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Time-course of venous wall biomechanical adaptation in pressure and flow-overload: Assessment by a microstructure-based material model

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ABSTRACT

Arteriovenous fistulae have been previously created by our group, through implantation of e-PTFE grafts between the carotid artery and jugular vein in healthy pigs, to gather comprehensive data on the time-course of the adapted geometry, composition, and biomechanical properties of the venous wall exposed to chronic increases in pressure and flow. The aim of this study was to mathematically assess the biomechanical adaptation of venous wall, by characterizing our previous in vitro inflation/extension testing data obtained 2, 4, and 12 weeks post-fistula, using a microstructure-based material model. Our choice for such a model considered a quadratic function for elastin with a four-fiber family term for collagen, and permitted realistic data characterization for both overloaded and control veins. As structural validation to the hemodynamically-driven differences in the material response, computerized histology was employed to quantitate the composition and orientation of collagen and elastin-fiber networks. The parameter values optimized showed marked differences among the overloaded and control veins, namely decrease in the quadratic function parameters and increase in the four-fiber family parameters. Differences among the two vein types were highlighted with respect to the underlying microstructure, namely the reduced elastin and increased collagen contents induced by pressure and flow-overload. Explicit correlations were found of the material parameters with the two basic scleroprotein contents, substantiating the material model used and the characterization findings presented. Our results are expected to improve the current understanding of the dynamics of venous adaptation under sustained pressure- and flow-overload conditions, for which data are largely unavailable and contradictory.

1. Introduction

Like other living tissues, blood vessels continuously adapt to “nonhomeostatic” mechanical stimuli by remodeling their inner structure, morphology, and biomechanical properties (Fung, 1993; Humphrey, 2002). This adaptive response of vascular tissues is mediated by the cell types residing at various depths within the wall, specifically the endothelial cells of the intima, the smooth muscle cells of the media, and the fibroblasts of the adventitia, which transduce the mechanical stimuli into biochemical and bioelectrical signals (Humphrey, 2001). Central to an improved understanding of the “homeostatic” affinity of blood vessels toward stability of their normal state is the quantification of the local mechanical environment experienced by vascular cells, so that the evaluation of intramural stress and strain distributions under both physiologic and pathologic conditions has attracted the attention of numerous researchers during the last decades.

The biomechanical adaptation of arterial tissue to persistently altered mechanical loads, such as pressure, flow, axial stretch, and combinations thereof, has received substantial attention owing to the enormous motivation for obtaining insight into the consequences of biomechanical factors on the pathophysiology of arterial disease, e.g. hypertension, atherosclerosis, and aneurysm formation; see Humphrey (2002) and references listed therein. By contrast, fewer studies (Wesley et al., 1975; Monos and Csengody, 1980; Dobrin et al., 1988; Han et al., 1998; Szentivanyi et al., 1998; Hayashi et al., 2003) have examined the respective adaptation of venous wall but results have been conflicting. Moreover, microstructural and biomechanical analyses have not been performed on the same tissue and at multiple phases during the process, as needed to fully comprehend the remodeling process. To fulfill those tasks, our group has recently employed an animal model of arteriovenous fistula for hemodialysis to gather comprehensive data on the evolution (from baseline to the ending steady-state) of the adapted geometry, composition, and biomechanical properties

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of jugular vein, exposed to step increases in pressure and flow by anastomosing it with the carotid artery via the interposition of an e-PTFE graft (Kritharis et al., 2010); see also the fluid mechanics study by Manos et al. (2010).

Compared to phenomenological material formulations, microstructure-based formulations are better candidates for vein wall biomechanical characterization in response to alterations in mechanical loads, allowing determination of the relationship

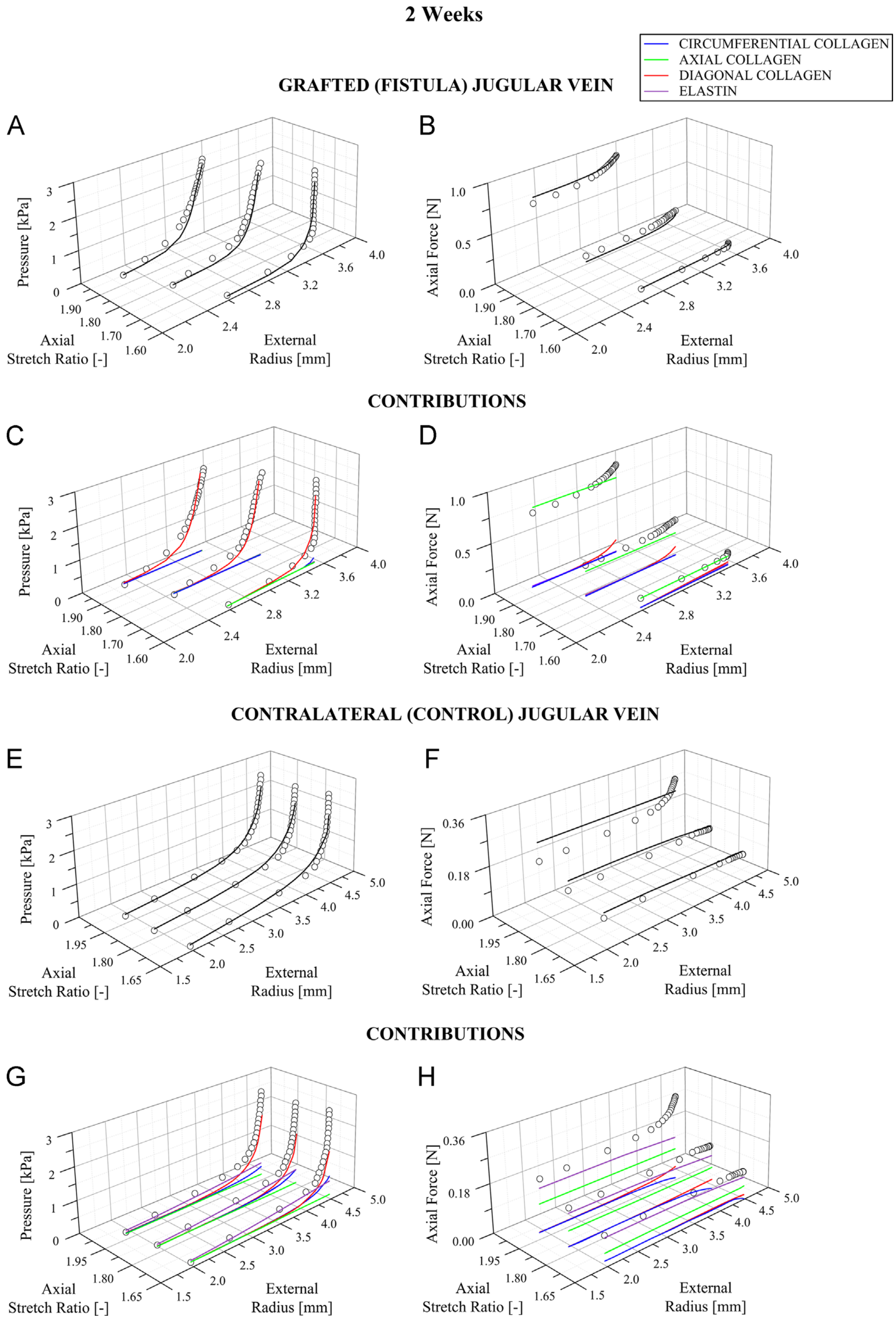

Fig. 1. Three-dimensional scatter plot of representative pressure (left) and axial force (right column) vs. external radius and axial stretch data (open symbols) for the 2-week group, together with the theoretical simulations by the quadratic and four-fiber family SEF and the contributions of each SEF term (solid lines). (A–D) Grafted vein (fistula): $b_{\theta\theta}=0.004$ kPa, $b_{zz}=0.053$ kPa, $b_{\theta z}=0.054$ kPa, $k_1^c=0.014$ kPa, $k_2^c=13.017$, $k_1^a=0.852$ kPa, $k_2^a=0.289$, $k_1^d=0.036$, $k_2^d=6.392$, $a^d=55.9^\circ$, $\varepsilon=0.287$. (E–H) Contralateral vein (control): $b_{\theta\theta}=1.798$ kPa, $b_{zz}=6.084$ kPa, $b_{\theta z}=1.110$ kPa, $k_1^c=0.301$ kPa, $k_2^c=0.284$, $k_1^a=1.465$ kPa, $k_2^a=0.112$, $k_1^d=0.065$ kPa, $k_2^d=0.643$, $a^d=52.0^\circ$, $\varepsilon=0.208$.