Abstract

Introduction: This dissertation summarizes our research published in seven articles where we described both the ways of utilization of porcine liver in biomedical research and the basic morphometric parameters of hepatocytes and liver connective tissue useful in experimental surgery followed by liver regeneration experiments. We set off with the description of anatomical concepts of human liver applied to clinical investigation followed by summary of porcine liver morphology with special stress on its potential clinical utilization. The studies in experimental surgery followed by liver regeneration where the porcine liver model proved its utility, reveals that the distribution of portal blood to the liver parenchyma, the number and the volume of mononuclear and binuclear hepatocytes, and the amount and the distribution of liver connective tissue being among the most useful ones.

Methods: For the mapping of portal vein branching we used μCT scans of porcine liver corrosion casts, and both the quantitative parameters of the hepatocytes and of the connective tissue were evaluated on systematic uniform random paraffin-embedded samples that were harvested from three different regions of interest (ROI) of liver parenchyma (peripheral, paracaval and paraportal). For the quantification, we followed standard stereological protocols. For the casting, we filled the vessel of liver with Biodur E20® resin, followed by corroding in potassium hydroxide. The quantification was performed on PAS- and aniline blue-stained histological sections.

Results: The liver of Prestice Black Pied pigs comprises of five to six hepatic lobes (quadrate lobe is fully developed in 35 % of cases only). Hepatic portal vein enters the liver in its cranial part on the level of the border between the right medial and right lateral lobes. Just before its entrance to the liver parenchyma the hepatic portal vein bifurcates into left and right branch, in one instance we observed a trifurcation – this caudal branch then supplied the right medial lobe. In total, the right branch of the portal vein supplies 19–40 % of the liver and the left branch 60–81 % of the liver in Prestice Black Pied pigs. Hepatic portal vein branches of the third generation are not exclusive suppliers of the respective liver lobes both in the left half of the porcine liver and both for the right medial lobe that, in the case of the hepatic portal vein trifurcation, can be fed by a direct portal branch. Nevertheless, it was possible to compartmentalize the porcine liver into eight segments according to Couinaud.

After the correction for tissue shrinkage, the mean number-weighted volume of porcine mononuclear hepatocytes was 3670 ± 805 μm^3 and the mean number-weighted volume of binuclear hepatocytes was 7050 ± 2550 μm^3 with the fraction of binuclear hepatocytes being 4 ± 2%. The numerical density of all hepatocytes was 146997 ± 15738 cells mm^{-3}. Peripheral regions of hepatic lobes contained the largest mononuclear hepatocytes with the smallest numerical density. However, the hepatocyte size and density, as well as the fraction of binuclear hepatocytes exhibited considerable interindividual differences even in healthy young animals.

There was also considerable variability in the fraction of connective tissue at all sampling levels: between sexes, among individual animals, liver lobes and ROIs. The mean fraction of connective tissue was greater in males than in females. In males, the mean fraction of interlobular connective tissue was 4.7 ± 2.4% and ranged from 0% to 11.4%. In females, the mean fraction of interlobular connective tissue was 3.6 ± 2.2% and ranged from 0% to 12.3%. The mean fraction of intralobular connective tissue (perisinusoidal summed with pericentral) was < 0.2 both in males and in females.

Conclusion: The volume ratio of the vascular territories of the left and right branches of the hepatic portal vein in our sample of porcine livers was reversed when compared to human liver. The morphometry of hepatocytes can be easily biased when the differences resulting from different position in ROI are not accounted for, especially, when tissue probes are harvested from the vicinity of large liver vessels and from the periphery of the liver lobes. Accodring to the analysis of the liver connective tissue, it is important to know the exact position of the tissue block within the liver – both the lobe and the ROI for the subsequent histological analysis. When the sampling scheme of experiments using the porcine liver reflects the differences between the lobes and the ROIs, the same quantitative information may result from a smaller number of samples and therefore provide a more efficient comparison to the situation in which the tissue blocks are harvested in a purely random manner.