



INVESTMENTS IN EDUCATION DEVELOPMENT

## **On heterogeneity of mechanical environment of vascular walls at a cellular level**

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Mechanical properties of the artery wall have been assumed to be homogenous in conventional analyses. However, it is not the case for microscopic analyses. Artery walls consist of components with various Young's modulus such as collagen (~1 GPa), elastin (~0.6 MPa), and smooth muscle cells (SMCs, ~10 kPa). Such heterogeneity should cause complex distribution of stress and strain depending on the histological structure. Aortic media has a concentric layered structure of a lamellar unit, a pair of elastic lamina (EL) mainly composed of elastin and a smooth muscle-rich layer (SML) mainly composed of SMCs and collagen. It is well known that the ELs are corrugated in an unloaded state and become straight over physiological pressure. Recently, we found that the corrugated ELs became straight upon isolation from the surrounding tissues. This indicates that the ELs bear compressive residual stress and the SMLs tensile in the circumferential direction in an unloaded wall. We also noticed that the waviness of the ELs in the unloaded aortic walls vary widely. To reveal the reason for this heterogeneity, we observed deformation of the ELs and SMCs in thin-sliced porcine aortic wall specimens during the circumferential stretch under a microscope in detail, and found complicated deformation at a microscopic level: Rotation and shear deformation was observed in SMCs, and ELs became straightened first without significant lengthening and then become elongated. Such deformation of ELs indicates that ELs with lower waviness bear higher load than ELs with higher waviness in a physiological state. To check this hypothesis, we cut off ELs in thin-sliced specimens stretched circumferentially mimicking a physiological state with a laser ablation technique and obtained results supporting the hypothesis, i.e., the gap produced by the ablation was wider in the ELs whose waviness had been lower in the unloaded state. Similar results were obtained for SMLs: SMLs adjacent to ELs with lower waviness had wider gap following ablation. Immunohistochemical analysis shows that SMCs adjacent to straight ELs were abundant with F-actin, suggesting that cells near ELs with lower waviness received higher mechanical stimulation. The reason for such heterogeneities is not clear at this stage. They might be caused by cellular activities such as remodeling and cell division. Microscopic mechanical environment is highly heterogeneous in the aortic walls. Microscopic viewpoint is crucial to elucidate the mechanism of the mechanical adaptation and remodeling of arteries.