Regional Frank-Starling relations in infarcted swine via dynamic real-time MRI

Francisco Contijoch[1], Walter RT Witschey[1], Jeremy McGarvey[1], Madonna Lee[1], Norihiro Kondo[1], Toru Shimaoka[1], Chikashi Aoki[1], Satoshi Takebayashi[1], Gerald A Zsido[1], Christen Dillard[1], Joseph H Gorman[1], Robert C Gorman[1], and James J Pilla[1]
[1]*University of Pennsylvania, Philadelphia, PA, United States*

Target Audience: Clinicians and scientists interested in the measurement of regional impact of ischemia and improved methods for evaluation of infarct dynamics.

Introduction: Non-invasive measurement of regional cardiac function is critical for the evaluation and development of pharmacologic, stem cell, and mechanical therapies to prevent adverse ventricular remodeling (1,2). Current methods require catheterization, have limited spatial resolution or field-of-view. Tyberg placed strain gauges directly on the epicardium to measure work (3). Current imaging methods provide a non-invasive and high spatial resolution approach, but are load-dependent since values obtained are influenced by the end-diastolic volume (preload) and arterial impedance (afterload). In this work, we developed an MRI method to quantify regional response to alterations in preload.

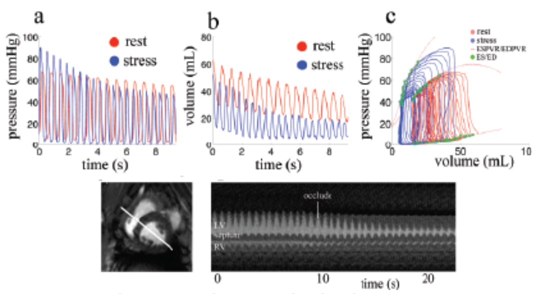

Figure 1: Real-time MRI during preload reduction experiment. **A)** LV pressure and **B)** LV volume during 10 s of continuous acquisition during preload reduction experiment. **C)** PV Loops were measured at rest and during continuous dobutamine infusion. **D)** 1D projection intersecting the LV parallel to the outflow tract illustrates temporal resolution during occlusion.

Method: A posterolateral myocardial infarction was created in swine via direct surgical ligation of the circumflex coronary artery or its branches (N=3, mean weight = 43kg, infarct size = 20% of LV mass). Balloon catheters were positioned in the inferior/superior vena cavae and inflated to perform an inflow occlusion. LV pressure was recorded via catheter (Millar Instr) and synchronized with MRI (LabView). Short-axis, golden angle radial, bSSFP imaging was performed with the following parameters: TE/TR = 1.45/2.9ms, BW=900 Hz/pixel, N=128, FOV=280 mm. Images were reconstructed using an iterative, conjugate-gradient, SENSE-based reconstruction with Nspokes = 34 on Gadgetron (4, 5). An intensity-based non-rigid registration algorithm was utilized to obtain strain (6). Time-varying wall thickness (WT) was calculated from epi- and endocardial contour. Natural radial strain was estimated as $\ln(WT_0/WT)$ and regional myocardial work density was calculated by integration of the pressure-strain loop generated for each cardiac cycle (7).

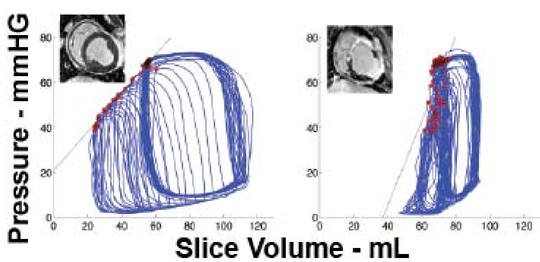

Figure 2: PV Loops in 3-week post infarct swine at two slice locations. Considerable differences are observed between remote (left) and infarcted (right) slices.

Results: Pressure-volume relations can be obtained using real-time MRI (Fig 1). However, in an infarct model, there are regional changes in function, which lead to changes in the observed PV loops depending on slice position (Fig 2). This necessitates a more regional measurement of myocardial work. With motion tracking, wall thickness and natural radial strain can be measured during the experiment (Fig 3 A-D). The pressure-strain loops vary depending on the loading condition (Fig 3 E) and can be integrated to obtain a measure of regional myocardial work density (RMWD). RMWD can be plotted for each heartbeat and each region of tissue (Fig 3F). A PSIR image was utilized to identify normal myocardium (blue), borderzone (green), and infarct (red) tissue used for subsequent analysis. The technique also allows for the development of regional Frank-Starling relations by plotting the measured RMWD vs. end-diastolic wall thickness (EDWT). The preload reduction experiment was divided into a pre-occlusion (high load) state and a full-occlusion (low load) state. The normal tissue performed 8.31 J/ m2 ± 2.71 during the high load period and 3.93 J/ m2 ± 0.87 during the low loading conditions (paired t-test p-value = 0.073). The borderzone tissue performed 3.70 J/ m2 ± 1.77 during the high load period and -0.52 J/ m2 ± 4.01 during the low loading conditions (paired t-test p-value = 0.198). The infarcted tissue performed 2.01 J/ m2 ± 2.31 during the high load period and -0.01 J/ m2 ± 3.59 during the low loading conditions (paired t-test p-value = 0.126).

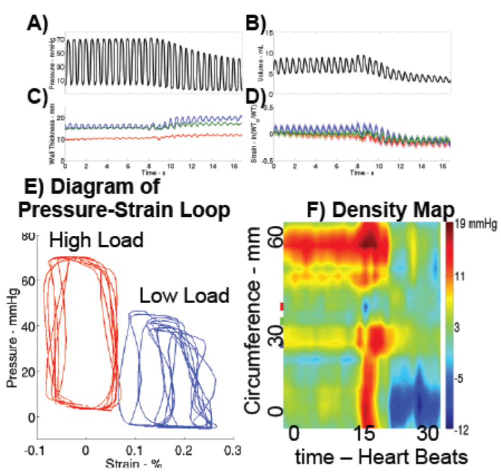

Figure 3: Strain and Work Density Results A) Pressure **B)** Volume **C)** Wall Thickness and **D)** Strain were measured for 3 points of interest during the preload reduction. **E)** Pressure-Strain loops can be generated for each region of interest for each heartbeat. **F)** Work Density can be calculate for all regions and heartbeats and plotted as an image.

Discussion: The three regions of interest show differential effects to the preload reduction. The normal tissue (blue) shows a decrease in RMWD as the occlusion progresses (wall thickness increases as filling decreases). The infarcted tissue (red) shows little change due to the occlusion. This is attributed to primarily passive material properties of an infarct. The borderzone tissue (green) shows somewhat mixed behavior. During normal loading, it experiences decreased work density (relative to normal myocardium). However, the borderzone tissue does appear to unload as the occlusion progresses.

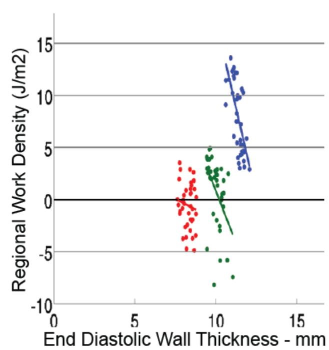

Figure 4: Regional Frank-Starling Relations Regional myocardial work for normal (blue), borderzone (green) and infarct (red) tissue is shown. The preload reduction causes a distinct change in wall thickness and work in normal myocardium. However, infarcted tissue does not show the same dependence on load.

Conclusion: We found evidence of depressed regional work density in the peri-infarct borderzone and a differential effect of loading conditions. Evaluation of the borderzone function is critical for the development of novel treatments to prevent heart failure. The presented method allows for evaluation of regional work density and loading conditions with high spatial and temporal resolution. This can aid development of novel medical therapies by improving the understanding of borderzone physiology during infarct remodeling.

References: [1] Blom et al. The Annals of Thoracic Surgery. 2007;84:2004-10. [2] Perin et al. JAMA. 2012;307(16):1717-26. [3] Tyberg et al. Cir. 1974; 49:748-754. [4] Greengard et al. SIAM Review, Vol. 46, No. 3, pp. 443-454. [5] Hansen MS, Sørensen TS. Magn Reson Med. 2012. [6] Rueckert et al. IEEE TMI. 1999;18:712-21. [7] Nakano et al. Circulation. 1990;82(4):1352-61.