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EVALUATION OF AORTIC RESIDUAL STRESSES: EXPERIMENTAL EVIDENCE AND CONSTITUTIVE MODELING

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Biomechanical factors such as mechanical stresses play fundamental roles in the genesis and development of vascular diseases [1]. These mechanical stresses are transmitted from the macroscopic to the cellular levels in the vascular tissue and influence the tissue's mechanobiology. Vascular tissue senses and responds actively to changes in its mechanical environment – a crucial tissue property the consideration of which in numerical models might also improve reliability of biomechanical simulations [2]. Predicting the stress state in an artery using passive constitutive models requires the prescription of residual stresses in the load-free configuration. However, for complex geometries the residual stress state is unknown and hypothetical assumptions are relied on [3]. The present work proposes a novel multi-scale framework for the arterial wall that accounts for smooth muscle cell (SMC) contractions and vascular wall's ability to adapt to the mechanical loading state which allows the direct estimation of the residual stress field. The framework could be used in finite element analysis (FEA) simulations to quantify and predict biomechanical stresses in arteries. In turn these analyses could contribute to better diagnoses and optimal treatment planning for vascular diseases.

A structurally derived constitutive model was used, where SMC and collagen fibers reinforce an otherwise isotropic ground matrix (elastin). Specifically, a reported SMC model [4] captured active vessels properties and the ground matrix remodeled towards a defined stress state at the vessel's physiologic loading. Collagen fibers are assembled by proteoglycans cross-linked collagen fibrils (CFPG-complex) [5] and are dynamically formed by a continuous stretch-mediated process and are deposited in the current configuration [6]. Multiplicative kinematics account for the straightening and stretching of collagen fibrils, and an orientation density function captures the spatial organization of collagen fibers in the tissue. Following the idea of the micro-fibers [7], the macroscopic stress at the material point was derived by integration over the unit sphere, which was implemented using spherical t-designs. The constitutive law was implemented at the Gauss-point level of a Q1P0 mixed finite element (FE) formulation in a FE environment. An adaptive time stepping algorithm was used, which related the size of the time increment to the maximum of the collagen mass increment. The material parameters for the passive constitutive model were identified from biaxial tensile test data on healthy arterial tissue harvested from mongrel dogs. Histological analyses of stained tissue slices were used to obtain volumetric fractions for the different

tissue constituents and to quantify the angular distribution of collagen fibers. Aortic tissue rings were obtained from the descending thoracic aorta of mongrel dogs, euthanized following an approved ethical protocol. Out of three adjacent rings, one was maintained in a buffer solution as a control while the other two were treated with a 1%vol Triton solution to increase the porosity of the cellular membrane and control SMC contraction by modulation of calcium concentration. Half of the treated rings were exposed to a relaxing solution containing EGTA to prevent SMC contraction, the other half was treated with a solution containing calcium and ATP to promote SMC contraction. All rings were opened by means of a single radial cut. Images of the rings were taken before and after the cut and analyzed with in-house algorithm using MatLab (The MathWorks, Natick, Mass). Inner and outer contours were fitted to circles or circular sectors to estimate inner and outer diameter and, in the case of the open rings, the opening angle. Plane stress FE models were used to replicate the passive and active in-vitro experiments. Specifically, SMC properties were estimated from the difference between passive and active opening angles.

Although simple mechanical assumptions and kinematics define the CFPG-complex, the passive model of aortic tissue implemented replicates the typical stiffening observed at physiologic strain level. Due to its highly nonlinear character, the passive formulation predicted a strong stress gradient across the vessel wall. Such stress gradients are thought to be non-physiologic, while the presence of residual stresses in the load-free configuration are able to reduce the gradients across the wall thickness. Integrating the vascular wall biology redistributed the stress both in the elastin and collagen fibers and homogenized the stress across the wall thickness, suggesting that collagen turnover and elastin remodeling recover the residual stresses in the load-free state. Activating SMCs produced an increase in opening angle, when compared to the passive state, with relaxed SMCs. This mirrors the results of the experiments. The computed residual stresses increased with the SMC contraction and further homogenized the stress distributions across the wall thickness.

The proposed model has a strong biological motivation and integrates both histological and mechanical information. The multi-scale histomechanical model sheds light on the impact of SMC contraction, and of collagen and elastin remodeling on the macroscopic properties of the tissue itself. Furthermore it predicts a homogenous stress distribution across the vessel wall that is a manifestation of a principle of optimal mechanical operation, which ensures a favorable mechanical environment. In conclusion, the constitutive concept developed yields a highly efficient and robust multi-scale approach that allows simulating in-vivo residual stresses of complex vascular geometry.

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