ANALYSIS OF HAEMODYNAMICS IN ARTERIOVENOUS FISTULAS

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Background
Haemodialysis is the most common treatment for end stage renal disease (ESRD) whereby an external machine (a dialyser) cleanses the blood, thus performing the function of the failing kidneys. For haemodialysis to be viable, a functional vascular access (VA) capable of managing 300-400ml extraction of blood per minute is required. Arteriovenous fistulas (AVFs) are preferred over other VA because of their association with prolonged survival, fewer infections, lower hospitalisation, and reduced costs in comparison with other types [1]-[3]. An AVF consists of a surgically created anastomosis joining a peripheral artery and vein. This joining can be accomplished in different configurations and in this study we concentrate on one configuration – an end-to-side anastomosis. This is where the vein is surgically cut and the end leading back to the heart is surgically stitched onto the side of the artery. The introduction of arterial blood flow, at a significantly higher blood pressure, into a vein should induce vein expansion and cause its walls to remodel. This expansion and remodelling, known as maturation, allows regular cannulation, accommodates the 300-400ml per minute required and is critical for successful long-term haemodialysis; however, some AVFs fail to ever mature. The maturation process is dependent on the local haemodynamics within the AVF with the endothelial cells lining the venous walls capable of sensing the flow conditions and releasing chemical messengers in response that influence how other cells within the venous wall behave. For instance, endothelial cells can release growth factors in response to low wall shear stress (WSS) which cause vascular smooth muscle cells (VSMCs) to proliferate and migrate into the inner lining of the venous wall. This proliferation, called intimal hyperplasia can result in a stenosis in a newly-formed or possibly in a matured AVF which would then require further endovascular intervention to remain patent for haemodialysis. With this in mind the question then is why some AVFs fail to ever mature with rates between 20-50% never considered a viable VA.

One hypothesis as to why this happens is that the haemodynamics within the AVF are not typical of what is usually experienced in the vasculature and depending on the AVF geometry can in some instances result in stenosis. There is significant variability between AVFs in different patients because of their individual vasculature, and different surgical techniques and locations. Modelling the haemodynamics within patient-specific AVFs is warranted to elucidate if there are particular geometrical features or perhaps the existence of certain flow conditions that cause failure. This could produce recommendations for future surgical techniques in AVF creation that could be employed to mitigate these effects.

Methods
As part of the Renal Dialysis Vascular Access (ReDVA) project four volunteers who required AVF creation were imaged before and after their surgery using a three Tesla (3T) magnetic resonance imaging (MRI) scanner at Ninewells Hospital. MRI techniques that do not require the use of contrast agent (contrast agents are restricted for patients with impaired renal function) were used to capture the vasculature geometry and the relevant velocity boundary conditions. Specifically, the multi-echo data image combination (MEDIC) method was used to acquire the geometry of the region of interest and the velocity of the blood flow at two locations, proximal and distal to the anastomosis location, were acquired using velocity-
encoding (VENC). Both of these methods can produce high resolution data, as shown in Figure 1, which in turn produce detailed representations of the AVF geometry and blood flow velocities for computational fluid dynamics simulations.

Figure Error! No sequence specified.: (a) Typical MEDIC image slice showing the vessels as bright spots, (b) typical VENC image at one instance in the cardiac cycle where the velocity of the flow is proportional to the intensity of the white (venous flow) / dark (arterial flow).

The MEDIC images were segmented using SimVascular (Stanford University, CA, USA), an open-source segmentation software,[4] with the resulting stereolithography (STL) geometry files then imported into Blender (Blender Foundation) for healing, for instance, a fillet had to be made in the anastomosis part of the STL because the MRI scan does not have enough resolution to display the curvature there. The advantage of this method is that it works by making a fillet inside the concave gap by filling it with a virtual clay and it does not modify the geometry globally, as a Laplacian filter does. The sculpt tool in Blender is used to fill in the gap, then a local smoothing is done manually. Also in Blender, the boundary patches of the STL are separated from the rest of the original STL with the following patches created: artery_inlet, artery_outlet, vein_outlet, and walls.

The complete STL is then meshed using snappyHexMesh with three layers over the walls patch. The octree has two levels, level 0 along the central lines, and level 1 near the walls. The mesh is refined to level 1 within a sphere centred in the anastomosis region to give it better resolution where velocity gradients are higher. A modified time-varying flow rate inlet boundary condition is applied as boundary conditions (BCs) for both the artery_inlet and the vein_outlet patches, which corresponds to the velocity data acquired from the VENC imaging sequence, whereas the artery_outlet patch is set as a zero pressure BC. This modified BC generates a paraboloid velocity profile on these circular patches, in order to mitigate entry and exit hydrodynamic effects. The time-varying flow rate curves are obtained from the VENC scans. Flow is applied on those two proximal patches, because (1) those velocities were obtained in the same slice at the same time, and (2) the VENC resolution is not as detailed at the artery_outlet, because it is a narrower vessel. Thus, the flow rate at artery_outlet ends up becoming the difference between the flow rates measured at the proximal (artery_inlet and vein_outlet) patches.

Three pulse cycles were simulated to guarantee that the flow field represents a series of the measured pulses. The difference of the time-averaged wall shear stress between the 2nd and 3rd cycle is less than 1%. A Newtonian model for blood viscosity was used: \( \mu = 3.5 \times 10^{-5} \text{ kg/(m.s)} \) and \( \rho = 1060 \text{ kg/m}^3 \), and the flow is assumed to be laminar. Ten time steps per cycle were saved, and at each of those the WSS (\( \tau_w \)), the magnitude of WSS (|\( \tau_w \)|), and the vorticity (\( \nabla \cdot V \)) were also computed and saved using run-time functions. Time-averaging of both WSS and magWSS was integrated along the run time using the fieldAverage run-time function. A modified fieldAverage function was set to start at the beginning of each cycle. Therefore, at the end of the cycle, the function would have averaged all the computed time steps. The time-averaged magWSS is the time-averaged WSS (TAWSS), and the time-averaged WSS is the time-averaged WSS vector (TAWSSV). Both are needed to calculate the oscillatory shear index (OSI) and the relative residence time (RRT), as shown in Equations 1 and 2, which are two additional variables that are used to quantify the disturbed flow at the surface of the arterial wall where the endothelial cells are located.

\[
OSI = 0.5 \times \left(1 - \frac{\int_0^T \tau_w dt}{\int_0^T |\tau_w| dt}\right) \tag{1}
\]

\[
RRT \sim [(1 - 2.0 \times OSI) \times TAWSS]^{-1} \tag{2}
\]

These were calculated in Paraview using the calculator filter, along with the local normalised helicity (LNH) using the saved velocity and vorticity, as shown in Equation 3. The LNH is a measure of helicity of the blood flow and is a way to visualise the strength and extent of helical flow in the AVF.
\[ LNH = \frac{(\nabla \times \mathbf{V}) \cdot \mathbf{V}}{|(\nabla \times \mathbf{V})||\mathbf{V}|} = \cos \theta \]  

(3)

Where \( \theta \) is the angle between the velocity and vorticity vectors. The LNH is a measure of the alignment/misalignment of the local velocity and vorticity vectors and has a range of \(-1 \leq LNH \leq 1\) where positive values are present in left-hand rotating flows and negative values are present in right-hand rotating flows, when viewed in the direction of the forward motion.[5] A sample plot of the results are shown in Figure 2.

The biggest computational challenge of computing a CFD simulation of an AVF is the high speed in small sized elements. The transient solution in limited by the Courant number (or CFL condition). Fortunately, the PIMPLE algorithm was able to converge to with Courant number set to 10, which shortened the computational time.

Figure 2: (a) The velocity vectors and the LNH within the AVF lumen, (b) the pressure (p), and (c) the WSS magnitude on the luminal surface of the AVF at one instance of the cardiac cycle.

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References