Understanding mechanisms by which injectable materials preserve cardiac function post-myocardial infarction

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Summary: Increasing infarct wall thickness by a bio-inert non-degradable injectable material was insufficient to prevent negative left ventricular remodeling after myocardial infarction.

With over 5.8 million people suffering from heart failure (HF), treatment of negative left ventricular (LV) remodeling after myocardial infarction (MI), the leading cause of HF, is a pressing clinical need. Injectable materials are being studied as a potentially minimally invasive therapy for treatment of MI. Several injectable materials such as fibrin, collagen and chitosan have been shown to preserve or improve cardiac function as well as prevent LV remodeling post-MI. However, it is unclear as to whether it is the structural support, the bioactivity of these polymers or a combination of both that leads to beneficial effects.

We examined how passive structural enhancement of the LV wall by an increase in wall thickness alone affects cardiac function post-MI upon injection of a bio-inert, non-degradable synthetic poly (ethylene glycol) (PEG) based polymer. PEG gels of storage modulus $G'$=0.5 ± 0.1 kPa were injected and polymerized in situ one week after total occlusion of the left coronary artery in rats. The animals were imaged using magnetic resonance imaging (MRI) at 7 days post-MI as a baseline and again post-injection 49 days after MI. Though infarct wall thickness was significantly increased in PEG gel injected vs. control animals, both groups showed significant decreases in cardiac function in terms of end diastolic volume, end systolic volume and ejection fraction 7 weeks post MI compared to baseline. The cellular response to injection in terms of inflammation and neovascularization was also similar in both groups.

![Fig. 1. A) PEG hydrogel injected in infarct region. P demarcates the region of injection. Photomicrograph taken at 10X and scale bar is 1mm. B) Infarct wall thickness at 7 weeks post-MI. Wall thinning was prevented in the PEG injected group compared to the control. ($^*p<0.01$) C) Comparison of ejection fraction baseline (1 week post-MI, pre-injection) and post-treatment (7 weeks post-MI) in PEG injected and saline injected groups. ($^*p<0.01$ PEG compared to baseline, $^§p<0.01$ saline compared to baseline)](image)

The results of this study demonstrate that passive structural reinforcement alone was insufficient to prevent post-MI remodeling, suggesting that bioactivity and/or cell infiltration due to degradation of injectable materials are likely playing a key role in the preservation of cardiac function, thus providing a deeper understanding of the influencing properties of biomaterials necessary to prevent post-MI negative remodeling and guiding the design of future cardiac biomaterials for MI therapy.