

At first glance macro- and microanatomy of the liver is well known and functional anatomy of the liver is well covered. At second glance however a surprising number of “white territories” need to be addressed, even when looking at a noncirrhotic liver. These “white territories” become real obstacles once modeling approaches are initiated. Liver perfusion, lymphatic drainage and biliary outflow define major mass transfer systems of the liver and will be in the scope of this review, describing the state of the art as well as “white territories” in our basic understanding of liver anatomy.

Liver perfusion is provided by portovenous and arterial inflow and hepatovenous outflow. Together the portovenous system and the hepatic artery provide blood to the sinusoidal system. Blood flow in the sinusoidal system is guarded by systemic and focal regulatory mechanisms. Systemic regulatory mechanisms are driven by endocrine and neural components.

Impaired liver perfusion leads to clinical symptoms in patients with liver outflow obstructions like the Budd Chiari syndrome and right heart failure. Arterial liver inflow obstruction leads to clinical symptoms in transplantation patients. Portovenous inflow obstruction is associated with portal hypertension as well as adaptive architectural and functional changes within the liver.

However differences in the focal ratio of portovenous and arterial supply to sinusoidal perfusion as well as the functional impact on a potential functional heterogeneity of the liver is still poorly understood. Precise spatially resolved evaluation of the vascular anatomy of the liver is warranted as a basis to understand spatially resolved liver perfusion. Evaluation of the vascular anatomy in man and mice involves histologic serial sections and 3d reconstruction as well as laser scan microscopy and radiologic imaging procedures. Sinusoidal perfusion is visualized using techniques like OPS. Hemodynamic monitoring is a quest especially in mice due to the small diameter of blood vessels.

Lymphatic drainage of the liver is not widely covered in literature. There are only single papers detailing the space of Disse as the starting point of the lymphatic system of the liver. Little is known on the regulation of the lymphatic flow.

Increased lymphatic flow is reported in liver cirrhosis. Distended lymphatic vessels in portal tracts are also observed in hepatovenous outflow obstruction.

However even the exact visualization of the connections of the space of Disse into draining lymphatic vessels is not available. Furthermore the functional impact of an increased lymphatic flow on hepatocellular function is not known. Lymphatic drainage is evaluated

employing fluorescent labeled dextrans potentially by the use of 2 photon microscopy. Reconstruction of the lymphatic system will involve also serial histologic sections and laser scan microscopy but also serial sections produced for EM evaluations.

Biliary outflow seems to be textbook knowledge down to membranous transporters providing secretion of molecules into the canaliculi.

Impaired biliary outflow is mainly due to an obstruction of the biliary system due to stones or tumors. Furthermore biliary outflow can be impaired for example by drugs affecting the molecular secretion machinery.

However even anatomical structures like the canals of Hering connecting the canalicular system to the ductular system is poorly understood. Also reactive changes of the canalicular system as well as the ductular system in mechanical biliary outflow obstruction need further work. Ductular changes can be visualized by serial histologic sections as well as laser scan microscopy. Functional evaluation of the canaliculi is achieved by 2 photon microscopy. A detailed evaluation of the canalicular system also involves electron microscopy.

Exploration of the „white territories“ will improve the current physiological computational models of the liver. Adding individual patient specific anatomical and physiological data is the prerequisite for developing individualized functional models of hepatic anatomy, perfusion and function. Individualized models are the prerequisite for the transition from systems biology to systems medicine. System medicine may support physicians by providing diagnosis and treatment support systems, predicting the course of disease under the influence of a given treatment strategy.