Mechanically Altering Infarct Properties Improves Regional and Global Function Secondary to Acute Myocardial Infarction

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Background

Acute myocardial infarction leads to structure changes that result in the alteration of infarct material properties. Following the insult, necrotic myocardium and the normal extracellular matrix are replaced by a disarranged collagen network, which ultimately leads to scar formation. These histochemical and cellular changes that occur directly alter the mechanical stiffness of the infarct and surrounding non-infarcted myocardium (border zone). Theoretical left ventricular (LV) modeling has demonstrated that infarct material properties have a profound effect on global and regional LV function and mechanically altering the stiffness of the infarct could improve function and mitigate remodeling.[1-2] In this study we have developed a method of stiffening the infarct in-vivo and utilized MRI to measure acute and chronic regional and global function.

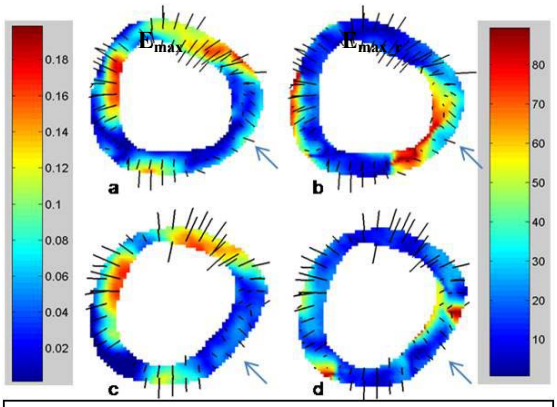

Fig 1. Maximum principal strain at 0mL (a) and 8mL (c). Maximum principal strain in the radial direction at 0mL (b) and 8mL (d). Arrows indicate the infarct area.

Material and Methods

This study was approved by the IACUC of the University of Pennsylvania. In order to adjust the infarct stiffness in-vivo, a device was developed that coupled the infarct to an external mesh using a fluid filled bladder placed between the infarct area and mesh. In addition, a port was exteriorized which allowed for adjusting the bladder volume thus infarct stiffness. To study the effect of the device on LV function a total of 8 animals were randomized to either control (4) or therapy (4). All animals received a posterolateral infarct with the therapy animals having the device placed at the time of infarct creation. One-week and 4 weeks post-infarct all animals were imaged (3T Siemens TIM Trio) to acquire global function and regional strain using the following parameters: Volumes; 2D Cine TrueFISP sequence, FOV=300mmx243mm, Matrix=192x159, FA=45, Slice=4mm, TR/TE= 3.2ms/1.6ms. Strain; 3D GRE 3D SPAMM tag sequence, FOV=260mmx260mm, Matrix=256x128, FA=15, Slice=2mm, TR/TE= 3.8ms/2.6ms, 3D SPAMM Prep Pulse. At the one-week time point, images were acquired for the therapy animals at bladder volumes of 0, 2, 4, 6, 8, and 10ml. Following the one-week imaging study the bladder was filled to 8ml and remained filled until the 4-week time point. Strain analysis was performed using a 3D OFM which tracks the 3D tags from end-diastole to end-systole.[3]

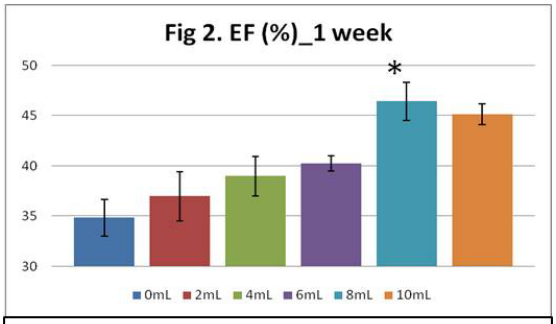

Fig 2. Acute testing at 1 week post infarction. Statistically significant difference between 8mL and 0mL ($p<0.005$).

Results

Maximum principal strain magnitudes (E_{max}) and vectors (E_{max_r}) for the one-week study at bladder volumes of 0ml and 8ml are shown in Figure 1. Stiffening the infarct caused a slight change in E_{max} for the infarct region (0.02±.001 (0mL), 0.03±.001 (8mL)) while E_{max_r} was significantly altered (77.6±1.3 degrees (0mL) and 22.4±2.7 degrees (8mL)). LV ejection fraction (EF) was also significant improved with infarct stiffening as depicted in Figure 2. Chronically stiffening the infarct significantly altered end-systolic volume (ESV) and EF compared to the control group (Figure 3).

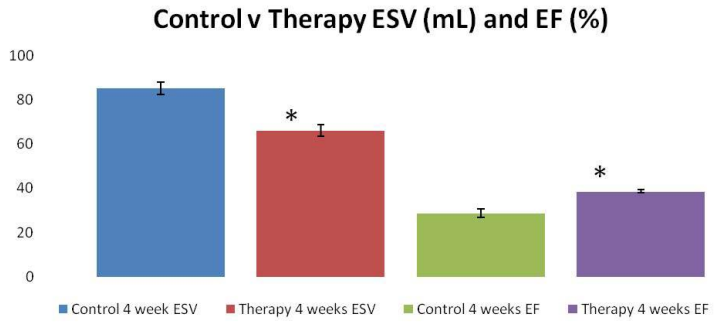

Fig 3. Left ventricular volumes at 4 weeks. Statistically significant decrease in ESV and increase in EF between therapy and control animals ($p<0.005$)

Conclusion

This study has demonstrated the ability to alter infarct material properties in-vivo by coupling the infarct to an external mesh. Stiffening the infarct shifted the mechanics of the region from a circumferential (stretch) to a more radial direction. This translated to diminished LV remodeling as evidenced by the improvement in EF and ESV at the chronic time-point, which correlates with the theoretical modeling. Clinically, stiffening the infarct by mechanical or cellular methods has the potential to mitigate infarct expansion and improve outcome.

References

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3. Xu.C, et al. Deformation analysis of 3D tagged cardiac images using an optical flow method. J Cardiovasc Magn Reson. 2010 Mar 30;12:19