Temporal Cardiac Manganese-Enhanced MRI with T1-mapping in Mice following Myocardial Infarction

F. liu[1,2], B. Waghorn[1,2], J. Liu[1], and T. C-C. Hu[1,2]

[1]Small Animal Imaging, Department of Radiology, Medical College of Georgia, Augusta, Georgia, United States, [2]Nuclear and Radiological Engineering / Medical Physics Programs, George W. Woodruff School, Georgia Institute of Technology, Atlanta, Georgia, United States

Introduction

Myocardial infarction (MI) can develop into either permanent ventricular dysfunction or dysfunction that can be improved with treatment. It is therefore necessary to investigate the viability of the myocardium when signs of left ventricular dysfunction are predominant [1]. Several imaging techniques are capable of detecting viable hibernating myocardium, each addressing a specific aspect of the problem [1]. Recent advances have improved the feasibility of studying ischemic heart disease with MRI [2]. Thus, it would be beneficial if MRI could be sensitized to accurately detect and quantify the regional viability following MI. As Mn^{2+} is an excellent T_1-shortening contrast agent for MRI and can also enter viable myocardial cells via voltage gated calcium channels, manganese-enhanced MRI (MEMRI) has been implemented in this study to estimate the dynamic uptake of manganese in a murine MI model and to assess changes in the uptake with disease progression post-MI. Viable cells have demonstrated a great affinity for manganese ions due to transmembrane potential, while injured cells fail to retain it [1]. Therefore, a temporal study using manganese-enhanced MRI (MEMRI) can potentially assess the remodeling process following the MI in murine models.

Methods and Materials

Adult male C57Bl/6 mice (n=9; 8-10 weeks old, 22.1±2.9 g) were divided into two groups for the MEMRI experiments: myocardial infraction (MI: open chest with left anterior descending coronary artery ligation) and sham operated (Sham: open chest without myocardial injury). The mice were anesthetized with 1-3% isoflurane in a 1:1 mixture of medical air and oxygen. A single dose of 190.1±0.9 nmoles/g body weight $MnCl_2$ was infused intravenously into the tail at a rate of 0.6 ml/hr. The imaging was performed on 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 volume coil was used to transmit and receive signals at ^1H frequency. The MRI studies included T_1-weighted ECG gated Gradient Echo Flow Compensated (GEFC) imaging (TE/TR=3.5 ms/35 ms, field of view=3.0×3.0 cm, slice thickness=1.0 mm, matrix=128×128, number of averages=6) and T_1-mapping ECG gated, flow-compensated Look-Locker imaging used with the following parameters: TR/TE=10 sec/2.5 ms, 50 echoes, field of view=3.0×3.0 cm, slice thickness=1.0 mm, τ=153 ± 18 ms, matrix=128×128, number of averages=2. Both pre- and post-$MnCl_2$ infusion T_1-map images were acquired with a T_1-weighted GEFC sequence to ensure the accuracy of the infusion at 2 days, 8 days and 29 days post-surgery (MI and Sham). The T_1 values for each T_1-map image were calculated using a custom written C^{++} program [4]. The mean T_1 value and ΔR_1 values for each ROI were calculated using Amide [5], where ΔR_1= (post- $MnCl_2$ infusion R_1) - (pre- $MnCl_2$ infusion R_1).

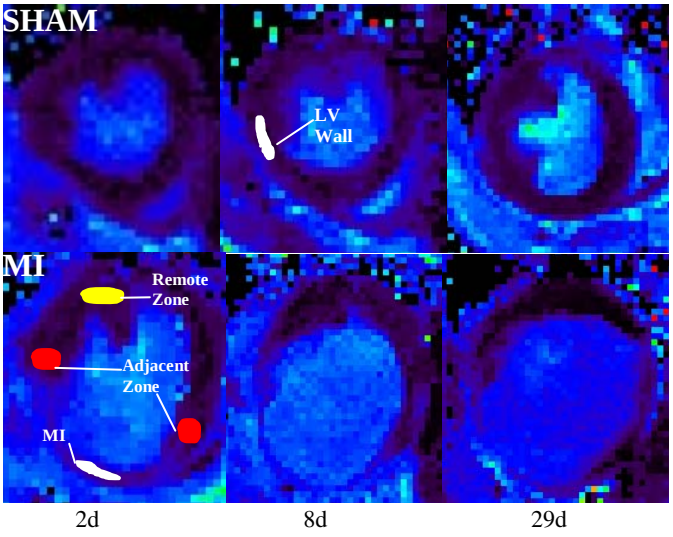

Figure 1: Example of short axis mouse heart T_1-maps at three different time points (2 days, 8 days and 29 days) post-surgery. The upper is for Sham operated and the ROI regions delineated at LV Wall; the lower is for MI and the ROI regions delineated at MI injury site, adjacent zones and remote zone.

Results

Both pre- and post-$MnCl_2$ infusion short axis T_1-maps for the MI and Sham mice are shown in Figure 1. Regions of interest (ROIs) were drawn on the T_1-maps for the left ventricular free wall (LV Wall), MI injury site, adjacent zone and remote zone. The change in relaxation rate, ΔR_1, for each ROI was calculated at three different time points (2.5±0.5 day, 8.5±1.5 day, and 29±1 day) post-surgery as shown in Figure 2. Reduced ΔR_1 values for the MI injury site indicated a reduction in the uptake of Mn^{2+} in MI mice versus the LV Wall of the Sham mice. Also, comparing the different ROIs, ΔR_1 for the sham group shows little temporal change as expected for normal cardiac system. Similarly, at the MI injury site ΔR_1 remains very low due to the MI. However, the increase in ΔR_1 for the adjacent zone of the MI injury site suggests potential Mn^{2+} flux modulation due to Ca^{2+} dysfunction, potentially allowing for monitoring of myocardial remodeling following MI.

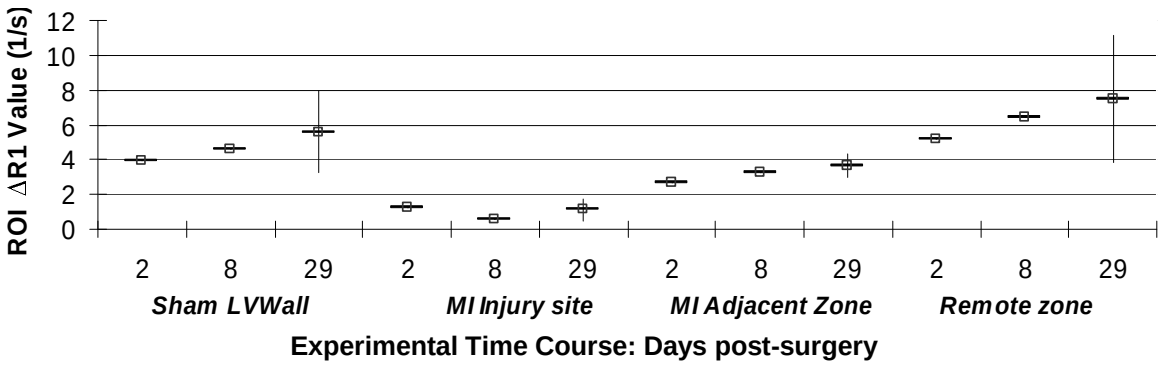

Figure 2: The ΔR_1 values for the ROI regions of sham operated and MI at three different time points.

Conclusions

Results in the current study suggests that T_1-mapping of cardiac MEMRI can be used to track and characterize the progress of MI in murine models, which may be useful for examining potential therapeutic interventions. Further data acquisition is required to draw conclusions with improved statistical confidence.

References

1. Daire JL, et al. *Magn. Reson. Med*. 2008; 59(6): 1422–1430. **2.** Hu TC, et al. *Magn Reson Med*. 2005 Jul; 54(1):196-200. **3.** Hu TC, et al. *Magn Reson. Med.* 2001; 46(5):884-890. **4**. Chuang KH, et al. *Magn Reson Med* 2006; 55(3):604-611. **5.** Loening A, et al. *Mol. Imaging*. 2003; 2:131-137.