

A multiscale framework for studying vascular morphology alterations during liver cirrhogenesis: a feasibility study

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OBJECTIVES

To date, little is known about the hemodynamic consequences caused by liver cirrhosis, especially at the cellular level. To gain more insight in the vascular morphology during cirrhogenesis, detailed 3D reconstructions of the hepatic circulation are vital. We have optimized two complementary techniques to acquire accurate 3D geometrical data of the rat liver circulation, covering the entire length scale of the hepatic vasculature.

METHODS

Vascular corrosion casting (VCC) entails injecting the casting resin PU4ii in the rat hepatic artery and portal vein. Lipiodol is added to the arterial mixture as a contrast agent to ensure a clear distinction between both vascular trees after micro-CT-scanning. The resulting datasets enable reconstructing detailed 3D geometries of the hepatic macro- and microcirculation.

The immunohistochemistry (IHC) protocol includes staining 350 µm thick liver slices with a generic endothelial marker antibody (*RECA*). To increase the liver slices' transparency and microscopic penetration depth, a modified version of the clearing protocol CUBIC is applied. Image stacks are subsequently recorded with a confocal microscope, and automatically segmented to visualize and analyze the microcirculation using in-house developed software.

RESULTS

We were able to gather and compare morphological parameters (radius, tortuosity, length, etc.) during cirrhogenesis. Our first results suggest that - even in the early cirrhotic stages - microcirculatory alterations manifest as the number of sinusoids per unit of volume reduces, while radius and length remain similar to normal liver tissue.

CONCLUSIONS

This framework allows quantifying the impact of cirrhosis on the hepatic angioarchitecture and may lead to novel insights in the cirrhotic pathophysiology.