Bio-fabrication methods and computational approaches applied to cardiovascular tissue engineering scaffolds and in-vitro models

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Cardiovascular tissue engineering

Concept: In 2020, 19 million deaths were attributed to cardiovascular diseases (CVDs), including stroke, and atherosclerosis [1].
Blood-contacting devices play a pivotal role in managing CVDs since one of the most common causes of their failure is the formation of blood clots [2].

From a tissue engineering perspective, the formation of a bio-engineered layer of endothelial cells on blood-contacting surfaces offers a promising approach to mitigate thrombogenic complications. It is well established that the native endothelium remains the gold standard for blood contact due to its natural anticoagulant and anti-inflammatory characteristics [3].

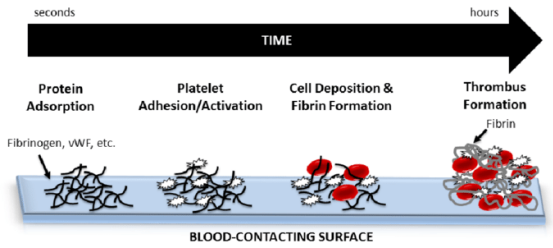
The PhD project aims to evaluate the structure of the native endothelium through the state of the art of imaging and replicate the cellular patterns in in-vitro tissues through bio-fabrication technologies.

It is known that a designed microstructure uniquely controls cell-biomaterial interactions and the initial endothelialisation phase.

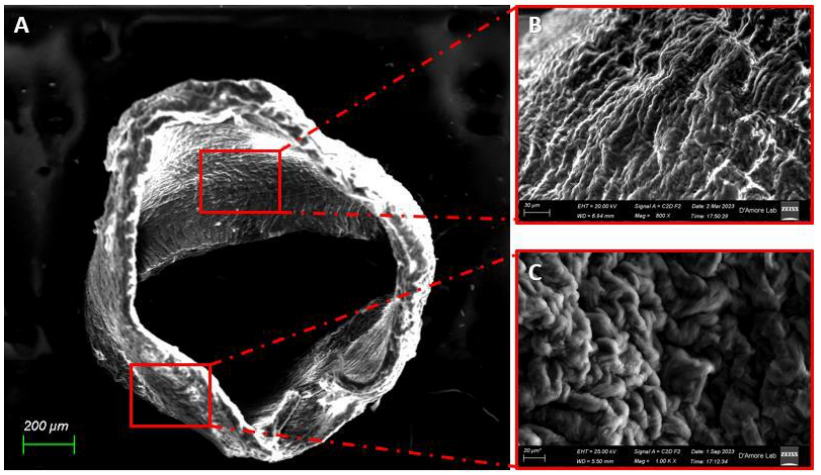
Scientific approach: The first phase of the project is the collection of both animal and human, pathological and healthy native tissues (e.g. coronary arteries) to evaluate the endothelium structure. Imaging analysis is carried out with a scanning electron microscope and a multiphoton microscope. Two different parameters are examined: the mean fiber angle θc that represents the angle between a fiber segment and the direction of alignment, and the orientation index OI, whose value is in the interval of 0.5 (for isotropic structures) and 1 (for anisotropic structures).
The second phase of the project involves the fabrication of patterned scaffolds combining two different bio-fabrication techniques: electrospinning, and lithography. Electrospinning is a cost-effective and versatile technique that allows the formation of polymeric micro- and nanofibers. Photolithography is a process that allows the transfer of geometric patterns on a mask on the surface of a wafer.
Scaffolds are then characterized with cellular tests to understand which pattern promotes the endothelium formation.

Research objectives: The PhD project aims to identify an optimal shape and size pattern that promotes the growth of a functional endothelial cell layer by manipulating parameters such as substrate stiffness, surface geometry, and topography. These data could help design and development of the surface of new medical devices.

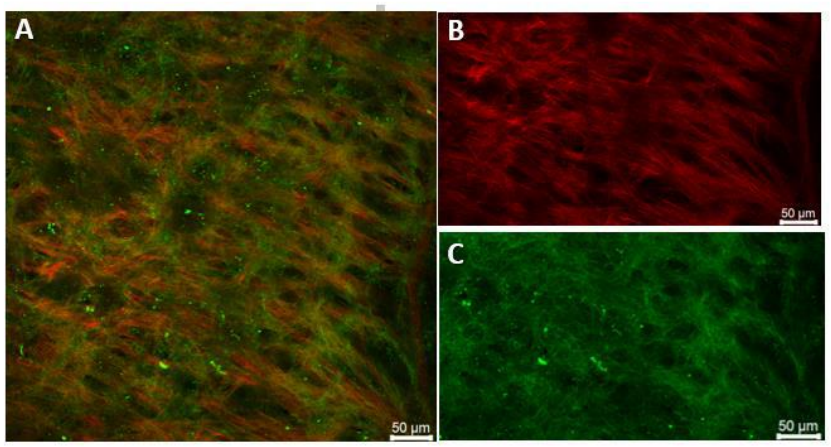
CLINICAL NEED



IMAGING ANALYSIS



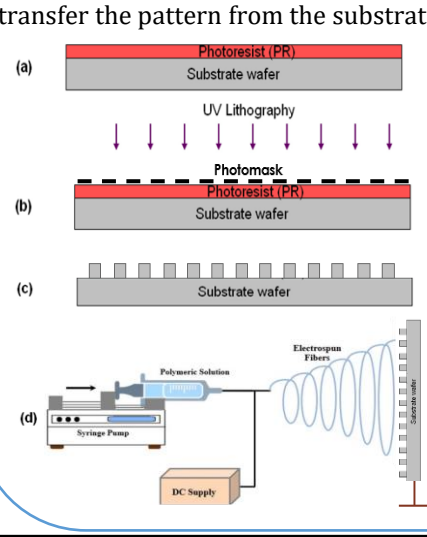
(A) SEM image of coronary artery cross-section 100X. (B) Intima side (C) Adventitia side

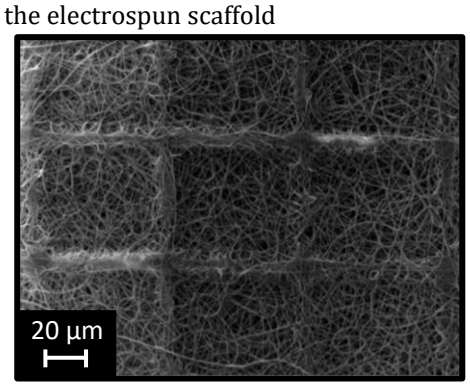


A) MPM analysis: Image stacks of 500 x 500 x 70 µm of intima side coronary artery. (B) In red, collagen fiber. (C) In green, elastin fibres

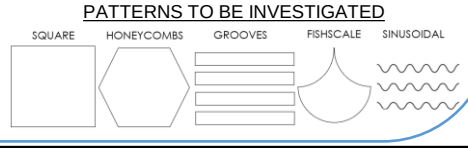
COMBINATION OF ELECTROSPINNING AND PHOTOLITHOGRAPHY

The patterned wafer acts as a collector for the electrospinning process in order to transfer the pattern from the substrate the electrospun scaffold





PATTERNS TO BE INVESTIGATED



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[3] V. W. M. van Hinsbergh, "Endothelium—role in regulation of coagulation and inflammation," *Semin Immunopathol*, vol. 34, no. 1, pp. 93–106, Jan. 2012, doi: 10.1007/s00281-011-0285-5.