Abstract

Considering the current knowledge on histology of microvessels suggested that quantification of the tissue microvessels itself should be accompanied by a description of the surrounding tissue components supplied by these microvessels. However, the microscopic anatomy of this tissue context can vary considerably on the scale of large-sized organs, such as the aorta of large mammals or the human brain. Given that the present knowledge on the variability of densities, spatial arrangement, and orientation of microvessels is usually limited to macroscopically small areas of these large organs, we consider mapping of the microvessels on a large macroscopic scale to be a matter of great importance. This became the unifying element of this thesis. The main findings based on six studies presented in the thesis were as follows:

Finding #1: The density and the penetration depth of the vasa vasorum has a considerable segmental variability in the porcine aorta. The density of the vasa vasorum was greatest in thoracic aortic segments, as was the depth of penetration into the tunica media, which exceeded previously published findings. The vasa vasorum density declined with age, but the relative depth of their penetration did not. The individual segments of the porcine aorta were not interchangeable for being used in further experimental studies on the vascularization of porcine aorta.

Finding #2: Both the numerical density as well as the length density of microvessels was greater in the grey matter that in the white matter of the human brain. These parameters were comparable between the brain cortex and the basal ganglia. Greater density of microvessels was statistically correlated with the loss of their preferential orientation.

Finding #3: Synthetic thin-walled tubular grafts examined in our study were not invaded by the ingrowth of vasa vasorum even after 6 months of being implanted in vivo into rabbit carotid arteries. The absence of the vasa vasorum did not prevent local differentiation of smith muscle cells within these highly permeable thin-walled grafts.

Finding #4: A software generator of virtual (phantom) image stacks simulating micro-CT scans was made available, including a realistic noise generator. The user input decided on precisely known geometrical characteristics of the microvessels-minicking objects, such as their volumes, surfaces, lengths, and numbers. The image data sets were processed on a micro-CT console and and the error between the true known and estimated data was quantified. The sensitivity analysis showed that resolution decreasing below 1/10 of the typical size of the microvessels resulted in a considerable error of the segmentation

procedure, thus introducing a bias threatening the conclusions drawn from the measurements.

Finding #5: Human abdominal aortic aneurysms (AAA) had a greater density of vasa vasorum profiles than samples of normal aortae. The density of the vasa vasorum positively correlated with the inflammatory infiltration, with the marker of hypoxia, with the expression of pentraxin 3, and with the macroscopic AAA diameter. The colocalization of increased vascularization of the AAA wall with the expression of a hypoxia marker was considered as a morphological correlate of hypoxia-induced neoangiogenesis. This phenomena was suggested to play a significant role in the AAA pathogenesis and to increase its susceptibility to rupture.

Finding #6: The data mapping the relative quantities of the main tissue components the wall of porcine carotid arteries suggested that, by excluding anatomical variations of branching, right-sided and left-sided vessels and vessels from castrated females and males can be pooled during experiments on these vessels. On the contrary, significant differences were found between the proximal, middle and distal sections of the carotid arteries, where the artery changed from elastic to muscular phenotype within a short interval of 2-3 cm. As the mapping of the vasa vasorum is still in progress, we hypothesize that the proximal segments with concentric elastin lamellae will be more densely and deeply penetrated with vasa vasorum than the distal segments due to the low diffusion permeability of elastin-rich proximal segments. However, this hypothesis must first be verified by data from an ongoing study. We also consider it useful to compare the structure of the pig carotid artery with another similarly large model in experimental cardiovascular surgery, which is the sheep carotid artery.

We believe that these conclusions entitle us to the following summary: Uniformity in the distribution, density or orientation of microvessels can not be reasonably assumed on a macroscopic scale in large organs (such as aorta or carotid arteries of large animals, or the human brain). The diversity of these microscopic parameters requires their thorough mapping. In the case of microscopic variability of organs of large animal models used in experimental medicine, this makes it possible to perform a power sample analysis to plan experiments with ethically justified numbers of individuals or tissue samples. Even with three-dimensional imaging methods such as high-resolution computed tomography, the calibration of all procedures that still lack standardization cannot be omitted. We strongly support the publication of primary measured data in each morphometric study.