Title: An integrative Multi-Scale Model of Extracellular Matrix Mechanics in Vascular Remodeling

Author: Katherine Yanhang Zhang

Department of Mechanical Engineering, 2Department of Biomedical Engineering,Boston University, Boston, MAyanhang@bu.edu

Cardiovascular diseases (CVDs) are the leading cause of death in the western world. It is responsible for 40 percent of all the deaths in the United States, more than all forms of cancer combined. While CVDs is a broad term used to describe a range of diseases that affect heart and blood vessels, arteriosclerosis or hardening of the arteries is presented in many of these diseases. The extracellular matrix (ECM) of the aortic wall plays an important role in the pathogenesis of arteriosclerosis, aortic aneurysms, etc. The aortic wall is largely composed of fibrous materials, collagen and elastin, and ground substance interspersed among organized layers of cells to form lamellar structures. The prevailing concept is that elastin and collagen are the primary load-bearing components of vascular tissue, respectively, in low-stretch or high-stretch regions of stress-strain curves. We previously investigated the interactions among these ECM constituents and how they affect vascular function [1,2]. However, understanding the layer-specific structural details of aortic wall and incorporation of that information in constitutive models of aortic behavior are much needed steps in biomechanics of aorta given the recent advances in medical imaging. In this work we developed a microstructural-based constitutive model that incorporates the structural information such as fiber orientation, undulation distributions and fiber density in describing the aortic mechanical response. Study of structural changes during normal stretching as well as elastin degradation was performed with second harmonic generation and two photon excitation fluorescence imaging. Fractal analysis of the images shows continuous engagement of medial collagen in contrast to the elastin which is engaged up to 20% stretch and the adventitial collagen which is recruited after 20% stretch. 2D fast Fourier transform analysis revealed realignment of the collagen fiber network during stretch while the orientation and distribution of the elastin structure was unchanged. Together these results provide a more comprehensive study of the structure function relationship with the goal of incorporating this information in understanding disease progressions and structurally based constitutive models. We have used a constitutive model for the planar non-equi-biaxial mechanical response of porcine aorta composed of two layers of isotropic ground substance and undulated collagen fibers. Using a constraint on the contribution of elastin to the adventitia layer, our parameter estimation results showed that medial collagen is engaged in load-bearing from the beginning of the biaxial loading whereas the adventitial collagen engaged later (at the stretch of about 1.2). This was consistent with our structural analysis of multi-photon microscopic images.

References

1. Chow, M. J., J. R. Mondonedo, V. M. Johnson, and Y. Zhang, 2013. Biomech. Model. Mechanobiol. 12, 361-372.
2. Zeinali-Davarani S., M. J. Chow, R. Turcotte, and Y. Zhang, 2013. Ann. Biomed. Eng., 41, 1528-1538.