Elucidating the role of substrate meso and micro topology in endothelial cell growth, proliferation and stability

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Concept. One of the current challenges in the field of biomedical devices is to address issues like mechanical mismatch, intimal hyperplasia, and thrombogenicity. The interaction between blood and the medical device's surface triggers coagulation and thrombus formation. To prevent this condition, patients are treated with lifelong therapy, using anticoagulants and/or platelet inhibitors. The most natural approach remains to cover the surface with host derived ECs or modifying the interface to elicit such effect.

Endothelial cells play a crucial role in maintaining vessel patency, acting as key regulators of vascular wall homeostasis and preventing thrombus formation.

It is known that wall shear stress (WSS) influences the phenotype of ECs, including the ability to adhere to a surface, and may be used to control cell differentiation [1]. For this reason the goal of this PhD project is to evaluate the WSS in the presence of different patterns to identify the one that best promotes cell growth.

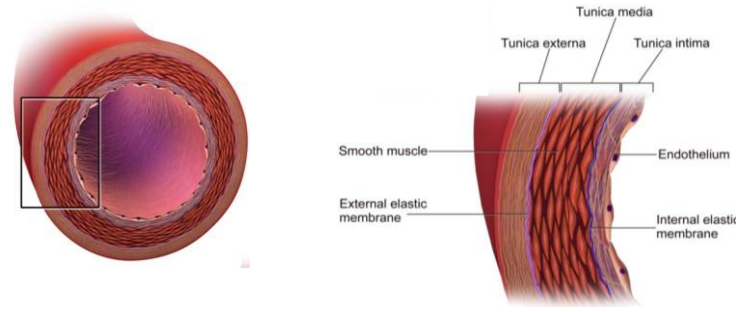
Scientific approach. Lithographic wafers with different polymeric electrospun patterns (honeycomb, square, fish-scale , etc) will be fabricated experimentally. Concurrently, identical geometries will be subjected to numerical evaluation utilizing computational fluid dynamics (CFD). This numerical analysis serves as a powerful tool, offering detailed insights into complex blood flow dynamics and shear stress distribution.

In addition to assessing the WSS, another crucial parameter could be the *ECAP metric (Endothelial cell activation potential*). This predicted parameter, relating oscillatory shear index and time-averaged wall shear stress, is employed to identify areas prone to high endothelial sensitivity [2].

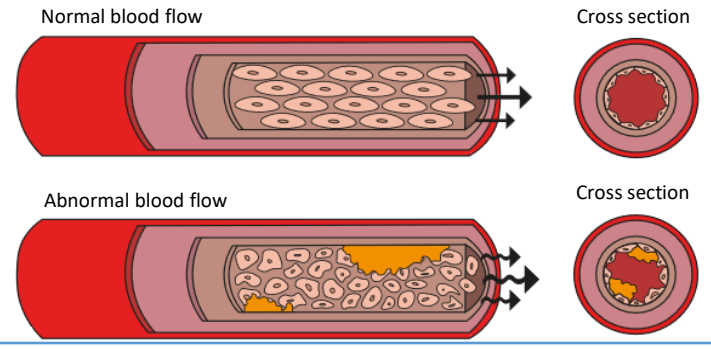
To validate the numerical models, the adhesion of cells on the substrates will be assessed. This validation endeavor will encompass the utilization of two distinct cellular assays aimed at evaluating cell traction force: Particle Tracking Microrheology and Three-Dimensional Traction Force Microscopy.

Research objectives. Recognizing the ability of endothelial cells to ensure blood homeostasis and since the substrate microtopography can be optimally modified to achieve cell alignment and stability, the goal of this PhD project is to identify an optimal shape and size pattern that promotes the growth of a functional endothelial cell layer by manipulating flow conditions. These data could help design and development of the surface of new medical devices.

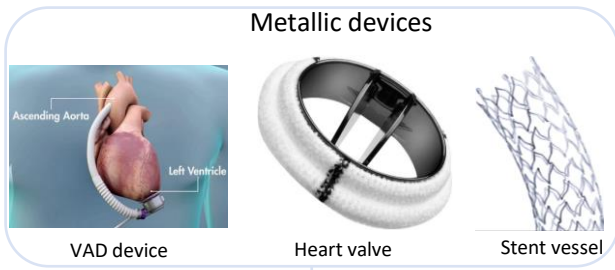
ANATOMY OF THE BLOOD VESSEL



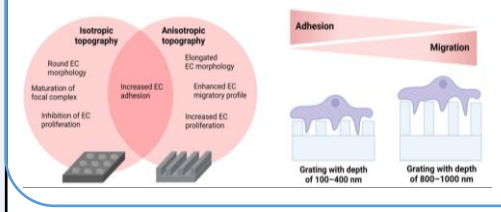
CLINICAL NEED



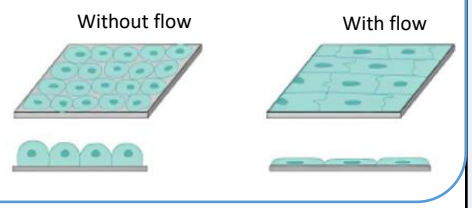
STATE OF THE ART



INFLUENCE OF THE PATTERN ON THE CELLS

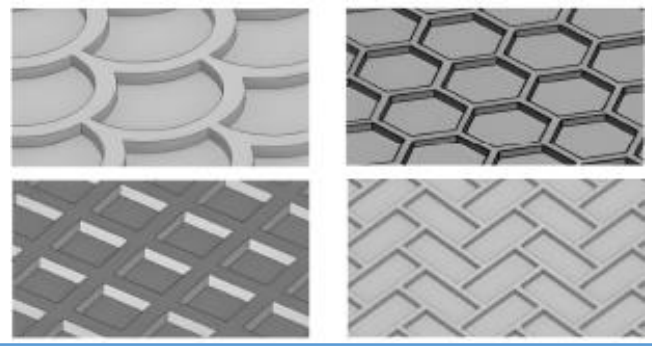


INFLUENCE OF BLOOD FLOW ON CELLS PHENOTYPE



PATTERNS TO BE INVESTIGATED VIA CFD SIMULATIONS

SPACING
20 µm
DEPTH
20 µm



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[1] Riha, et al. "Roles of hemodynamic forces in vascular cell differentiation." (2005).

[2] Mutlu, et al. "How does hemodynamics affect rupture tissue mechanics in abdominal aortic aneurysm: Focus on wall shear stress derived parameters, time-averaged wall shear stress, oscillatory shear index, endothelial cell activation potential, and relative residence time." (2023).

[3] Khalili, et al. "A review of cell adhesion studies for biomedical and biological applications." (2015).

[4] Bachmann BJ, et al. "Honeycomb-structured metasurfacesfor the adaptive nesting of endothelial cells under hemodynamic loads." (2018).