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Synchrotron X-ray PIV of Blood Flow in an Optically Opaque Bifurcation Model

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ABSTRACT

Particle image velocimetry (PIV) of biological flows is commonly conducted on *in vitro* models using planar PIV. This requires optical access to the model and is restricted to obtaining two components of velocity for a single plane of the domain. X-ray PIV provides the ability not only to image opaque specimens, such as *ex vivo* blood vessels, but also to acquire the velocity field within the entire domain. This paper investigates the fluid dynamics of blood flow in an optically opaque *in vitro* model, chosen to be consistent with that of a healthy human carotid bifurcation. The velocity profile of the internal carotid artery (ICA) is seen to develop a region of low wall shear stress identified on the outside wall of the ICA. Additionally, the use of gas micro-bubbles has proven successful in providing a stronger signal for X-ray PIV experiments.

1. INTRODUCTION

The study of biological fluid mechanics is essential to the understanding of arterial disease, currently the leading cause of death and morbidity in the developed world. Conducting research on living tissue is essential for determining the effect that the flow dynamics, and the resultant stresses induced by these complex flows, have on the development and progression of arterial disease. However, the opacity of living tissue means that optically based imaging methods are unable to accurately and quantitatively assess internal fluid dynamics, such as in the deep vasculature. X-ray particle image velocimetry allows the investigation of optically opaque specimens, overcoming this difficulty.

The study of bifurcations are of interest as it is generally upstream of a bifurcation that aneurysms are seen to develop [8] and downstream in the internal carotid artery that stenoses are seen to develop. The complex geometry of carotid bifurcations within the body has been extensively investigated with computational fluid dynamics (CFD), using various medical imaging techniques to define the geometry. However, structuring investigations in this manner does not lead to the determination of which geometrical features are causing the undesirable hæmodynamics within the flow. Additionally, although it seems that CFD can predict the flow dynamics in anatomically realistic *in vitro* models, given the questions over the validity of various modelling assumptions [1, 10], it has been suggested that validation with *in vivo* data should be conducted whenever possible [2, 5].

Previous *in vitro* studies using synchrotron X-rays have used various tracer particles to seed whole blood [3, 9], however these particles are not compatible with blood and thus cannot be used for *in vivo* experiments. Some studies have used the red blood cells (RBC) themselves as the tracer particles [6, 7], reducing interference to the blood. However, although using RBCs as tracer particles for *in vitro* studies has been successful, the relatively small phase difference between whole blood and tissue creates very low signal from the blood compared to the noise created by the tissue. The current study uses a commercial ultrasound contrast agent DEFINITY® (Bristol-Myers Squibb Medical Imaging Inc) as the tracer particles, overcoming the limitation of signal without interference to the blood. DEFINITY®, when activated, produces a homogeneous injectable suspension of perflutren lipid microspheres [11]. The increase in signal helps in the reduction of exposure time and thus interframe time, enabling further progression towards physiologically real flow rates. Although contrast agent is not required for *in vitro* research, the current study develops the techniques required for *in vivo* research by investigating whole blood flowing through an optically opaque *in vitro* model, chosen to be consistent with that of a healthy carotid bifurcation [12].

2. METHOD

The experiment described below was conducted at the SRring-8 synchrotron located in Hyogo, Japan. The undulator beamline, 20XU (downstream hutch), was used and the broadband synchrotron radiation was filtered by a Si-111 double crystal monochromator to provide a beam energy of 25keV. The beam size was approximately 4mm x 6mm.

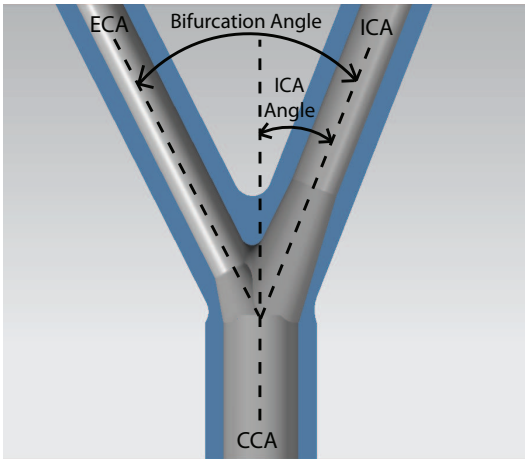

Figure 1: Main parameters for defining bifurcation geometry.

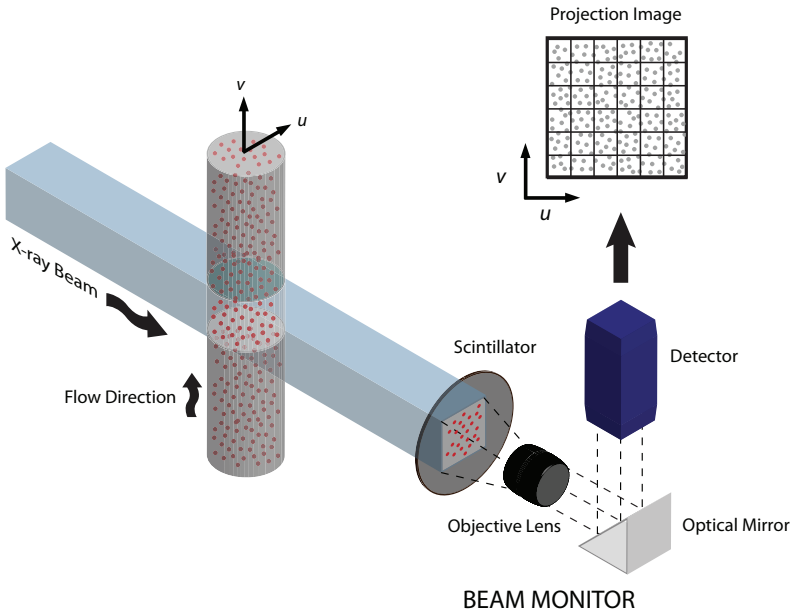

Figure 2: Schematic setup of basic X-ray PIV configuration. Image courtesy of Stephen Dubsky.

2.1 Geometry

The investigation of carotid bifurcations commonly uses several geometric parameters to define the geometry (Figure 1), all of which are well defined by Thomas *et al.* [14]. The inlets and outlets of the bifurcation are defined by the diameter of the common carotid artery (CCA), external carotid artery (ECA) and the internal carotid artery (ICA). Additionally, the bifurcation angle and the ICA angle are used to define the angles at which the ICA and ECA diverge.

The planarity angle (tilt into the page) was chosen to not be considered as a technique has been developed to determine the velocity profile throughout the entire domain from only one projection [3], subject to the geometry being symmetric about the depth.

Studies into bifurcation geometry have investigated both the size and shape for multiple demographics, such as age and disease. The current study uses this previous work to define its geometry, with the following diameter ratios [12] and angles [14] used, representing the shape and size of a young, healthy carotid bifurcation.

$$\frac{\text{ICA}}{\text{CCA}} = 0.64 \qquad \frac{\text{ECA}}{\text{CCA}} = 0.56$$

$$\text{ICA Angle} = 21.6^{\circ} \qquad \text{Bifurcation Angle} = 48.5^{\circ}$$

The complex geometry of a bifurcation is difficult to manufacture without introducing undesired surfaces due to machining, which have a significant effect on the fluid dynamics. This study utilised the advances in 3D-printing to manufacture a model from the Objet^{TM} FullCure® acrylic-based photopolymer material. The high resolution technique, with a layer thickness of 16μm, ensured the models were accurate on the small scale being investigated.

2.2 X-ray configuration

Figure 2 shows the basic configuration required for X-ray PIV. The bifurcation model is placed into the beam such that the X-rays produced by the synchrotron penetrate the volume. The X-rays then pass through a scintillator to produce visible light, enabling a visible light camera to be used. The area of interest is magnified by a 10x Nikon plan apochromatic objective lens and the visible light is then reflected by a mirror onto the camera sensor, ensuring the camera is not exposed to the X-ray beam. This setup produced an effective pixel size of 0.46μm.

2.3 Experimental setup

The set-up consisted of a micro syringe connected to the CCA of the bifurcation model via silicon tubing, with the ICA and ECA separately led to atmospheric pressure. Whole blood was pumped by a micro syringe pump (World Precision Instruments Inc UMP2) at a flow rate of 18μLmin^{-1}. The flow was allowed to reach steady state before images were acquired. The model was placed such that the geometry being imaged was symmetric about the depth. Images were acquired using a 4 megapixel high speed (500fps) intensified camera (IDT X5*i*). The field of view was 1.1x0.8mm^2 and the region of interest of the model was chosen to be the transition from the CCA to the ICA.

An exposure of 5ms was used with a corresponding interframe time of 40ms. To eliminate any temporal inconsistencies of the equipment during the experiment, oversampling was used to decrease the time required. Images were acquired at a frame rate of 100fps, four times the required rate, thus requiring a frame interval of 4 for the PIV analysis. This means that the PIV process was integrated between frame 1 and 5, 2 and 6, and so on. The data were analysed using the code described in Fouras *et al.* [4].

3. RESULTS

Figure 3 shows the correlation averaged vector field for the ICA overlayed onto an X-ray image of the model geometry. The

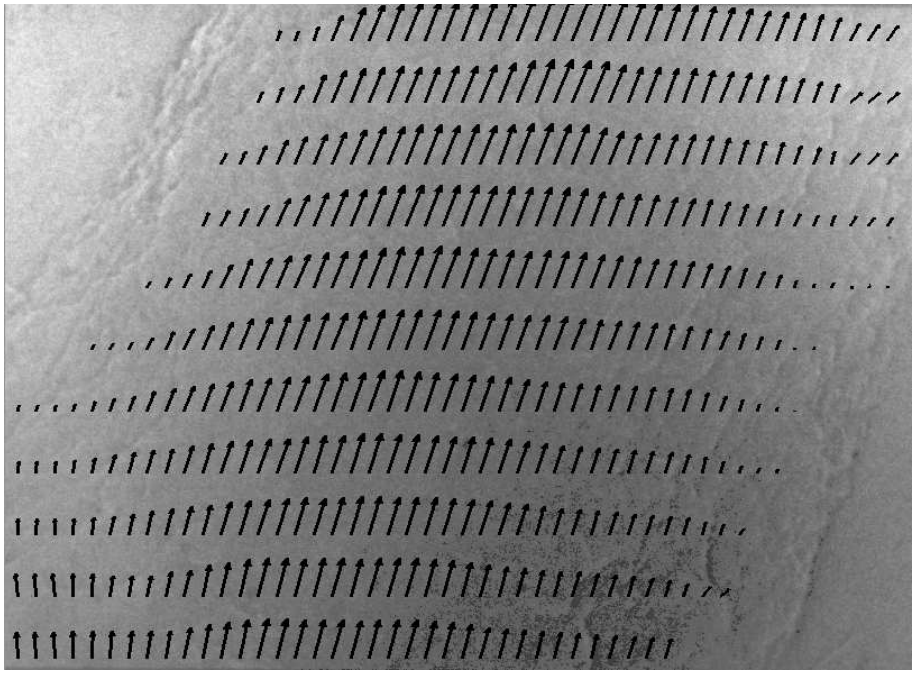

Figure 3: Correlation averaged vector field for the ICA overlayed onto an X-ray image of the model geometry.

interrogation windows used were 30x30μm^2 in area with 16 pixel spacing; 200 consecutive instantaneous correlation peaks were used for the correlation average. It is clearly seen in the first row of vectors (bottom of the figure) that the transition from CCA to ICA and ECA is affecting the velocity, with a parabolic profile developing as one moves closer to the wall. As the blood flows further downstream of the CCA into the ICA it is seen to gradually adopt a fully developed parabolic flow profile.

The slow increase from zero to maximum velocity on the outside wall compared to the inside wall of the ICA implies a lower wall shear stress (WSS) on the outside wall. This is in strong agreement with Steiman *et al.* [13], who also found the WSS to be higher at the inside wall. It is in low WSS areas that plaque deposits are seen to form, causing stenosing of the vessel, with this result suggesting the entrance of the ICA on the outside wall to be a advantageous location for this sort of development.

4. DISCUSSION

The ability to obtain *in vitro*, *ex vivo* and eventually *in vivo* PIV data is helping establish the knowledge base of the development and progression of arterial disease. With further advancements being made in synchrotron technology (such as the Australian synchrotron) and camera technology (such as faster and more sensitive sensors), likely to enable even shorter exposure times, the ability to acquire data of physiological realistic rates is within grasp. The current study has successfully shown that DEFINITY® can be used as a contrast agent for imaging blood flow within *in vitro* models. This knowledge will help *in vitro* X-ray PIV to image flow rates much higher than previously capable, whilst ensuring that the same techniques are readily transferable to *in vivo* investigations.

Future studies will investigate the velocity flow field and WSS of pulsatile blood flow, using a 5 Fourier mode approximation of a cardiac cycle, acquiring the velocity profile for the entire domain then using the technique described in Fouras *et al.* [3]. Various models of bifurcation, stenosis and aneurysm will be investigated with the aim of gaining further understanding into the fluid dynamics of whole blood within physiologically real geometries.

5. CONCLUSION

This paper has further demonstrated the ability of X-ray PIV for the investigation of biological systems. The velocity profile of the ICA in an opaque *in vitro* bifurcation model has been measured, with the region of low WWS identified on the outside wall of the ICA, thought to be an ideal location for the development of stenosis. Additionally, the use of gas micro-bubbles has proven successful in providing a stronger signal for PIV experiments whilst not negatively altering the properties of whole blood in a biologically harmful manner.

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