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MULTI-LEVEL MODELLING OF THE HEPATIC PERFUSION

Charlotte Debbaut[1*], Diethard Monbaliu[2], Pieter Cornillie[3], Christophe Casteleyn[4], Manuel Dierick[5], Jan Vierendeels[6], and Patrick Segers[1]

[1]IBiTech – bioMMeda, Department of Electronics and Information Systems, iMinds Future Health Department, Ghent University. Campus Heymans – Blok B, De Pintelaan 185, B-9000 Gent, Belgium. Charlotte.Debbaut@Ugent.be and Patrick.Segers@Ugent.be, www.biommeda.elis.ugent.be
[2]Abdominal Transplant Surgery, University Hospitals Leuven, & Department of Microbiology and Immunology, KU Leuven. Herestraat 49, B-3000 Leuven, Belgium. Diethard.Monbaliu@uzleuven.be
[3]Department of Morphology, Faculty of Veterinary Medicine, Ghent University. Salisburylaan 133, B-9820 Merelbeke, Belgium. Pieter.Cornillie@ugent.be
[4]Laboratory of Applied Veterinary Morphology,, Department of Veterinary Sciences, Faculty of Pharmaceutical, Biomedical and Veterinary Sciences, University of Antwerp. Universiteitsplein 1, B-2610 Wilrijk, Belgium. Christophe.Casteleyn@Uantwerpen.be
[5]UGCT, Department of Physics and Astronomy, Ghent University. Proeftuinstraat 86, B-9000 Gent, Belgium. Manuel.Dierick@Ugent.be
[6]Department of Flow, Heat and Combustion Mechanics, Ghent University. Sint-Pietersnieuwstraat 41, B-9000, Gent, Belgium. Jan.Vierendeels@Ugent.be

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INTRODUCTION

Liver transplantation is a successful treatment for end-stage liver failure. Unfortunately, there is a structural shortage of donor livers. The inclusion of lower quality livers (e.g. donation after cardiac death) may help enlarging the donor pool. These organs are, however, more susceptible to ischaemia-reperfusion injury, partially aggravated by static cold storage. Hypothermic machine perfusion (HMP) has therefore been proposed as an alternative preservation technique, allowing better and longer preservation. Since liver HMP still faces potential hazards (sinusoidal endothelial injury and flow competition [1]), it is essential to clarify the determinants of the intrahepatic haemodynamics. To this end, we investigated and modelled the hepatic vasculature and perfusion across different length scales.

METHODS AND RESULTS

The vasculature of a human liver, discarded for transplantation, was corrosion cast by simultaneous injections of resin (Batson's #17, Polysciences, USA) in the hepatic artery (HA; including barium sulfate as contrast agent) and portal vein (PV). The vascular replica was first imaged in globo (± 110 μm resolution) using a high-resolution micro-CT scanner (UGCT, Belgium) to image the first blood vessel generations (macrocirculation). Thereafter, a lobe (88 x 68 x 80 mm³) was dissected and scanned (± 71 μm resolution) to investigate vessel generations distal to the macrocirculation (mesocirculation). In a third step, a small sample (2.0 x 1.5 x 1.7 mm³) was dissected from the liver cast to image the microcirculation (± 2.6 μm resolution). Image processing resulted in 3D reconstructions and topological

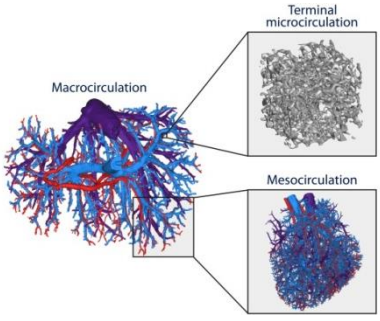

Figure 1. Visualisation of the hepatic vasculature at different length scales.

data of the hepatic vascular trees (HA, PV and hepatic veins (HV)) and the sinusoidal network (Fig. 1). Branching topologies and geometrical features were quantified for the macro- and mesocirculation based on data from vessel generations 1-13 (e.g. radii ranging from 13.2 to 0.08 mm, lengths ranging from 74.4 to 0.74 mm). The microcirculation showed a complex network of interconnected and intertwined sinusoids (mean radius of 6.63 μm, mean porosity of 0.15). Based on these data, various computational models were developed to simulate liver perfusion at different length scales. An electrical analog model of the whole liver blood circulation was developed based on the macrocirculation data [2]. This model allows simulating pressure drops and flows throughout the liver for natural blood flow as well as HMP (Fig. 2). Next, a 3D computational fluid dynamics (CFD) model of the microcirculation was developed. Simulations (Fig. 3a; based on 3D reconstructions) revealed anisotropic permeability characteristics within liver lobules (higher permeability parallel to the central vein; lower permeability in radial and circumferential directions) [3]. The latter results were incorporated in a new 3D porous medium liver lobule model, including vascular septa at the lobule borders (Fig. 3b).

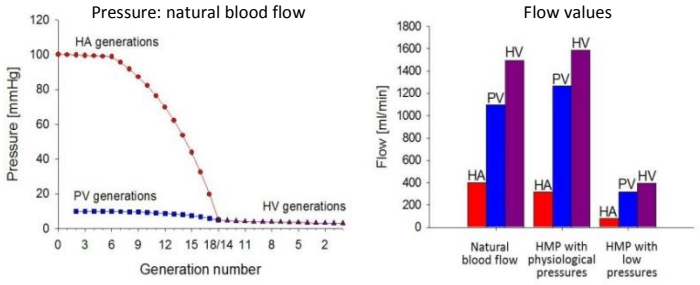

Figure 2. Results of the electrical analog model: pressure profiles and flow values for natural blood flow and HMP conditions.

CONCLUSION

A multi-level framework of models was developed to simulate hepatic perfusion at different length scales. Unique 3D morphological and geometrical data have been obtained from the macrocirculation down to the microcirculation, as well as novel models and insights into the haemodynamic behavior of the liver (e.g. during HMP). This approach can be extended to other applications (e.g. living donor liver transplantation and liver pathologies such as cirrhosis) and organs (e.g. kidneys).

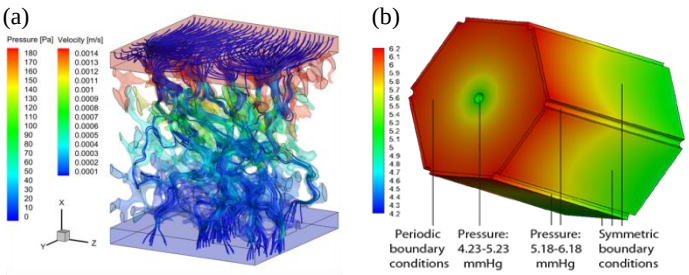

Figure 3. Results of micromodels: (a) pressure contours (and streamlines) of (a) a sinusoidal structure and (b) a porous lobule model.

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