JOHNS HOPKINS
BIOMEDICAL ENGINEERING

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Engineered Boundary Conditions Direct Cardiac Myogenesis and Contractility

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Abstract: We have developed an *in vitro* assay to study structure-function relationships in myocardium; combining ultrastructural analysis with functional readout of contractile force. Rather than recapitulating the whole heart, or even an entire ventricle, we have focused on evaluating the deformation of 2-dimensional (2D) myocardial sheets that mimic the lamellar layers of the ventricular wall. This myocardial sheet is integrated into a free-standing, thin film of polydimethylsiloxane (PDMS) elastomer. Thus, we have created a biological and synthetic, bilaminate structure, referred to as a muscular thin film (MTF). We can engineer MTFs with specific contractile properties by controlling the microcontact printing parameters of extracellular matrix proteins used to direct 2D myogenesis. Specifically, we can recapitulate both normal myocardium and the pathologic muscle structures characteristic of pressure-overload hypertrophy, dilated cardiomyopathy and the infarct border-zone. For physiologic experiments, the MTFs are fashioned into cantilevers, mounted in normal Tyrode's solution in an organ bath maintained at 37ºC and electrically stimulated to contract. Initial results show that the loss of uniaxial cardiomyocyte alignment as seen at the infarct border-zone corresponds to a 10-fold deficit in the peak systolic stresses. Quantification of sarcomere alignment at the sub-micron scale correlates this poor contractility with a deceased number of aligned sarcomeres and an increased distribution width of sarcomere orientation angles. The next step will be engineering MTFs with tissue microstructures that mimic normal, pressure-overload and dilated cardiomyopathy disease states in order to better understand the biomechanics, towards developing novel therapeutic strategies.

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