo 120 XT) and lens train was used to generate the light sheet and illuminate the domain. The light sheet thickness was 1 mm which was achieved using Dantec Dynamics 80X74 cylindrical lens setup. To synchronize the laser pulses and image capture, a TSI synchronizer was used. TSI Insight 4G software was employed to capture the images and process the images into velocity maps.

Light reflection from the wall boundary of the model, stationary objects and laser flare can cause error in the displacement vectors calculation. Therefore, to enhance the signal to noise ratio prior to cross-correlation, subtraction of average intensity background and intensity capping was performed (Raffel et al. 2018). A particle displacement vector field was computed across the images using a cross-correlation method. The analysis was phased-locked with 25 pair of images captured for each eight time points shown in Figure 4. Processing also consisted of the ensemble averaging PIV algorithm to compute the vector field at each time point. A recursive Nyquist iterative grid generation engine was used with the start and final window dimensions of 64*64 and 32*32 pixels respectively and a window grid overlap factor of 50% was adopted. The post processing included vector validation with interpolation used when local vector disagreement surpassed an arbitrary threshold. The resulting velocity fields were plotted using Tecplot 360 data presentation software.

Results

Figure 5.a shows the fluid velocity decreases along the centreline of the phantom distal of the graft outlet at the peak flow rate. In data not explicitly shown, this distal reduction in velocity was observed at all times. The pattern is evident in the velocity maps shown in Figure 6. The velocity of the jet increased as flow accelerated to the peak of the cycle; however, this was not observable spatially. Proximal to the phantom walls during peak flow, a low velocity region can be seen close to the distal end of the graft (Figure 5.b). Figure 6 shows time evolving velocity maps during the acceleration and deceleration phase of systole. A jet flow was observed at the trailing edge of the graft which diffuses through to the end of the phantom. However, the low velocity region observed in Figure 5.b close to the wall remains persistent through all time steps recorded.

To show recirculating flow, velocity streamlines and vectors are shown at the graft trailing edge (Figure 7). Noticeable recirculation was initiated at the trailing edge during acceleration (t_4). The recirculation increased in size as flow accelerated to the peak flow. However, the recirculation zone reduced in size as the flow decelerated to t_7, and there was no observation of complete recirculation at this time point. This transition of velocity at the phantom wall distal to the graft from forward at t_3 to reversed at peak flow, then forward at t_8 is indicative of oscillating shear stress.

Figure 8 shows the radial shear rate profiles at $X_{(axial)}/D_{(radial)}=0.07$ away from the graft outlet for the onset, peak and end of recirculation observed in Figure 7. Low shear rates were observed in the centre of the lumen and increased close to the wall. The near wall oscillation and sudden changes in shear rate became more severe as the flow accelerated to the peak followed by a drop to mid deceleration phase. The negative shear rate value near the centre of the lumen at peak flow was not due to the recirculation. No particular haemodynamic behaviour was observed at the centre of the lumen at the graft trailing edge. In fact, the negative value was due to the confounding effect in the data. The confounding effects include micro air bubbles trapped between the rings on the exterior surface of the phantom during pressure box filling or fluid circuit. The air bubbles caused an oversaturation of the light and biased the cross-correlation at this region.

Discussions

The flow dynamics in a grafted silicone phantom was examined to investigate the potential flow disturbances downstream of the graft. It was hypothesized that compliance mismatch between the graft and artery affect the haemodynamics. The axial velocity gradient along the artery showed the effect of the compliance mismatch. The velocity was higher at the centre of graft outlet and decreased downstream of the graft. The flow velocity components perpendicular to the wall shown in Figure 7 indicate positive transmural pressure and dilation of the compliant phantom. The velocity was lower in the phantom region compared to the graft region in accordance with the conservation of mass principle. This is in agreement with Casciaro et al. (2018) who showed a strong jet at the graft outlet in the iliac artery in computational simulation. Hence, the agreement between the CFD study and the PIV results provides validity to the observations.

The observed low velocity region proximal to the phantom wall and flow separation at graft trailing edge can be associated with the compliance mismatch between the graft and parent artery. During the late acceleration and early deceleration phases, the diameter of the phantom was higher than the effectively rigid graft thus inducing recirculation zone. The strongest recirculation was observed at peak flow. The flow pattern observed was similar to the well-known step wall flow pattern (Le et al. 1997). As flow further decelerates (t8), the artery contracted to its natural diameter and the effect of compliance mismatch is minimal.

Another potential reason for recirculation was the presence of the metal graft wireframe leading to local instability in flow at the wall. Benard et al. (2003) observed intra-stent-graft hemodynamics and reported the existence of recirculation at three regions between the strut wire mesh. While not reported by Benard et al. (2003), these recirculation regions may propagate into the distal region and contribute to the recirculation patterns observed in Figure 7. However, circulation was not observed at t_3 or t_8. This potentially implies that the recirculation was caused by compliance mismatch at the graft-phantom boundary, and not by the mesh struts. The flow disturbances downstream of the grafts were hypothesized to be most likely due to the compliance mismatch between the graft and parent artery, and less likely due to the geometry of the mesh that leads to smaller regions of recirculation (Kolandaivelu et al. 2011). However, the current study lacks a rigid comparator to ensure that the recirculation was only due to the compliance mismatch and if similar haemodynamic behaviour occurs in cases wherein calcification distal of the graft causes stiffening of the arterial wall.

High shear rate fluctuation at peak flow (Figure 8) was associated with the changes in the recirculation region. It has been reported that flow recirculation and separation can induce oscillating or low wall shear stress proximal to the wall which are key factors for endothelial cell damage, intimal thickening and atherosclerosis initiation (Rouleau et al. 2010; Wentzel et al. 2012; Meng et al. 2014). A CFD study by Raptis et al. (2017) showed considerable reduction of post-operative WSS compared to physiological values. Hence, the low velocity magnitude, recirculation, and shear rate fluctuation observed in Figures 7 and 8 is in agreement with these findings and implies a potential for endothelial cell damage, intimal thickening and may ultimately lead to restenosis at the graft trailing edge. Increased understanding of stented haemodynamics may reduce the rate of EVAR patients who currently experience limb occlusion within 6 months of stent-graft implant (3-10%) (Maldonado et al. 2007; Mestres et al. 2009).

The carotid artery waveform was scaled and used for this study to match the typical Reynolds and Womersley number in the iliac artery. However, the Womersley number was selected from the lower end of the feasible scale (San and Staples 2012). This low simulated Womersley value may have led to observation of smaller recirculation haemodynamics than could occur in typical patients. While the physiological iliac waveform sometimes exhibits a small backflow during diastole, the effect on systolic haemodynamics is minimal. Although the backflow was not investigated in this study, it may lead to recirculation distal of the stent graft due to compliance mismatch. This study measured the velocity field during systole for which the carotid and iliac artery shows similar waveforms. In addition, the haemodynamic disturbances at the graft trailing edge were due to pressure changes and compliance mismatch, not flow direction.

The phantom used in this experiment was designed to closely mimic physiological conditions. However, the optical opacity of the graft meant that flow within the graft region was not captured. Therefore, no conclusion could be drawn regarding the flow disturbances within the graft. However, the graft lumen is reasonably rigid and many CFD studies have thus been able to accurately model intra graft haemodynamics (Karmonik et al. 2011; Polańczyk et al. 2012; Polanczyk et al. 2015; Boland et al. 2016; Karanasiou et al. 2017; Raptis et al. 2018; Tasso et al. 2018).

The lack of specific intra-graft haemodynamics does not affect the observation of the flow disturbances downstream of the graft. At some stages of the cardiac cycle, the shear rate observed was less than 100 s-1. In, contrast to blood, which exhibits non-Newtonian behaviour for shear rates below 100 s^{-1} (Waite and Fine 2007), the working fluid used in this study was Newtonian. Therefore, using non-Newtonian fluid might yield improved outcomes.

The phantom geometry used in this research was highly simplified. The transition from the abdominal aorta to the common arteries includes bifurcation, curvature, and tortuosity that was not included in the phantom. Furthermore, in cases wherein EVAR is necessary, the geometry is often affected by aneurysm. However, modelling the complex geometry of the intra stent-graft region was not deemed necessary in this research that concentrated on the haemodynamics observed at the transition of the rigid graft to the compliant phantom. To observe recirculation at the trailing edge of the stent-graft, only the primary flow characteristics and the vessel mechanical properties were desired. Boersen et al. (2017) developed a more precise, but effectively rigid model of the EVAR to enable PIV analysis of haemodynamic features in the renal and iliac artery. The researchers observed some interesting effects due to the bifurcation, which this present study was not intended to capture. However, Boersen et al. stated that the use of a more compliant model usually results in lower WSS and shear rates. Geoghegan PH et al. (2017) study also showed that wall rigidity leads to overestimation of WSS by 61%.

Similar to this study, Boersen et al. (2017) did not consider out of plane flow. The out of plane flow potentially generated by complex geometry of the EVAR lumen is transverse to recirculation characteristics, would be very difficult to capture, and may ultimately make it difficult to capture the recirculation in the primary flow. In particular, planar PIV uses a light sheet to capture motion of particles within the light sheet, not transverse to it. Hence, while a more accurate model may have yielded more accurate flow dynamics, the ability to capture such dynamics using planar PIV was expected to be limited. If observation of out of plane flows was deemed necessary, stereo-PIV or tomographic PIV (Nguyen et al. 2019; Medero et al. 2020) or phase contrast MRI could be utilised (Yamashita et al. 2007).

Since recirculation is an important clinical parameter for restenosis risk, it is thus also an important consideration during stent-graft testing. Hence, experimental processes that utilise fluid/boundary interaction are critical to enable observation of stent-grafted haemodynamics. PIV offers a unique ability to observe such flow patterns in-vitro. Future PIV studies may enable stent-gaft design optimisation and thus improve patient outcomes.

Conclusion

PIV was used to investigate the effect of compliance mismatch between silicone phantom and endovascular graft on flow disturbances and limb occlusion. This study showed that it is possible to assess the elements of the performance of endovascular grafts using PIV. The results illustrated that the compliance mismatch between the graft and parent artery induces flow separation and shear stress oscillation proximal to the wall and trailing edge of the graft. These flow patterns can lead to intimal thickening, limb occlusion and graft blockage. In addition, the flow separation became more severe at peak flow. This in turn shows the importance of conducting pulsatile flow experiments. The outcomes emphasize the need to assess candidate endovascular graft designs in compliant phantom under pulsatile flow conditions.

References

Figure Captions

Figure 1. Elements used in the experiment (a) Compliant silicone phantom of iliac artery, (b) endovascular graft

Figure 2. An element of the compliant phantom with unit width, height, and length

Figure 3. Schematic diagram of circulatory mimicking loop: A) reciprocating piston pump, B) flow straightener, C) electromagnetic flowmeter, D) silicone phantom in pressure box, E) header tank with weir, F) aortic graft

Figure 4. Pulsatile flow waveform for one cardiac cycle with phase location at point of interest (t/T= (t_1) 0.109, (t_2) 0.153, (t_3) 0.219, (t_4) 0.263, (peak) 0.307, (t_6) 0.351, (t_7) 0.395, (t_8) 0.461)

Figure 5. Velocity magnitude distribution from graft trailing edge through phantom outlet at peak flow (t5); (a) along the axis, (b) near the wall (Y/D=0.04)

Figure 6. Time evolving velocity map for all measured time points locations on the cardiac cycle. Note that the dominant flow direction is right to left, and the right edge of the plot is fixed to the trailing edge of the graft. The figures are one diameter high, three diameters wide, and have a true aspect ratio.

Figure 7. Velocity streamlines at t3, t4, peak flow, t6, t7, and t8. The plots are zoomed at proximal trailing edge of the graft to show the flow disturbances easier. X/D represents distance from the trailing edge of the stent graft. Note the magnification of the figures.

Figure 8. Radial shear rate at X/D= 0.07 from trailing edge of the graft outlet at t3, peak flow, and t8 time points