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LEUKOCYTE DEFORMATION IN CARDIAC ASSIST DEVICES

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SUMMARY

Ventricular Assist Devices (VADs) are pumps which support failing hearts. While considered by some surgeons as gold standard treatment, current VADs have many complications related to the imposed stress on the blood. In particular, damage to the leukocytes may contribute to infections, currently the biggest post-surgical problem. Our aim was to create a numerical model of a leukocyte which can be used to investigate leukocyte deformation in VADs. The leukocyte was modelled as a compound liquid droplet and solved in OpenFOAM using the multiphaseInterfoam solver. Initial results are presented for different shear rates, extensional versus planar shear, and for different nucleus sizes.

Key words: *leukocyte, compound drop, ventricular assist device*

1 INTRODUCTION

Over 500,000 people in the UK have heart failure and there are around 10,000 deaths each year [1, 2]. For the majority of patients heart failure is treated with a cocktail of drugs, or a pacemaker. However, in the worst cases patients really need a new heart. Around 14,000 patients are admitted to hospital annually with the most severe symptoms, unfortunately, fewer than 200 heart transplants are performed each year [3, 4].

Cardiac assist devices can be used to help the failing heart to pump blood around the body. Ventricular Assist Devices (VADs) work in parallel with the native heart to augment the function of the left, or both, ventricles. Blood perfusion is restored, improving quality of life and halting or even reversing the disease progression. 2 year survival rates for low risk VAD patients are now comparable with those of transplant patients [5]. However, although considered by some surgeons as gold standard treatment [6], current VADs have many complications related to the imposed stress on the blood. Much of the work done to date has focussed on the damage done erythrocytes, the red blood cells, under shear stress and numerical modelling of haemolysis has shown some success in assisting in the design of new devices. There has been far less work on the influence of fluid dynamic stress on leukocytes, the white blood cells.

Infections occur in 30% of VAD patients [7] and are the biggest long term cause of death [8]. Damage to leukocytes likely lowers a patients immune defence, reducing their ability to fight infections. Additionally cell microparticles (MPs) which break off can start the clotting cascade leading to thrombosis, a cause of device failure, heart attacks and neurological dysfunction. Reduced leukocyte numbers and circulating MPs were found in VAD patients [9, 10] and in the CentriMag VAD *in vitro* [11].

Leukocyte deformation under vascular flow conditions, and in pipettes, has been studied experimentally and numerically before, most notably by Kan *et al* [12, 13]. However, the shear stresses involved in those conditions are far smaller than those experienced by the leukocytes in cardiac assist devices: approximately < 10 Pa compared with > 100 Pa. In addition, the time scales involved are longer than those in cardiac assist devices: for example, depending on the flow rate blood spends approximately < 0.5 s within the device, compared with > 20 s in the pipette.

The aim of this work is to develop numerical models of leukocytes which can be used to investigate leukocyte deformation under the high shear, short exposure conditions typical of cardiac assist devices. Here we present the numerical model and initial results for varying shear rate, nucleus size and shear type. These demonstrate the viability of the model and reveal the differing influence of the nucleus in neutrophils versus lymphocytes.

2 METHODS

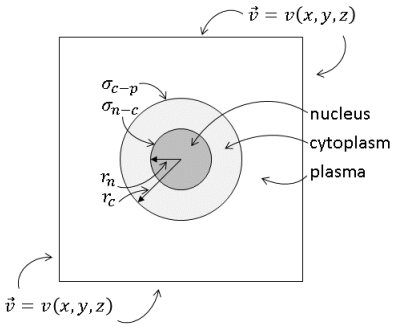

Figure 1: Leukocyte modelled as a sphere with concentric nucleus

The liquid-like behaviour of leukocytes is widely accepted [12] and so the leukocyte was modelled as a compound drop as shown in figure 1. The model then consisted of three fluids: plasma, cytoplasm and nucleus. The Navier-Stokes equations were solved using a finite volume method and the Volume of Fluid (VOF) method was used to calculate the volume fraction of each fluid and the positions of the interfaces. The surface tension at the plasma-cytoplasm (σ_{c-p}) and cytoplasm-nucleus (σ_{n-c}) interfaces represented the cell and nuclear membranes respectively. The methods were implemented in OpenFOAM (foam-extend-3.2) using the multiphaseInterFoam solver.

The cells were assumed to be spherical with concentric spherical nuclei. The nucleus of the neutrophil occupies 21% of the volume of the cell [12] and so the ratio of nuclear radius (r_n) to cell radius (R_c) was $r_n/r_c = 0.585$.

The cell was positioned at the centre of a cube with side length $4r_c$. The model was three-dimensional and the shear rate was specified using velocity boundary conditions on all cube faces. By specifying the velocity boundaries as a function of position any general shear rate could be applied. The velocity at the cell centre was always zero and so there was no displacement. The velocity field was initiated using the potentialFoam solver to ensure continuity of mass.

The cell was exposed to constant shear for the same fixed time in all simulations. Deformation of the cell and nucleus were examined at the end of the simulation.

3 RESULTS

3.1 Shear Rate Magnitude

Extensional shear was obtained by applying the velocity boundary condition $\vec{v} = G/2(2x, -y, -z)$ and the value of G was varied resulting in a range of shear rates. At low shear rates there was minimal deformation (figure 2). At high enough shear rates the cell deformed to a prolate ellipsoid, whereas the nucleus became an oblate ellipsoid, in agreement with work by Kan *et al* [12].

3.2 Size of Nucleus

In lymphocytes the nucleus occupies 44.4% of the volume [13] and so a cell with a nuclear radius $r_n/r_c = 0.76$ was created in order to compare the deformation of lymphocytes with neutrophils. For the low shear rate the cell with the smaller nucleus (like a neutrophil) had negligible deformation whereas the cell with the larger nucleus (like a lymphcyte) had a slightly prolate shape (figure 3).

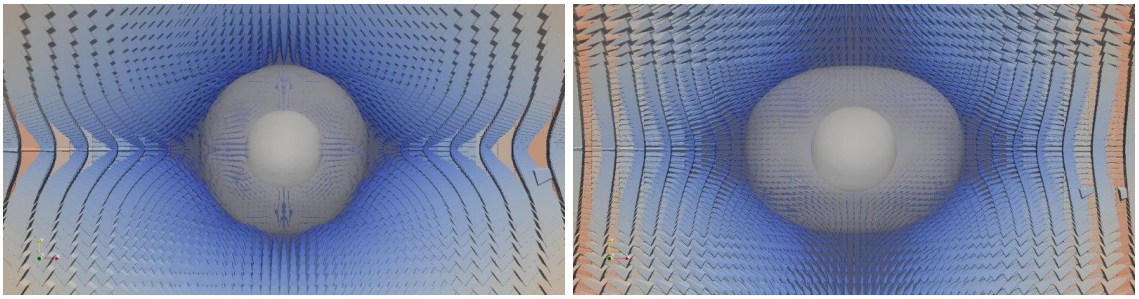

Figure 2: Influence of shear rate magnitude on cell deformation

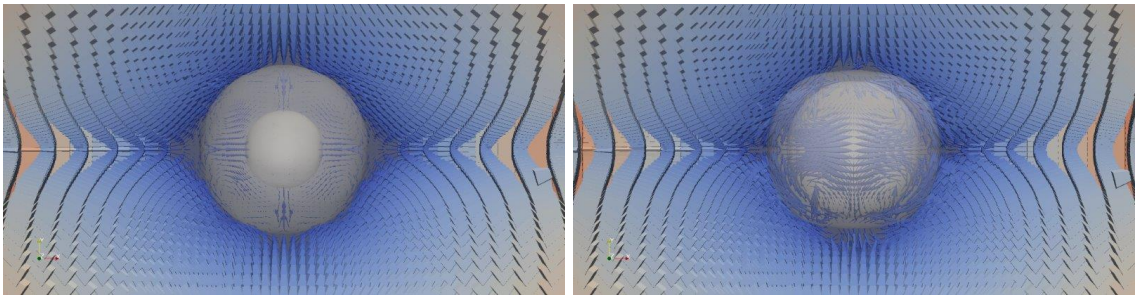

Figure 3: Influence of nuclear size on cell deformation

3.3 Shear versus Extension

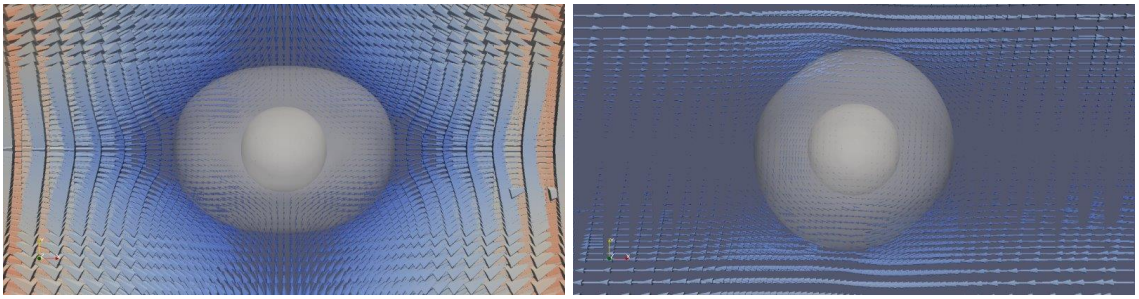

Figure 4: Comparison of extension and plane shear

Planar shear was obtained by applying the velocity boundary condition $\vec{v} = G(y, 0, 0)$. The cell deformed such that its long axis was inclined in the direction of the velocity (figure 4).

4 CONCLUSIONS AND FUTURE WORK

A model of a leukocyte was created and initial results show that it can be used to investigate cell deformation under different types of fluid dynamic shear stress (extension and plane shear), and for different types of leukocyte (neutrophils and lymphocytes). Future work will involve investigating the changes in deformation as the leukocytes travel through cardiac assist devices (figure 5) and the subsequent relaxation of these cells.

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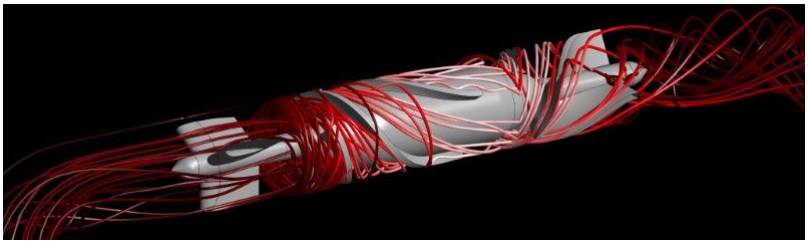

Figure 5: Pathlines through the HeartMate II VAD

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