Myocardial infarction quantification and function assessment with Manganese Enhanced MRI (MEMRI) in mice on a clinical 3T scanner

B. Delattre[1], V. Braunersreuther[2], J-N. Hyacinthe[1], F. Mach[2], and J-P. Vallée[1,3]

[1]Faculty of Medicine, University of Geneva, Geneva, Switzerland, [2]Division of Cardiology, Department of Medicine, University Hospital, Foundation for Medical Researchers, Geneva, Switzerland, [3]Work supported in part by the Center for Biomedical Imaging (CIBM), Geneva and Lausanne

Introduction:

Manganese (Mn), a calcium analog, is an interesting contrast agent that enters excitable cells via L-type voltage dependant channels. Due to a strong T1 shortening effect when accumulating in tissue Mn can be used as an efficient marker of cell activity [1],[2]. In previous studies [3],[4] it has revealed a strong efficiency in the assessment of transmural fibrotic scar myocardial infarction in a mice model of permanent coronary occlusion. Wether Manganese Enhanced MRI (MEMRI) is also able to detect non transmural infarct in mice is not known. The aim of our study was to set up a MEMRI protocol to assess subendocardial myocardial infarction in a mouse model of coronary occlusion reperfusion on a regular 3T clinical MR scanner.

Methods:

All experiments were done in C57/BL6 wild type male mouse (n=11, m=24±2 g). During surgery mice were anesthetized with 2% isoflurane in oxygen, and artificially ventilated. Infarction model used was a 60 minutes ischemia induced by ligation of left ventricular descending coronary artery followed by reperfusion. Imaging was performed 24 hours after reperfusion on a clinical scanner magnetom Trio 3T TIM system (Siemens Medical Solutions, Erlangen Germany) with a dedicated 2 channels receiver coil for mice (Rapid biomedical GmbH, Rimpar Germany). To perform the MRI exam we adapted 2 clinical sequences commonly used in cardiac patients by the implementation of a modified low SAR pulse to achieve sufficient spatial resolution. A turboflash cine sequence assessed myocardial function before and after Mn injection: in plane resolution 344 µm, slice thickness 1 mm, typically 4 slices, TR/TE 11/5 ms, flip angle 30°, GRAPPA with acceleration factor 2, 3 averages, typical acquisition time 3 min. A T1-weighted turboflash sequence using Phase Sensitive Inversion Recovery reconstruction [5] (PSIR) assessed myocardial viability: in plane resolution 156 µm, slice thickness 1 mm, typically 4 slices, TR/TE 438/7.54 ms, flip angle 45°, TI 380 ms, GRAPPA with acceleration factor 2, 2 averages, typical acquisition time 2 min 30. Both sequences were ECG and respiratory gated. Mn solution was made of 15 mM $MnCl_2$ diluted in NaCl 0.9% vol. Mn was perfused by an intraperitoneal line at a typical rate of 4 ml/h for approximately 5 min during the MRI exam in order to assess the wash-in kinetics in the myocardium. After experiment the infarct size was quantified by TTC staining and correlated to the measurements derived from MRI based on a threshold method. The threshold was defined from the mean signal intensity in an area showing a strong function default observed in the cine images. Myocardial function analysis was performed with in-house software that allows evaluation of wall thickening with projection of radial segments covering the entire muscle.

Results and discussion:

First experiments were done in normal mice (n=7) to determine the Mn concentration needed to achieve a maximal enhancement in viable myocardium. We found that 200 nmoles/g body weight was optimal for the PSIR sequence used. To assess myocardial infarct size in mice who had infarction (n=4) we did PSIR images of the whole myocardium 60 min after Mn injection. We determined with the Mn kinetics measured that this delay was suitable to have a sufficient contrast between viable myocardium and infarcted area (results not shown), which is in agreement with other studies [4]. An example of PSIR images and TTC staining is shown in figure 1. The spatial resolution achieved allows to observe a subendocardial infarction area. This quantification method showed a reliability of 92 ± 2 % compared to TTC staining which is considered as the gold standard. Figure 2 shows the estimated infarct volume reported on total left ventricular myocardial volume estimated with MEMRI versus the estimation done with TTC. The results show a significant correlation between the 2 methods. Left ventricular regional function was assessed by comparing myocardium thickening between diastole and systole for 100 rays covering the whole myocardium. Figure 3 shows the results obtain before and after Mn injection for normal (n=3) and infarcted mice (n=4). Compared with the normal group, wall thickening is widely reduced in anterolateral region for infarcted mice while it is slightly augmented in septum probably due to a compensation mechanism. There is no significant difference in wall thickening before and after Mn injection, which means that cine measurement could be used in future experiments where Mn will be injected before the MRI exam.

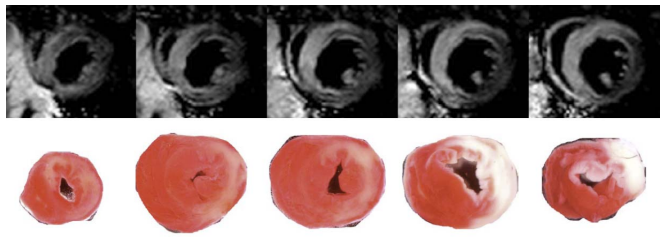

Fig. 1 : Comparison between whole heart PSIR images taken 60 min after Mn injection and TTC staining in myocardial infarct in mice.

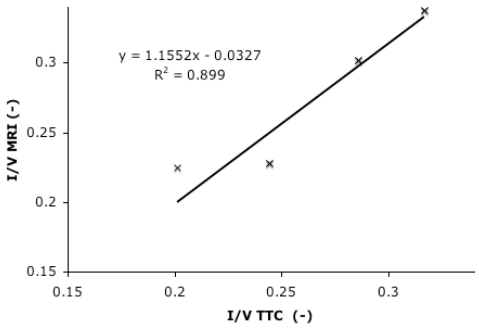

Fig. 2 : Infarcted volume reported on total left ventricular volume estimated by MEMRI versus TTC estimation for infarcted mice (n=4).

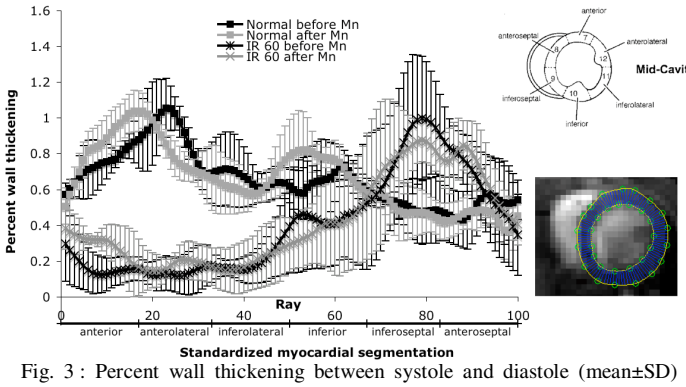

Fig. 3 : Percent wall thickening between systole and diastole (mean±SD) for 100 rays covering the whole myocardium in one slice (see right insert), for normal mice (n=3) and infarcted mice (referred to as IR 60) (n=4) before and after Mn injection.

Conclusion:

This study shows the feasibility of accurate non transmural infarct size quantification by MEMRI in a mice model. Proposed cine sequence, even in presence of Mn, depicts accurately infarct related contraction deficit. This validated protocol allows longitudinal study of cardiac disease model on clinical 3T scanner, a widely available platform.

References : [1] Silva et al. NMR Biomed 17 :532-543 (2004) ; [2] Wendland NMR Biomed 17 :581-594 (2004) ; [3] Saeed et al. Eur Radiol 10(2): 310-8 (2000) [4] Hu et al. NMR Biomed. 17 :620-626 (2004) ; [5] Kellman et al. MRM 47(2): 372-83 (2000) ;