From microscale events to clinical implications: investigating thrombosis through microfluidics and biocompatible membrane design

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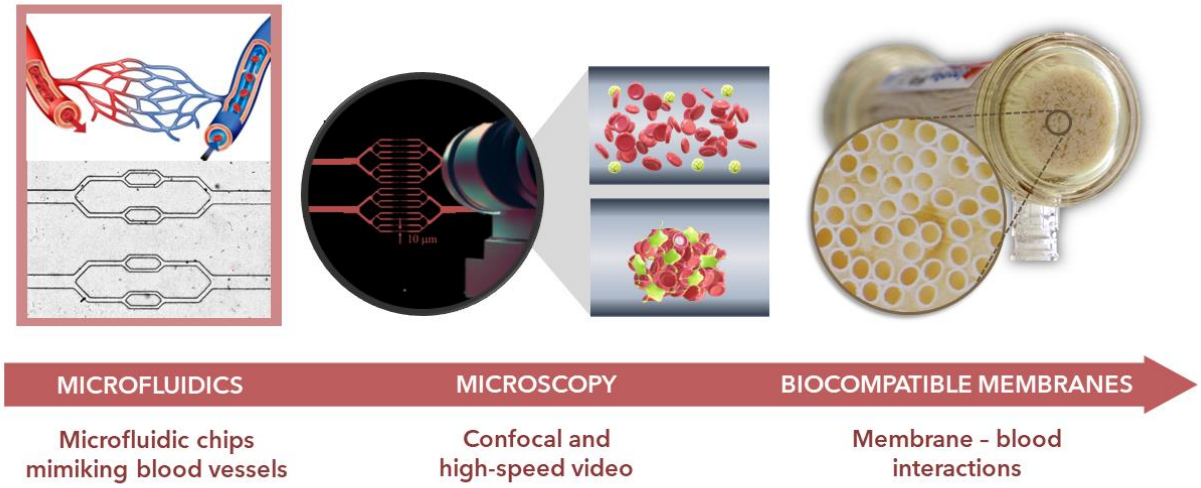

Thrombosis, a complex process involving the aggregation of red blood cells (RBCs) and platelets within blood vessels, poses significant cardiovascular risks, such as myocardial infarction and stroke. Understanding the underlying mechanisms of thrombosis is essential for developing targeted therapeutic strategies. In recent years, microfluidic systems have emerged as powerful tools for investigating thrombosis, as they can replicate the physiological conditions of blood flow within microscale channels [1].

This research project aims to study the impact of fluid-dynamic conditions on RBC and platelet aggregation mechanisms throw microfluidics, with a particular focus on elucidating the role of RBCs in thrombus formation and stability. While RBCs are known to interact with platelets and influence thrombosis, the precise contributions and underlying mechanisms are not fully understood [2].

The project begins with designing and fabricating microfluidic devices that accurately mimic the geometric and flow conditions of blood vessels [3]. Key features such as stenosis, bifurcations, and surface functionalization with coagulation-activating substances, enable the emulation of pathophysiological conditions associated with thrombosis [4]. Precise control over flow parameters, including velocity and shear stress, allows for the simulation of physiological and pathological blood flow conditions. Microfluidic platforms, coupled with advanced imaging techniques such as confocal microscopy and high-speed video microscopy, enable real-time visualization and analysis of the interactions between RBCs, platelets, and the surrounding fluid flow [5].

Quantitative measurements, including RBC deformation, platelet aggregation, thrombus growth, and velocity profiles of RBCs and aggregates, can be obtained using image analysis algorithms. The project can be divided into two phases, listed below.

- The primary phase will be devoted to the investigation of the influence of shear forces on the kinetics and morphology of RBC and platelet aggregation during thrombotic events. Additionally, the research aims to systematically explore the impact of various factors, such as haematocrit, platelet concentration, and rheological properties of blood, on thrombus formation and stability. The effect of the addition of coagulation-activating agents to mimic inflammatory states on thrombus formation will be investigated as well.

- In a subsequent phase, the study will focus on investigating the interaction between haemodialysis membranes and blood, particularly regarding thrombus formation. This research addresses the development of more biocompatible membranes capable of preventing thrombus formation during dialysis, especially in cases where heparinization of the circuit is not feasible or desirable due to patient-specific clinical issues.

In conclusion, this Ph.D. project utilizes microfluidics to investigate the role of fluid-dynamic conditions on RBC and platelet aggregation during thrombosis events, providing insights into underlying mechanisms and contributing to the development of more biocompatible dialysis membranes. The findings will enhance our understanding of thrombotic processes and pave the way for improved therapeutic interventions and membrane designs, ultimately benefiting patients at risk of thrombosis-related complications.

References

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