Development of a mathematical model for microindentation of aortic valve leaflets to aid in the determination of local micromechanical properties

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Calcific aortic valve disease (CAVD) is the most common heart valve disease, affecting over 25% of the population in developed countries. The hallmark of early CAVD is focal changes in the mechanical properties of the extracellular matrix (ECM) in the valve leaflets. In particular, proteoglycan-rich lesions begin to form on the surface of the fibrosa layer of these leaflets. Maladaptive remodeling of the ECM is hypothesized to negatively influence valve cell function, ultimately resulting in stiffened leaflets that do not function properly. To date, the local micromechanical properties of healthy and diseased valve leaflets have not been characterized. The objectives of the present study are to measure local micromechanical properties of the three layers of porcine aortic valve leaflets (fibrosa, spongiosa, and ventricularis), and of these proteoglycan-rich lesions, and to develop material models for these layers and the lesions that take into account material non-linearity and heterogeneity. Leaflets will be obtained from healthy swine as well as those with early stage CAVD; comparison between the material models developed for the two cases will help identify changes in the local micromechanical properties of the aortic valve leaflets during the onset of CAVD.

To obtain the experimental data, a microindenter will be used to deform the surface of the leaflets. From these experiments, we will obtain the indenter depth and the corresponding force. We will also know the shape and size of the indenter and the shape and size of the tissue region deformed by the indentation.

Each layer of the aortic valve will be modelled as a hyperelastic material, whose functional form will be assumed based on previous experimental studies. To calculate the material parameter values for the model at each measurement location we will use non-linear optimization along with an inverse finite element method. More specifically, we will assume values for each of the parameters, run finite element simulations of the indentation, compare the resulting deformation

to the measurements, adjust the parameter values, and iterate until convergence. Because the rate of convergence of these inverse finite element simulations is dependent on the initial values of the material parameters, a good initial guess would reduce the computational time required per measurement location.

Contact problems, such as the indentation of soft tissue have been well-studied, with analytical solutions available for problems in which the material is assumed to be linear elastic and undergoing small strains. However, in the present study, neither of these assumptions is valid; therefore, inverse finite element methods are required. Also, the presence of the three-layer structure adds additional complexity to the problem.

In summary, microindentation will be used to obtain force-displacement data for porcine aortic valve leaflets, which may or may not contain lesions indicative of the early stages of CAVD. At each measurement location, we will also have measurements of the thicknesses of the lesion (if present) and the three leaflet layers. From this information, the objective of our proposed problem is to develop a method to determine the mechanical properties of the lesion and the leaflet layers at each measurement location and to do so in such a way as to ensure the uniqueness of the solution. This proposed method could be one that gives an analytical solution to this problem, or more likely, provides an approximate solution that could be used as an initial condition for inverse finite element simulations. In addition, because both the fibrosa and the ventricular layers have been shown to be anisotropic, a secondary objective of our study would be to develop a method of obtaining additional experimental data that would enable us to account for this anisotropy in material models of these layers.