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A STRUCTURALLY-BASED CONSTITUTIVE MODEL OF HEART FAILURE

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The progression of heart failure is associated with substantial changes in myocyte organisation and composition of the cardiac extracellular matrix (ECM) that lead to an alteration in the mechanical behaviour and, hence, the impairment of cardiac function. The collagen network is a major load-bearing component of the myocardium and is a primary determinant of the passive mechanical properties of the heart. The main goal of this study is to develop a structurally-based constitutive model of the myocardium that can directly link the organisation of collagen, acquired using high-resolution images, to the mechanical function of the heart, as characterised by ex vivo left ventricle pressure-volume curves.

High-resolution three-dimensional (3D) images of 12-month-old spontaneously hypertensive rats (SHR) and age-matched Wistar-Kyoto (WKY) rats as control were obtained using extended-volume confocal microscopy. The collagen network was segmented from the images and an intensity covariance matrix was constructed and analysed to describe the collagen organisations in the 3D confocal images. The eigenvalues of the covariance matrix were used to quantify the shape of the collagen, while the eigenvectors were used to represent the orientation. Two morphological parameters (elongation and flatness) derived from the eigenvalues were used to quantify the structural differences between the control (WKY) and failing (SHR) hearts. Microstructural constitutive equations that incorporate quantitative parameters of the collagen morphology were developed and then applied to computational models of WKY and SHR hearts to assess their ability to reproduce measured pressure-volume (PV) compliance curves.

A comparison of the collagen elongation and flatness parameters revealed distinct differences between WKY and SHR hearts. In particular, the dominant collagen shape in the WKY heart was an elongated structure, whereas the collagen shape in the SHR was more sheet-like. The role of the collagen remodelling in the passive myocardial mechanics was demonstrated using constitutive models that incorporated structural parameters derived directly from the confocal images to predict the passive LV function of both WKY and SHR hearts. The value of this study is not limited to predicting the mechanical behaviour of myocardial tissue but could also provide insights into the relationship between the structure and function of the myocardium in health and disease that may eventually pave the way for a more effective treatment for HF.