STRAIN-CONTROLLED ENZYMIC COLLAGEN DEGRADATION CAN EXPLAIN THE HEALTHY NATIVE MYOCARDIAL FIBER ORGANIZATION

AN IN-SILICO APPROACH

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Introduction

Myocardial fiber organization is one of the main contributors to the mechanical behavior of the heart. From a mechanical perspective, we can understand why this organization is essential for the heart's functionality, but the underlying biological structuring mechanisms remain unclear. Here, we developed a computational model to test the hypothesis that, in combination with cell active forces, strain-mediated enzymic degradation can explain the healthy native myofiber/collagen organization.

Methods

An existing macroscale mechanics model of the left ventricle (LV) was used to extract the strain-time profiles at different transmural locations in healthy conditions [1]. The output of the macroscale model was given as input for a remodelling model which involves the interaction of cells, collagen fibers, and the remaining isotropic matrix [2] (Fig. 1). The multiscale framework was adopted to test which strain-dependent enzymic degradation profile can capture the remodelling response of the tissue at different transmural locations. Motivated by literature [3,4], two strain-dependent collagen degradation functions were chosen; namely, the V-shaped and monotonic functions, which characterize the directional strain-dependent degradation rate of collagen fibers (Fig. 2).

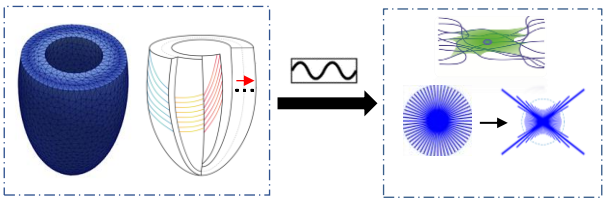

Figure 1: The multiscale computational framework: deformations from the LV model at different transmural locations (left) provide input to the cell-mediated remodeling model which predicts the resulting organization of collagen fibers after remodeling (right).

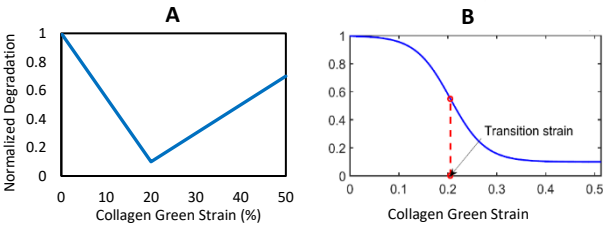

Figure 2: V-shaped (A) and monotonic (B) strain-dependent degradation functions affecting the collagen organization [3,4].

Results

The computational model was able to predict the emergence of the native myocardial fiber organization under the assumption of a V-shaped degradation function. The resulting predicted helix angle agreed well with experimental data of helix angle orientations from endo- to epicardium (Fig. 3A). The monotonic decreasing function displayed larger deviations from experimental data. The cell-mediated mechanisms (pre-stretch in Fig. 3B) did not have considerable influence on the results but provoked relatively larger variations at smaller deformations (mid-wall to epicardium).

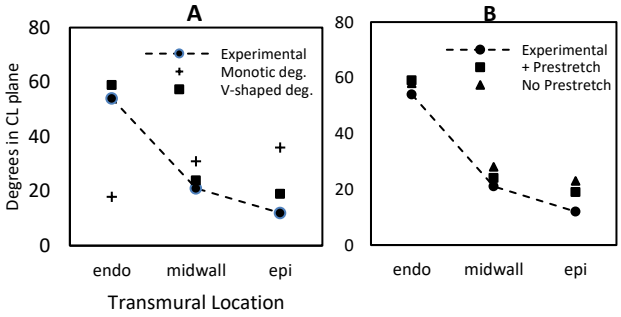

Figure 3: Model-predicted collagen fiber angle and native helix angle [1] at three points along the equator (A) for monotonic and V-shaped degradation functions (B) with and without cell-mediated pre-stretch.

Discussion

The results showed that the healthy myocardial fiber organization can be explained by strain-controlled enzymic degradation. The effect of cell-mediated mechanisms is smaller and primarily apparent at smaller deformations. In the future, our theory could be tested at additional transmural locations, as well as under pathological deformations.

References

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Acknowledgements:

This work is supported by the partners of Regenerative Medicine Crossing Borders (www.regmedxb.com) and powered by Health~Holland, Top Sector Life Sciences & Health.