Dissertation abstract

The dissertation thesis consists of seventeen papers dealing with quantitative histological assessment of vascular wall and with application of morphometry in atherosclerosis research as well as in biomechanics of elastic arteries. History of microscopic morphometry with an emphasis on stereology is reviewed in the Introduction. The principles of mathematical morphology and of stereological estimation of volume, surface, area, length, and numerical density of objects in tissue blocks are explained in the Methods. The key rules of unbiased sampling of histological series and designing morphometric studies are summarized. The distribution of the overall observed variance in biological experiments, its sources and management are discussed. Procedures necessary for three-dimensional reconstructions based on scanned histological series are described.

We proved that inflammatory process was significant in patients with ruptured aneurysm of abdominal aorta (AAA). There were more pronounced inflammatory infiltrates in areas of neovascularization in ruptured AAA than in asymptomatic AAA patients. Histological findings were in agreement with higher cytosol cytokine levels (IL-6, IL-8, TNF-α), enhanced collagen III metabolism and degradation in ruptured AAA. We found lower volume fraction of the contractile phenotype of smooth muscle cells, higher volume fraction of collagen, and minimal to normal elastin volume fraction within the tunica media of AAA than in normal aorta. Apolipoprotein E-deficient (apoE-KO) mice fed with a cholesterol-rich diet for five months developed accelerated atherosclerosis of thoracic aorta with atherosclerotic lesions of higher volume than the group fed for two months only. In another study, heterotopic heart transplantation in apoE-KO mice didn't prove itself to be a reliable experimental model for study of atherosclerosis regression, although the lesions found in aortic sinus were more stable in some of the transplanted than in non-transplanted animals. In another study, no regression of initial atherosclerotic lesion was achieved by syngeneic heterotopic transplantation of thoracic aorta segments of 12-week-old apoE-KO mice to wild-type recipients of the same age. On the contrary, neointima formation, arteriosclerosis and degradation of elastin 19 prevailed in all transplanted specimens, even in control groups. It was suggested that the minute and sensitive wall of juvenile aorta suffered from severe disturbance of vasa and nervi vasorum caused by the invasive intervention in the transplanted animals, so that it became vulnerable to inflammation and transplant arteriopathy. The reproducibility of the promising regression model in 12-week-old mice was derogated by the striking dependence of the results upon the operation technique. Thoracic to abdominal aorta transplantation did not offer a method which would enable us to study atherosclerosis regression in 12-week-old apoE KO mice.

The mean distance between adjacent elastic lamellae was higher in paired transversal sections through abdominal than thoracic segments of porcine aortae. Volume fraction of elastin within tunica media did not differ between paired samples of thoracic and abdominal porcine aorta. We assessed volume fractions of collagen and smooth muscle, as well as elastin length density in porcine aorta. Computer simulation performed with a composite model of aortic wall and based on histomorphometry suggested that in the aorta the residual strain in the extracellular matrix (mainly in elastin fibres) was much more important for the proper function of the arterial wall than the tone of smooth muscle cells. In another paper, morphometric analysis succeeded mechanical uniaxial traction tests in order to supply a twolayer composite mathematical model of the aorta with sufficient data.

A three-dimensional geometry model of canine heart ventricles considering anisotropy of the cardiac muscle was presented. Simulation of excitation of the cardiac conducting systém and myocytes was done with cellular automata and coupled with a finite element model of heart mechanics. We developed a computer model of the blood flow and vascular wall mechanics in AAA. Morphology of the model including its boundary conditions was based on real patient-specific geometry data obtained with computer tomography. Dependence of wall stress contours and velocity profiles upon the realistic geometry of vessel lumen, thickness of arterial wall and intramural thrombus, and branching was simulated during the cardiac cycle. This approach was suggested to be suitable for follow-up study of patients with high surgical risk but smaller aneurysms observed for the aneurysm growth, where simulations could be correlated with surgeon's clinical experience. Stereological quantification of microscopic structure of blood vessels was found reliable, and reproducible. Most of the stereological methods used nowadays had been designed as unbiased, and assumption-free. Description of morphological properties of tissue specimen with use of continuous variables and systematic unbiased sampling permitted us to apply standard statistical procedures and tests to morphometric data. Due to our experience, stereological quantification might be useful for other topics of vascular research, e.g. for describing histology of hypertensive aorta remodelling in a model of chronic renal failure in rats, for assessment of alteration of aortic wall caused by application of biological glues into a model of aortic dissection, or for description of angioarchitectonics of microvessels in normal and tumourous lymph nodes.