Introduction: The ischemically injured myocardium contains a mixture of viable and non-viable tissue post-myocardial infarction (MI); thus, a method to discern the various zones would be of great value in clinical management. The traditional approach in treatment attempts to salvage the viable peri-infarcted areas, by pharmaceutical intervention. A popular route of treatment is providing Angiotensin Converting Enzyme inhibitors (ACEi) to reduce QT dispersion (QTD) following MI. Increased QTD is a marker of electrical instability predisposing to ventricular arrhythmias in the infarcted areas. Captopril, an ACEi, is widely used as an effective reducer of mortality and morbidity following MI, primarily due to its ability to improve left ventricular remodeling following the cardiac event. The physiological effect of Captopril has on the peri-infarcted regions post-MI has not been well interpreted. Studies show promise in the field of cardiac imaging using manganese as a contrast agent to track changes in tissue viability. In this study we would like to examine, using a murine model: (1) the sensitivity of manganese enhanced MRI (MEMRI) T1 mapping to detect peri-infarction sites, and (2) the sensitivity to differentiate pre- and post-ACEi treatment. This non-invasive imaging technique could provide a potential diagnostic method to monitor pharmaceutical intervention and therefore improve diagnostic assessment of ischemic damage, thus improving patient care.

Methods: The left anterior descending coronary arteries of male C57Bl/6 mice (7-10 weeks old), were ligated to induce MI. One group then received captopril (1 mg/kg BW) administered in their drinking water for 7 days (n=7); comparable to the 65 mg daily dose post-MI administered to clinical patients. The other group received no treatment (n=9). MnCl2 (282 nmol/g BW) was infused at a rate of 0.6 ml/hr 7-10 days post-MI. The mice were then imaged in a 7.0 T 20 cm horizontal bore Biospec MRI spectrometer (Bruker Instruments, Billerica, MA) equipped with a micro imaging gradient insert (950 mT/m). A 35 mm inner diameter coil was used to transmit and receive at 1H frequency. Mn2+ signal enhancement was monitored with a T1-weighted ECG gated Gradient Echo Flow Compensated (GEFC) pulse sequence with the following parameters: matrix= 128x128; TE= 3.5 ms; TR = 35ms; slice thickness= 1.0 mm; FOV= 3.0x3.0 cm; and NA= 2. The short axis T1-map GEFC images were acquired with an ECG gated, flow compensated Look-Locker pulse sequence with the following parameters: matrix= 128x128; Inter TE/TR= 2.5 ms/10sec; slice thickness= 1.0 mm; FOV= 3.0x3.0 cm; NA= 2; inversion time/interval= 9/150 ms; echo images= 50. The analysis of the resulting images was performed using an in-house computer program (Myoplotter), developed in MATLAB (Natick, MA) that segmented the cardiac image into 24 sectors and reported the T1 value of each, which has an inverse relationship with the uptake of Mn2+.

Results: Variation in Mn2+ uptake due to MI is shown in the myocardium (Figure 1). There is minimal variation between the treatment and the control group within the MI zone (Figure 2); however, the sectors adjacent to the infarct regions showed a higher percent change with and without ACEi treatment (26.5%) in the T1 values between the groups (Figure 3). The most impacted areas of note were sector #19 (p=0.019) and sector #10 (p=0.066), both within the peri-infarct region.

Conclusion: Differential Mn2+ uptake between the experimental and control mice were observed in the peri-infarct regions, indicating the MEMRI with T1 mapping implementation is sensitive enough to show a difference with and without pharmaceutical intervention by ACEi. This agrees with the idea that the necrotic regions in, and healthy regions far away from, the infarct zone are less likely to be affected by treatment than transitional areas. Further research is warranted on why the Mn2+ uptake in peri-infarct regions is different in the treatment group. There is also room to improve the MEMRI T1 mapping technique, along with histological validation, to be more sensitive in demonstrating preclinical models with potential translational impact.

References: