Biomimetic Heart Valve Tissue Virtual Experiments

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In the current study, a set of virtual biaxial stretch experiments were conducted on porcine pulmonary valve leaflet tissue photomicrographs via an image-based finite element approach. Stress distribution evolution during diastolic valve closure was predicted at both the tissue and cellular levels. Orthotropic material properties at distinct stages of diastolic loading were applied. Virtual experiments predicted tissue- and cellular-level stress fields, providing insight into how matrix-to-cell stress transfer is influenced by the inhomogeneous collagen fiber architecture, tissue anisotropic material properties, and the cellular distribution within the leaflet tissue. To the best of the authors' knowledge, this is the first study reporting on the evolution of stress fields at both the tissue- and cellular-levels in valvular tissue, and thus contributes toward refining our collective understanding of valvular tissue micromechanics while providing a computational tool enabling further study of valvular cell-matrix interactions.

Introduction: Valvular extracellular matrix (ECM) is largely comprised of collagens, elastin, and glycosaminoglycans, which in coordination confer valves their mechanical integrity and unique functional characteristics. Nonlinear and anisotropic, the mechanical behaviors of aortic and pulmonary valve leaflet tissues have been comprehensively quantified and constitutively modeled via biaxial testing. It has been observed that progressive collagen fiber rotation into the principal direction of loading, uncrimping, and transverse compaction collectively enable the tissue to withstand diastolic transvalvular pressure. Toward understanding valvular failure mechanisms, previous studies have aimed to determine stress distributions in heart valve leaflet tissues by finite element analysis and homogenization of the collagen fiber distribution. However, these previous linear elastic, isotropic or nonlinear, anisotropic tissue-level models have yet to incorporate the embedded valvular interstitial cells (VICs).

Materials and Methods: To understand how external mechanical forces can translate into altered VIC stress states, in the current study we adapted our image-based finite element analysis technique to investigate stress evolution at both the tissue- and cellular-levels during diastole. Anisotropic tissue-level finite element models were incorporated, wherein three sets of linearized elastic orthotropic material properties were applied in virtual biaxial experiments to simulate stiffness changes associated with distinct stages of diastolic loading.

Results and Discussion: The results of the current study indicate that the stress transmitted from the ECM to the VICs is dependent on the heterogeneous collagen fiber architecture, VIC distribution, and the anisotropic tissue properties (**Figure 1**). The stress a representative VIC is subjected to may be influenced by interactions with neighboring VICs and/or the surrounding ECM, and is predicted to vary with location around the perimeter of the cell nucleus. Several factors may contribute to the stress distribution that evolves within heart valve leaflet tissues, such as the orientation of collagen fibers, morphologies and/or sizes of the VICs, and the local composition and degree of crosslinking of the ECM.

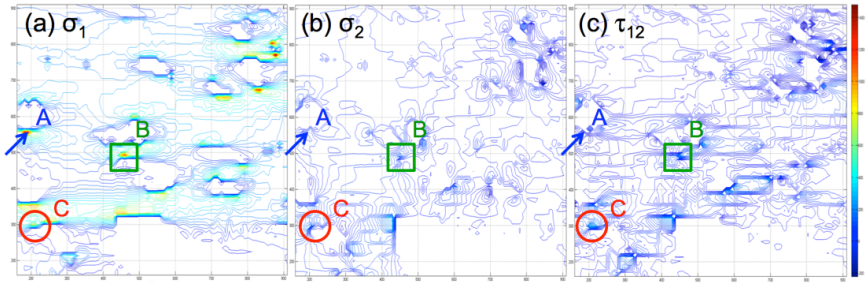

Figure 1. Stress distribution of the anisotropic finite element model under 30% equibiaxial strain. (a) σ1 at location A is 1,292.15 kPa, at location B is 1,139.38 kPa, and at location C is 746.84 kPa. (b) σ2 at location A is 81.72 kPa, at location B is 82.4 kPa, and at location C is 185.33 kPa. (c) τ12 at location A is -111.48 kPa, at location B is 161.76 kPa, and at location C is 301.01 kPa. Color key: blue = -200 (kPa) and red = 1500 (kPa).

Conclusions: The virtual experiments conducted herein complement previous studies of VICs and valve mechanics by predicting stress distribution evolution within the ECM and at the level of an individual VIC. This approach, incorporating the collagen fiber architecture, VIC distributions, and the anisotropic material properties of the ECM, provides a tool for comprehensively quantifying stress during diastolic valve closure.