

Developing Blood Vessel-on-a-Chip Platform for Studying Vascular Mechanobiology

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Introduction

Cardiovascular disease is a leading cause of death worldwide, with atherosclerosis which is driven by localized vascular dysfunction. Plaques preferentially form in regions of disturbed flow, such as arterial branches, highlighting the role of shear stress [1]. Endothelial cells (ECs) act as mechanosensors. Laminar flow promotes a quiescent state, whereas disturbed flow induces inflammation and atherogenesis [2]. These responses highlight the need for physiologically relevant flow models.

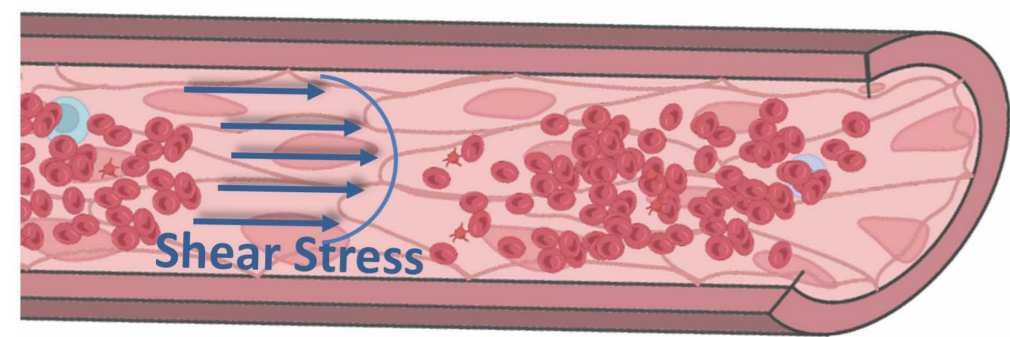


Figure 1. Representation of blood flow-induced shear stress on endothelial cells lining the vessel wall.

Materials & Methods

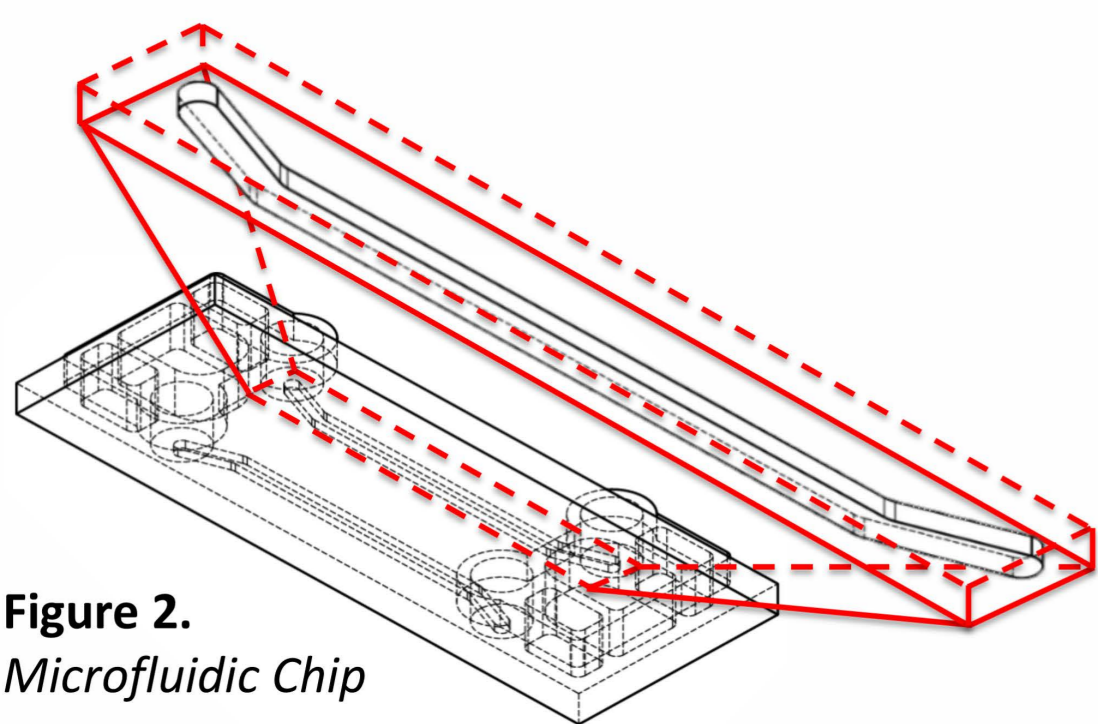


Figure 2. Microfluidic Chip

Computer Assisted Design Modeling (CAD) / Computational Fluid Dynamics Simulation (CFD): A commercially available microfluidic chip (BeOnChip, Be-Flow) geometry was modeled and imported into a CFD platform to simulate fluid flow and evaluate velocity and shear stress, under physiologically relevant conditions.

Seeding of Brain ECs (BECs): BECs were seeded in fibronectin-coated microchannels until monolayer was formed and subjected to flow.

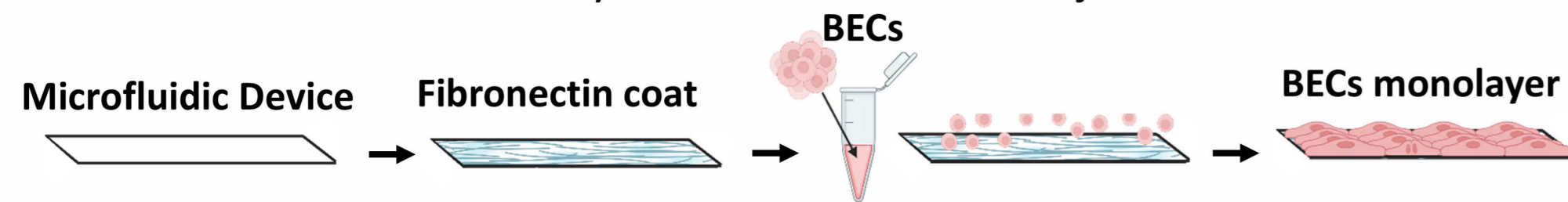


Figure 3. Schematic diagram of BECs seeding

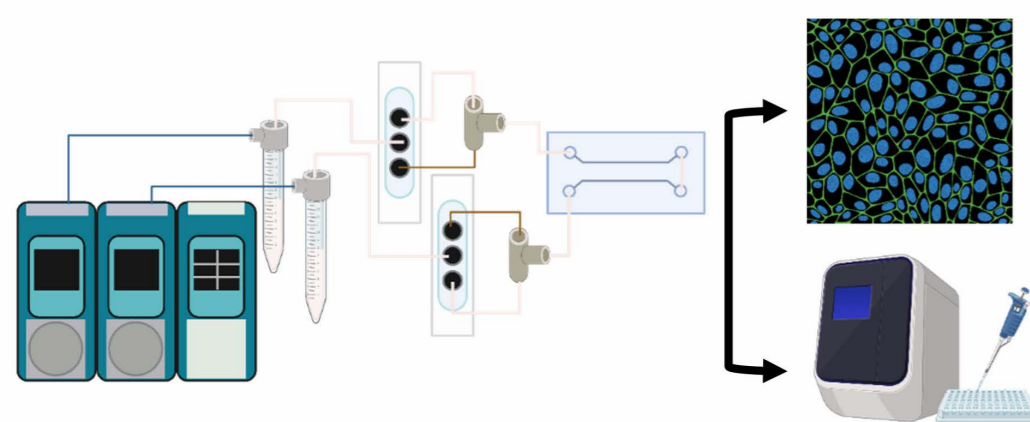


Figure 4. Experimental workflow of flow stimulation and analysis

Categorization of endothelial cells post-flow: A pressure-driven microfluidic pump was used to apply flow to cells. Post-flow, cells were analyzed using immunostaining to evaluate morphological changes while qPCR for gene expression.

Results

CFD simulations reproduces relevant physiological conditions

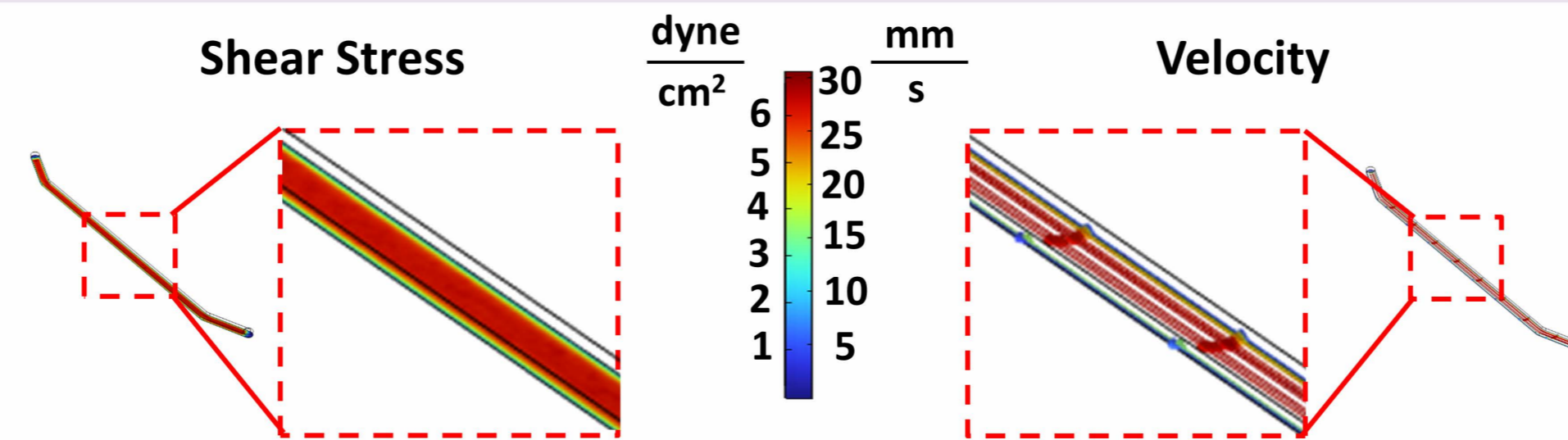


Figure 5. Shear Stress (left) and Velocity Fields (right). COMSOL Results revealed minimal spatial variations in shear stress and velocity within the microchannel. Laminar flow was maintained, while geometric transitions produced localized changes in shear stress and velocity.

Flow induces endothelial elongation and alignment

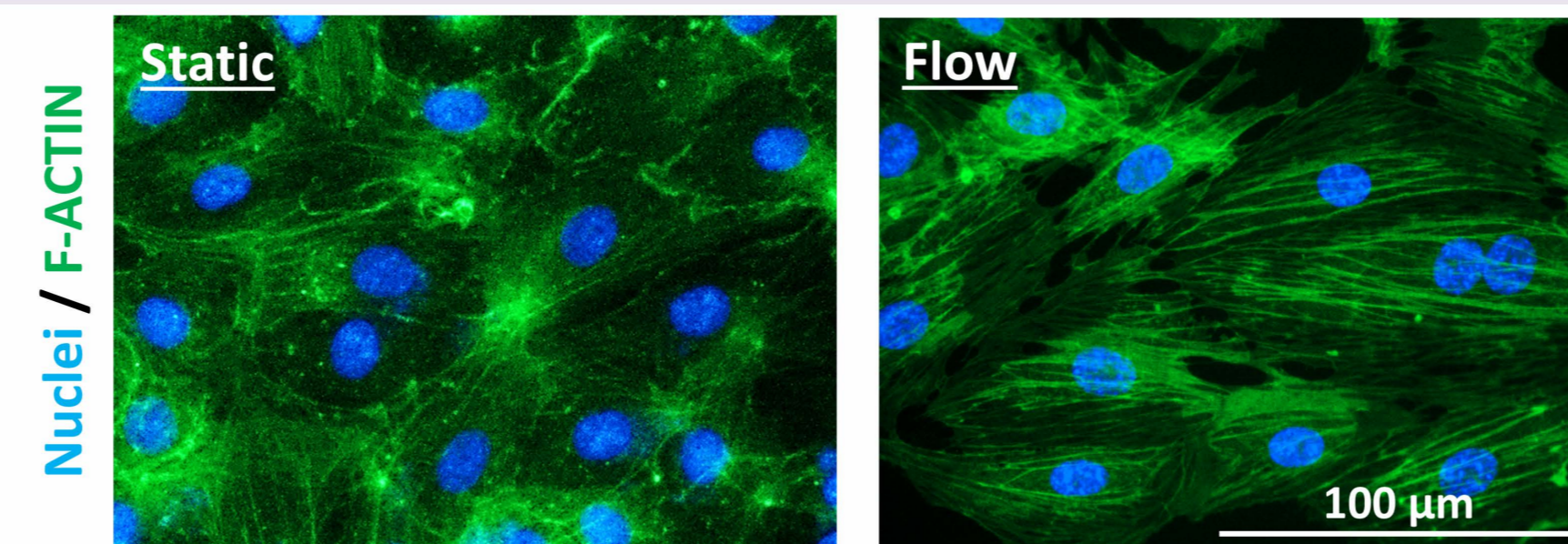


Figure 6. Immunofluorescence imaging revealed distinct morphological differences. Static controls displayed a random, cobblestone morphology, while flow-exposed cells exhibited elongation and alignment along the direction of shear stress.

Quantitative analysis shows the directional organization of BECs after flow

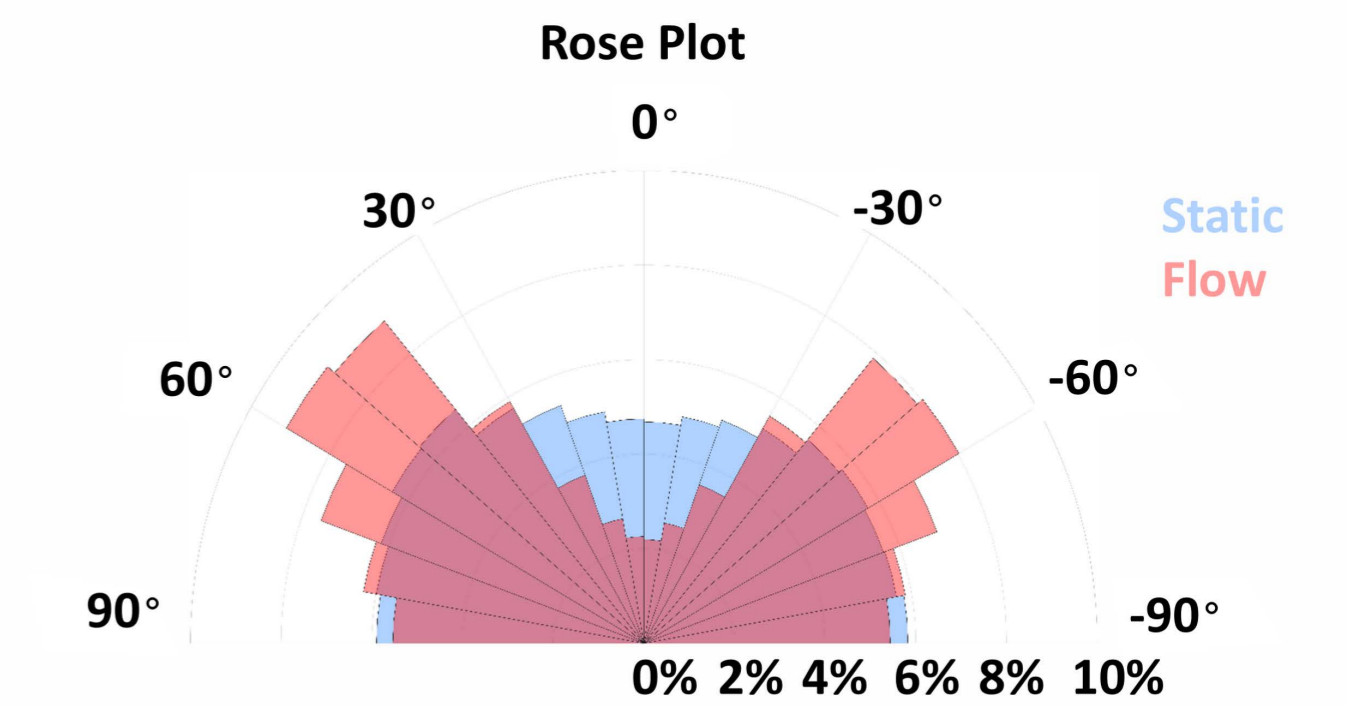
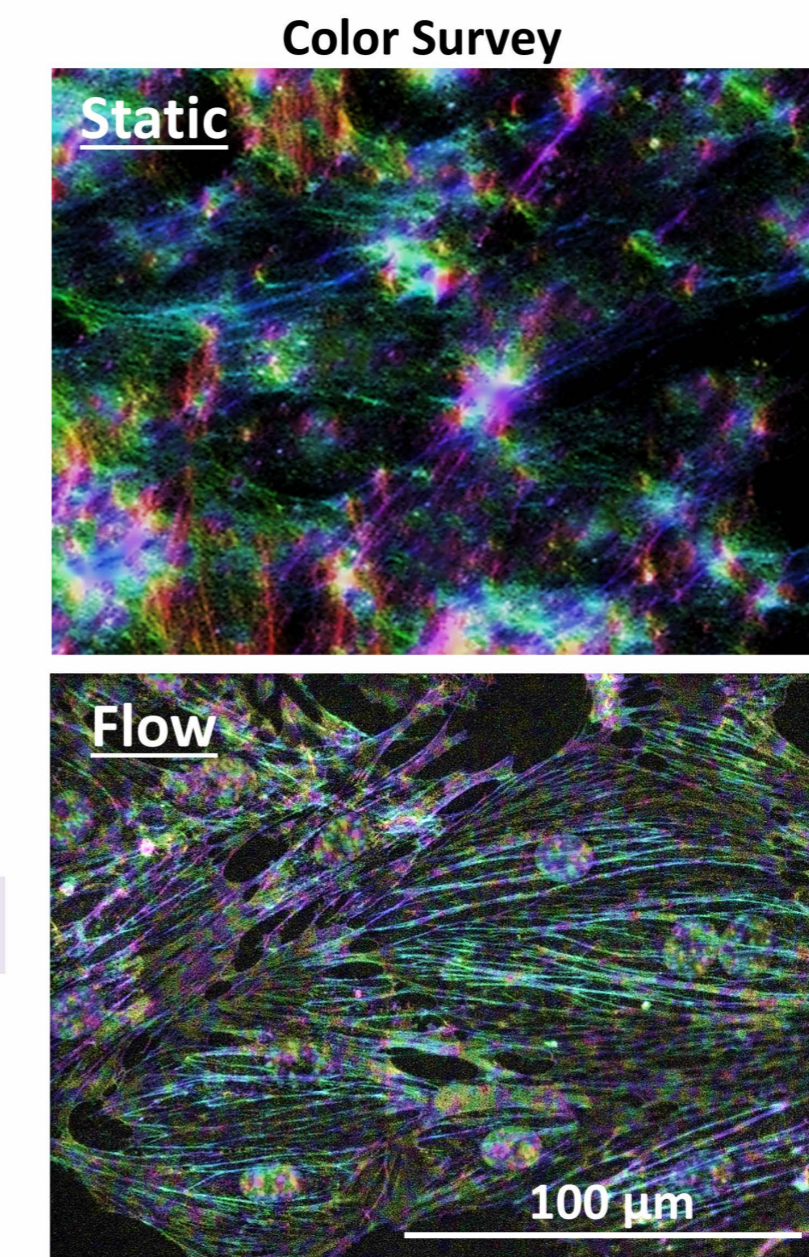


Figure 7. Flow induced endothelial elongation and alignment. Compared to random morphology in static controls. Orientation analysis revealed isotropic distributions under static conditions and strong alignment under flow. Rose plots revealed the orientation of cells.

Shear stress increase the flow-sensitive gene expression in BECs

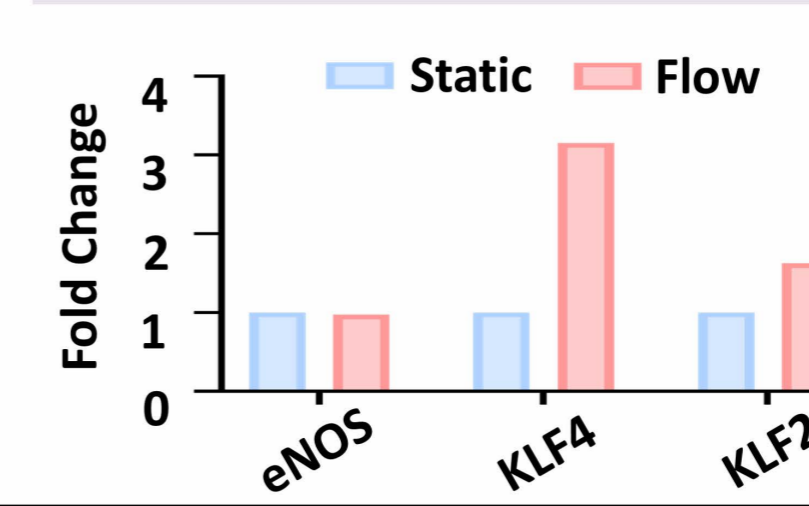


Figure 8. Flow induces KLF2 and KLF4 expression in BECs. Flow exposure altered expression of shear-responsive genes in BECs. RT-qPCR showed increased expression of KLF4 (~3.1-fold) and KLF2 (~1.6-fold), while eNOS remained unchanged (~0.97-fold) compared to static controls.

Conclusion

This study demonstrates that microfluidic modeling combined with CFD simulations can recapitulate physiologically relevant vascular flow conditions. Experimental results confirm that flow induces endothelial alignment and activates shear-responsive gene expression, validating this platform

Acknowledgements

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Future Work

Future work will focus on performing biological repeats of these experiments, more complex vascular geometries and co-culture systems to better mimic in vivo conditions. Additionally, longer-term flow studies and expanded gene and protein analyses will be performed to further characterize endothelial responses.

References

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