AUTHENTICALLY COMPLEX VASCULAR BIO-MIMETIC MICROFLUIDIC CHIP

Marco Miali[†]*, Giuseppe Pascazio[*] and Paolo Decuzzi[†]

[*] Departmento di Meccanica, Matematica e Management (DMMM)
Politecnico di Bari (POLIBA)
[†]Laboratory of Nanotechnology for precision medicine
Italian Institute of technology (IIT)
e-mail: marcoelvino.miali@poliba.it / marco.miali@iit.it
e-mail: giuseppe.pascazio@poliba.it
e-mail: paolo.decuzzi@iit.it

ABSTRACT

In the last years microfluidics gained a central role in biomedical and biological applications, thanks to technological progress achieved in designing and manufacturing in vitro models for the manipulation of fluids. The use of complex systems increases their feasibility for a more realistic and tailored studies *in vitro* finalized to satisfy increasingly challenge in biological and medical field.

Here, we propose an innovative bio-mimetic microfluid chip obtained directly by soft-lithography with PolyDiMetilSiloxane (PDMS) of a natural '*Hederal elix*' leaf. The natural template ensures the ability to mimic a human cardiovascular system organized in a complex 3D configuration. The ability of the chip to replicate human cardiovascular system makes it a widespread bio-alternative of standard process.

The functionality of the geometrical configuration in human cardiovascular systems has been demonstrated by Murray [1], and afterwards for the lymphatic vessels of ~~the~~ leaves by Price et al. [2]. As a proof of concept, the geometrical law proposed by Murray for the cardiovascular system was firstly verified to hold also for the leaf under investigation, thus ensuring the geometrical feasibility of the bio-device. More in the detail, a topology study revealed channels dimensions from 70 up to 300 um making the bio-microfluidic chip suitable to mimic arteriole and precapillary vessels. Presenting different branches in a unique device ensures the complexity of the chip exploiting the natural template of the leaf and, respecting Murray's law, the proposed bio-device confirms the direct proportionality between flow-rate and cross-sectional area. Study of the fluid dynamics was assessed by performing the u-PIV experiment, returning useful data in terms-of velocity and flow-rate inside channels and branches.

Further, the chip has been biologically functionalized by creating an endothelium monolayer able to cover continuously all the inner surface of the channels.

Adhesion experiments were performed: (a) by flowing Cancer Tumor Cells (CTC), and in particular MDA-MB-231 breast cancer cells, in order to verify adhesion trend vs channel flow rate; (b) by flowing Nano Particle (NP), having spherical and discoidal shape, in order to assess the adhesion for different channels.

To gain deeper insight of the physics behind NPs circulation inside human micro-vasculature, a numerical model of the proposed bio-devise is employed, by means of a Lattice-Boltzmann Method (LBM), an approach particularly efficient to simulate the dynamics of the fluid in micro-circulation also in the presence of transported particles [3]. Here we use the model to predict vascular transport of NPs and compare experimental results for adhered NPs. The analysis are carried out using the real geometry of the leaf channels, obtained directly from a 3D microscopy acquisition.

REFERENCES

[1] MURRAY, Cecil D. The physiological principle of minimum work: II. Oxygen exchange in capillaries. *Proceedings of the National Academy of Sciences*, 1926, 12.5: 299-304.

[2] PRICE, Charles A.; KNOX, Sarah-Jane C.; BRODRIBB, Tim J. The influence of branch order on optimal leaf vein geometries: Murray's law and area preserving branching. *PloS one*, 2013, 8.12: e85420.

[3] COCLITE, Alessandro, et al. A combined Lattice Boltzmann and Immersed boundary approach for predicting the vascular transport of differently shaped particles. *Computers & Fluids*, 2016, 136: 260-271.