Dual Manganese- and Delayed-Enhanced MRI Detects Myocardial Border Zone Viability in a Murine Myocardial Injury Model

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Background: Delayed enhancement MRI (DEMRI) identifies the non-viable anatomy of the myocardium. This non-specific technique may overestimate the non-viable territory. On the other hand, manganese (Mn^{2+})-enhanced MRI (MEMRI) identifies only the biologically active intracellular accumulation of Mn^{2+} by the viable myocardium. We performed dual-contrast myocardial assessment to complement DEMRI with the biological data of MEMRI using a diabetic murine myocardial injury model to better delineate the viable myocardium within in the peri-infarct border zone *in vivo*.
Hypothesis: Combined MEMRI/DEMRI will identify the viable myocardium in the border zone.
Methods: Left anterior descending coronary artery (LAD) ligation was performed in 3 adult C57BL/KLS-lepr^{db}/lepr^{db} (*dbdb*) and 7 heterozygous mice. Cardiac MRI was performed using a 3T GE Signa Excite clinical scanner with dedicated mouse coil (Rapid MR International) on weeks 1, 2, and 4 post LAD ligation. MEMRI was obtained after a 1cc/kg intraperitoneal (IP) injection of Mn^{2+} contrast agent (EVP1001-1, Eagle Vision Pharmaceutical Corp.). Twenty four hours later, delayed enhancement MRI was acquired with 0.2mmol/kg Gadolinium IP injection. Infarct volumes were determined manually using Osirix software. Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) were measured and ejection fraction (EF) was calculated.
Results: The scar volume percentage was significantly lower using MEMRI when compared to DEMRI at weeks 1, 2, and 4 (13±8%* vs. 33±12%, 14±6%* vs. 23±8%, 17±3%* vs. 35±12%, *$p<0.05$, respectively). Similarly, the total scar volume demonstrated lower measurement using MEMRI vs. DEMRI at weeks 1, 2, and 4 (60±36μm^3* vs. 155±49μm^3, 74±39μm^3* vs. 124±49μm^3, 86±26μm^3* vs. 176±71μm^3, *$p<0.05$, respectively). This difference between MEMRI and DEMRI scar volumes indicate border zone viability. Furthermore, the longitudinal measurements of LVEDV (0.038±0.007ml, 0.047±0.015ml, and 0.047±0.024ml), LVESV (0.029±0.004ml, 0.037±0.012ml, and 0.035±0.017ml) and EF (24.1±5%, 23.2±4%, and 22.9±4%) indicate myocardial injury, LV remodeling, and persistence of peri-infarct border zone.
Conclusions: Dual-contrast MEMRI-DEMRI patterns may identify at-risk, but viable myocardial cells within transmural DEMRI regions in a murine myocardial injury model.

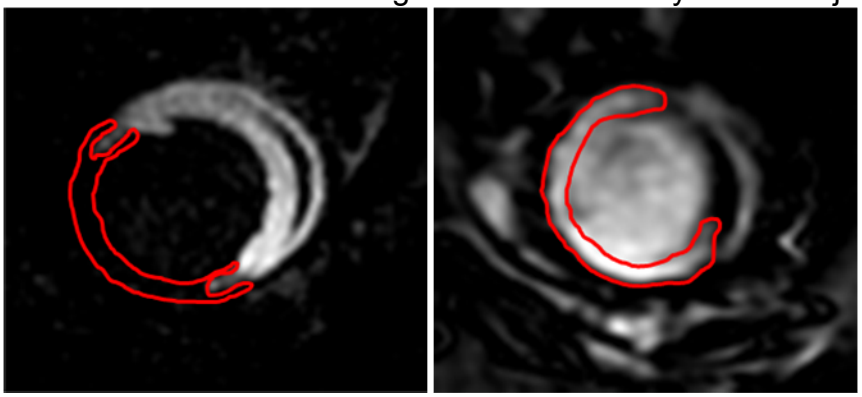

Figure. Corresponding MEMRI and DEMRI short axis images of the myocardial scar. Mn^{2+} defect (left) and corresponding larger Gd defect (right) can be seen visually (red ROI outlines the MEMRI and DEMRI scars).