ABSTRACT

Left ventricular (LV) remodeling is nominally an adaptive process that restores biomechanical function following myocardial injury and/or sustained alterations in loading conditions. This remodeling can materialize as changes in myocardial geometry, composition, and mechanical properties. When these changes fail to restore LV biomechanical function, remodeling is termed maladaptive. It is generally accepted that maladaptive LV remodeling underlies the progression to heart failure in various forms of heart disease. The central hypothesis of this study is that we can leverage echocardiographic imaging techniques to non-invasively quantify changes in biomechanical function and mechanical properties in a serial manner throughout the progression towards heart failure. The corollary to this hypothesis is that the observed changes in function and mechanical properties can, at least in part, be attributed to a reorganization of collagen within the extracellular matrix. Large animal models of myocardial infarction and left ventricular pressure overload were integrated with echocardiographic imaging, computational modeling, and multi-photon microscopy to test this hypothesis. We posit that this delineation of disease-specific LV remodeling outcomes, with focus on regional mechanical changes throughout the myocardium, will promote translational strategies that can interrupt this deterministic process.