MICROFLUIDICS DEVICES TO INVESTIGATE BLOOD CELL DYNAMICS DURING THROMBUS FORMATION DRIVEN BY SHEAR-GRADIENTS ON MICROSTENOSIS

Francisco J. Tovar-Lopez[1], Thach Nguyen[1], Mahyar Nasabi[1], Vijay Sivan[1], Arnan Mitchell[1], and Warwick S. Nesbitt[2]

[1] Microplatforms Research Group, School of Electrical and Computer Engineering, RMIT University, Melbourne, Victoria, 3001, Australia

[2] Department of Microbiology, University of Melbourne, Melbourne, Victoria, 3010 Victoria, Australia

ABSTRACT

We report on a microfluidic experimental platform and a computational fluid dynamics model to study blood cell dynamics at micro-scale stenoses where local strain-rate microgradients trigger platelet aggregation. The manner in which stenotic flow affects blood cell mass transport at physiological flow rates; and how this modulates platelet aggregation, remains unexplored. We present the design and experimental validation of a microfluidic device that incorporates asymmetric flow focusing of several fluidic streams to study the hemodynamic variables promoting platelet aggregation at shear-gradient mechanisms as well as a computational model to investigate local forces enhancing platelet transport.

KEYWORDS: blood clotting, microfluidics, cfd, volume of fluid, shear gradients.

INTRODUCTION

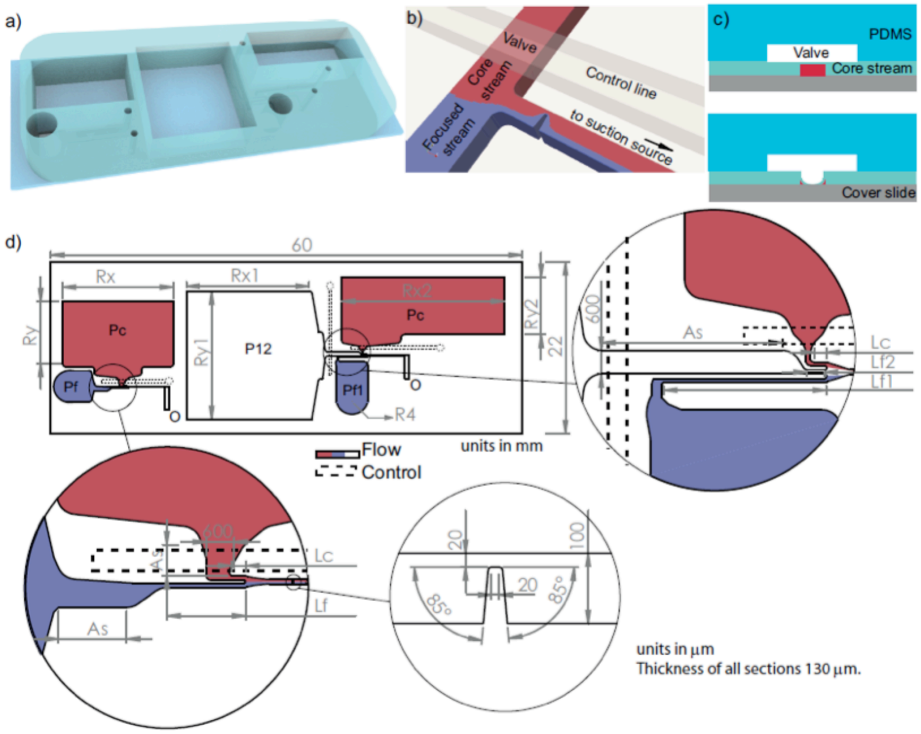
In order to investigate blood cell transport under conditions of complex flow through a stenosis, we have developed a microfluidic platform that both, mimicks a stenosed vessel[1], but also enables the control of blood flow streams. We also present a computational model to investigate the interaction of blood cells at stenosis sites. Control of blood streams is achieved using hydrodynamic flow focusing platform using a single flow driver (Fig. 1). To date, methods employing flow focusing have relied on positive pressure driven delivery of the sample via syringe pump; a method that has a number of practical limitations in the context of blood handling and experimentation. Our microfluidics platform generates different tunable streams of steady flow. The fluid sample is loaded directly into a reservoir, without having to preload the sample on a syringe. The hydraulic resistances of the feeder segments control the thickness of the streams. The flow is induced by a syringe pump in suction (refill) mode but any suction device can be used.

EXPERIMENTAL

Fig. 1 presents the overall device design and layout. On chip sampling was implemented to minimize contact with glass or plastic materials and long dead volumes by using a reservoir where the fluid sample is loaded close to the micro-contraction. A manually operated pneumatic valve was incorporated into the chip using multi-layer soft lithography to allow easy purging of the fluid lines as air bubbles can lead to resistance changes and disruption of streamline control. The dimension of the channel was 130μm×100μm. A micro-contraction used in previous investigations on blood micro-flows (thrombosis) ([1,2]), was fabricated to illustrate the capability of the technique in flow visualization.

COMPUTATIONAL MODEL

Figure 2 presents snap shots of a computational model that was developed to investigate the red cell-platelet dynamics at the stenosis. The role of red cells in promoting local changes in shear gradient forces to enhanced transport to stenotic walls was investigated. A transient multiphase model (3 phases) was developed in OpenFOAM to solve the equations of motion of fluid using Volume of Fluid to model cell interphases from red cells and platelets. Blood cells were modeled as different phases (phase 1 and phase 2), in plasma (phase 3).



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RESULTS AND DISCUSSION

Using this experimental platform and the computational model we identify the blood flow streams that principally contribute to platelet aggregate formation in a shear gradient driven model [1]–[3], present evidence of platelet stream crossing at microflows (Fig. 2). We demonstrate that relatively thin surface streams located at the channel wall are the primary contributor of platelets to the developing aggregate under shear gradient conditions. Furthermore we delineate a role for red blood cell hydrodynamic lift forces in driving enhanced advection of platelets to the stenosis wall and surface of developing aggregates. We show that this novel microfluidic platform can be effectively used to study the role of mass transport phenomena driving platelet recruitment and aggregate formation and believe that this approach will lead to a greater understanding of the mechanisms underlying shear-gradient dependent discoid platelet aggregation in the context of cardiovascular diseases.

CONCLUSION

This paper presented an alternative way to generate and manipulate fluids streams at the microscale. Several considerations that emerged from our experimental experience in the laboratory on handling biological fluids (blood), including the necessity of generate fluid streams in the same channel, and the necessity of having a simple flow system operated by a single source actuating the flow (syringe pump), were the driving force to create the present platform. On the other hand we presented our progress on modeling the platelet transport enhanced by local changes in red-cell hydrodynamic forces.

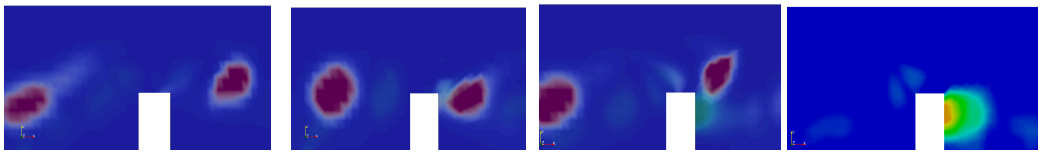

Figure 2: Computational fluid dynamics model to investigate red cell (red areas) and platelet (green areas) interaction at shear micro gradient flows. Red cells move along the stenosis enhancing platelet transport. Platelet accumulation and enhanced transport driven by red cell migration was observed in the model similar to experiments with blood.

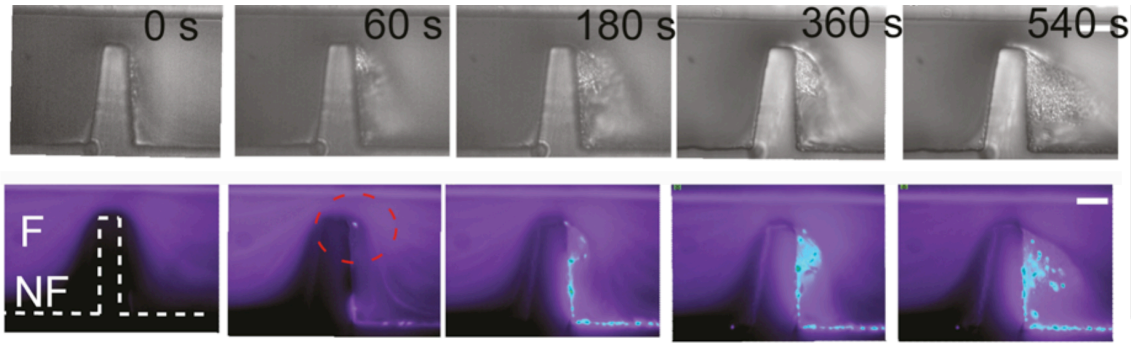

Figure 3: Experiment of blood flow streams where platelet stream crossing at microflows was observed,

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CONTACT

* FJTL.tovar.lopez.fj@gmail.com