Endothelial cells response to combined loading from flow and substrate deformation: A quantitative analysis

Martina Genta

Master Thesis in Biomedical Engineering
Department of Mechanical and Aerospace Engineering, Politecnico di Torino, Italy
Email: martina.genta92@gmail.com
Supervisor: Umberto Morbiducci (umberto.morbiducci@polito.it)

Extract from the Supervisor's reference letter

… Master Thesis project was focused on the study of endothelial cells response to combined loading from flow and substrate deformation. Martina's thesis work was carried out within an experimental in vitro framework and was integrated by a computational study aimed at the simulation of the substrate deformation under stretching condition. Part of Martina's thesis project was developed at ETH (Zurich, Switzerland) within the Zürich Heart project …

Martina's Master Thesis has been developed in the cardiovascular framework with the aim of developing a new innovative ventricular assist device. This specific need is due to the drastic increase of the percentage of population affected by cardiovascular diseases in the next decades. Indeed, along this trend, the development of new and innovative solutions has become the next step towards the decrease of health problems.

Within this context, the Zürich Heart project focused on the development of a new left ventricular assist device (LVAD) based on a hyperelastic hybrid membrane. Thanks to the deformation of the membrane, the blood is pulsed from the ventricle directly to the aorta allowing the patience to receive the correct cardiac output. Compared with the state of art, the disruptive and challenging idea of this project is to cover with autologous endothelial cells the inner part of the device, and in particular the membrane, in order to have a full integration and a total hemocompatibility of the device inside the human body.

Martina's work focused on this specific challenge, that is the study and the analysis of endothelial cells response to combined loads from flow and substrate deformation.

The in vivo reaction of endothelial cells to different loads is well known, but, on the other side, few studies in vitro have been performed in a complex environment. As a consequence this Master Thesis was essential for the investigation of cells behaviour under complex loading conditions and for the definition of their survival limits.

In order to achieve this goal a systemic study of cells behaviour under different environmental conditions is required. Martina dealt with this problem from two different perspectives: a pure biological cells behaviour and a mechanical analysis of the flow conditions and deformation of the membrane.

Regarding the first part, a bioreactor has been used in order to simulate the conditions that cells will experience inside the device. Firstly, the two loads, shear stress and deformation of the membrane, were applied separately and then different combinations were tested aiming at determining the survival limits of cells and the threshold above which one stimulus, either shear stress or stretching, prevails on the other.

Moreover, from a more mechanical point of view, a complementary computational study of the membrane has been performed aimed at investigating the influence of initial conditions on the final applied stretch, and also the influence of boundary conditions (clamping) applied to the system. Finally, a pure mechanical characterization of the material of the membrane, PDMS, has been performed in order to extract the exact law that describes the hyperelastic material, allowing to obtain the precise values that cells experience inside the bioreactor.

Overall, the results obtained combining the biological study and the mechanical tests, allowed to identify not only the different behaviour of cells in complex environments, but also to determine which is the most detrimental area of the membrane for their survival. As a consequence, Martina's Master Thesis was fundamental to define the right values needed to obtain a healthy and confluent monolayer of cells, paving the way for a new era of ventricular assist devices.

…

ISBN: 978-88-6296-000-7