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A MULTI-LEVEL COMPUTATIONAL MODEL TO CHARACTERIZE THE HEPATIC CIRCULATION IN HUMAN CIRRHOSIS

G. Peeters*[1], C. Debbaut[1], P.Cornillie[2], E. Pauwels[3], D. Monbaliu[4], W. Laleman[5], P. Segers[1]

[1]IBiTech – bioMMeda, Department of Electronics and Information Systems, iMinds Future Health Department, Ghent University. De Pintelaan 185 – Block B, B-9000 Gent, Belgium. Geert.Peeters@UGent.be;Patrick.Segers@UGent.be;Charlotte.Debbaut@UGent.be; 0032 9 332 33 79
[2]Department of Morphology, Faculty of Veterinary Medicine, Ghent University. Salisburylaan 133, B-9820 Merelbeke, Belgium. Pieter.Cornillie@UGent.be
[3]UGCT – Department of Physics and Astronomy, Ghent University. Proeftuinstraat 86, B-9000 Gent, Belgium. Elin.Pauwels@UGent.be
[4]Abdominal Transplant Surgery, University Hospitals Leuven, & Department of Microbiology and Immunology. Herestraat 49, B-3000 Leuven, Belgium. Diethard.Monbaliu@uzleuven.be
[5]Hepatology, University Hospitals Leuven, & Department of Liver and Biliopancreatic disorders, KU Leuven. Herestraat 49, B-3000 Leuven, Belgium. Wim.Laleman@uzleuven.be

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Background and aim

Liver cirrhosis is a chronic liver disease progressively degenerating liver tissue architecture and function by the formation of fibrosis and regenerative nodules. This disruptive process deteriorates the hepatic (micro)circulation and may lead to an increasing intrahepatic vascular resistance. The healthy liver consists of repetitive anatomical units at the microscopic level, commonly represented as hexagonal lobules comprising sinusoids (hepatic-specific capillaries). In cirrhosis, however, this anatomical architecture is greatly affected by sinusoidal capillarization and shunt formation. More elaborate research is necessary to better understand the hemodynamic consequences of cirrhotic disease. Multi-level numerical models may provide deeper insight into the perfusion characteristics of the dysregulated microcirculation and the impact of regenerative nodules on hepatic hemodynamics.

Methods and results

a. Macrocirculation: the effect of regenerative nodules

The impact of regenerative nodules, reducing the volume of perfused tissue, was analyzed using a simplified 3D geometry of the liver, including a dual vascular supply (Fig. 1). All vascular trees (hepatic artery, portal vein and hepatic vein) were modeled as single bifurcations. Initially, the computational fluid dynamic (CFD) model was calibrated to perfusion data (pressures and flows) of a healthy liver [1]. Darcy's law was applied to define various porous media volumes in order to match the permeability values to the expected pressure drops.

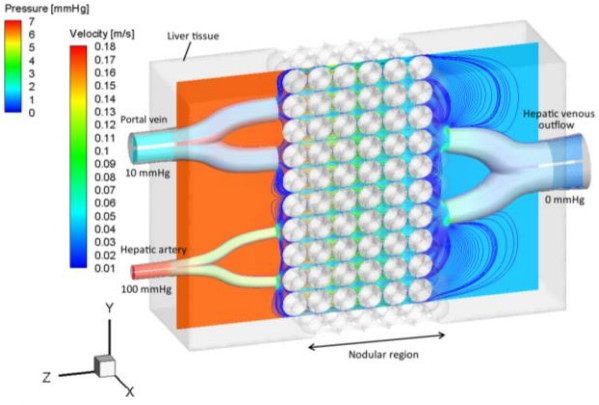

Fig. 1 Pressure distribution and velocity streamlines of a section through the nodular region (simulation with a nodular vol% of 81.2%).

Subsequently, regenerative nodules were introduced into the CFD model as impermeable spheres in the liver tissue between the inlets and outlet (Fig. 1).
The results indicate that increasing volume percentages of regenerative nodules correspond to higher pressure drops over the nodular region (Fig. 2a) and significantly lower hepatic venous outflows (Fig. 2b). Hence, the inclusion of regenerative nodules severely increases the intrahepatic vascular resistance (Fig. 2c), impeding the perfusion of liver tissue, with a steep increase beyond about 65 volume%.

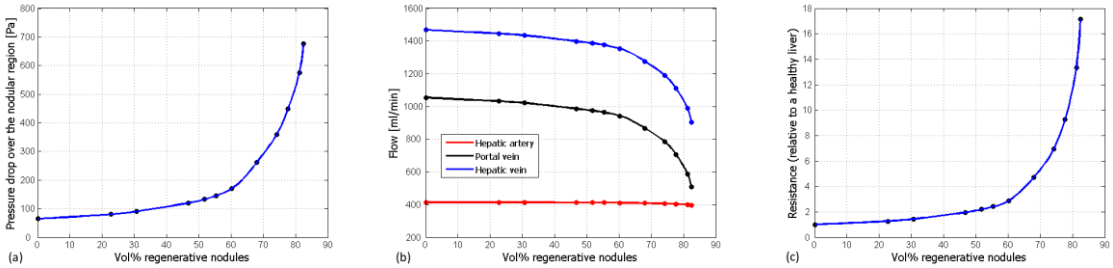

Fig. 2. The pressure drops over the nodular region (a) and vascular resistance (c) increase due to regenerative nodules. The flows through the vascular trees (b) decrease as a consequence of the regenerative nodules.

b. Microcirculation: the effect of sinusoidal dilatation and shunt formation

Vascular corrosion casting and high-resolution micro-CT scanning of a human cirrhotic liver generated detailed datasets of dissected microsamples. Image processing resulted in anatomically correct 3D reconstructions of the microcirculation. Two cubic samples (150 x 150 x 150 μm^3) were virtually dissected and defined as the fluid domains for the numerical CFD simulations of blood flow in three orthogonal directions (radial (r), circumferential (θ) and longitudinal (z)) (Fig. 3).
The hemodynamics of both cirrhotic liver samples indicate that the pressure gradients are markedly lower when compared to a normal liver sample (e.g. 33, 6 and 170 Pa for cirrhotic sample 1, 2 and a normal sample, respectively [2] in the radial direction). This implies a locally decreased resistance, suggesting the presence of local compensation mechanisms (dilated sinusoids and shunt vessels in cirrhotic sample 1 and 2, respectively). These compensations counteract the increased liver resistance caused by regenerative nodules (see section a) and dynamic contraction mechanisms (stellate cells, NO-concentration etc.).

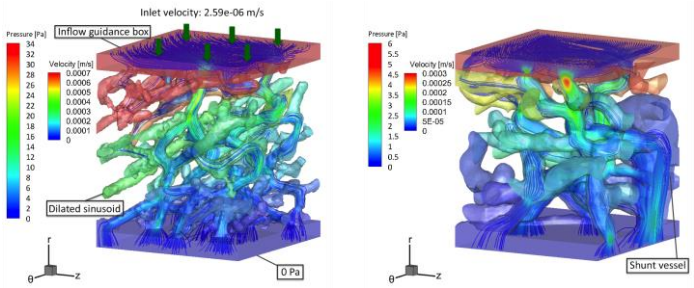

Fig. 3 Pressure distribution and velocity streamlines of cirrhotic sample 1 (left) and sample 2 (right).

Conclusions

Numerical modeling allows quantifying the perfusion characteristics of the cirrhotic macro- and microcirculation, i.e. the effect of regenerative nodules, dilated sinusoids and shunt vessels. Future research will focus on an anatomically more realistic macro-model and to the coupling of the macro- and microcirculation.

References

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