A Physiologically-Driven Biaxial Bioreactor System to Investigate Valve Interstitial Cell Phenotypic State after Surgical Repair

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Despite the phenomenal level of reliability of heart valves, more than five million people are diagnosed with valvular disease in the United States each year, with approximately 95,000 annular valve replacement surgeries and 20,000 mortalities per year [1]. Though ring annuloplasty for mitral regurgitation is beneficial in the short-term, it has been shown to be less promising in the long term, with repair failure as high as 60% [2, 3]. Mechanical stress is a strong etiological factor: alterations in mechanical loading caused by surgical repair lead to stress-induced changes in mitral valve interstitial cell (MVIC) function that affect both tissue structure and composition, ultimately leading to repair failure. In this work, we develop a robust experimental-computational approach that allows us to answer specific questions on mitral valve (MV) mechanobiology and provides insight into the micromechanics of surgically repaired valves. This work is thus three-fold: the first part focuses on the design and development of a planar biaxial bioreactor system. The second part involves the use of an established finite element model of the mitral valve [4] to estimate in vitro pre-stresses and functional stresses before and after different surgical repair scenarios. We then use the biaxial bioreactor system to apply the estimated stresses to stimulate MV samples and follow-up with downstream biological assessments of the valves. To develop robust tools that can help improve surgical repair, we must first understand the underlying mechanisms of MV compensatory response after ring annuloplasty by linking tissue-level stresses to MVIC response. A wide array of experimental studies have captured phenomena that drive VIC homeostasis—the current challenge lies in transforming this wealth of information into a holistic understanding of how cell response dictates long-term disease and repair failure. The integrated experimental-computational approach that we present in this work will serve as a platform for identifying biomechanical treatments that optimize surgical repair and elucidate mechanisms of disease progression.

Figure 1. (A) Biaxial bioreactor system. (B) MVIC deformation quantified by the nuclear aspect ratio (NAR) for the three groups: Control, Pre-Stress, and Normal Stress; both pre-stress and normal stresses are estimated from the inverse finite modeling approach. The difference between the three groups is statistically significant (p<0.01).


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