The mechanics of healing myocardial infarcts are a critical determinant of left ventricular function and the risk of an array of post-infarction complications including catastrophic rupture and progression to heart failure. Yet it has proven remarkably difficult to devise therapies to improve post-infarction prognosis by manipulating the scar formation process. Recent studies help to explain why: collagen alignment is a more important determinant of LV function than collagen content or overall scar stiffness, the primary targets of most interventions. Agent-based models are developed to evaluate the mechanisms by which mechanical environment directs collagen deposition and remodeling by cardiac fibroblasts and to better understand the effects of therapeutic interventions on the evolving scar structure. Results suggest different environmental cues regulate scar formation for different tissues and predict that a number of regenerative and device therapies that alter infarct mechanics – including stem cell injection, polymer injection, surgical reinforcement, and peri-infarct pacing – will alter scar structure, in some cases reducing the efficacy of the therapy. Moving forward, computational models of infarct healing suggest unexpected, novel approaches to...