

Assessment of Cardiac Functions and Inflammation Burden of Ischemic Injury with Integrated Functional and Cellular MRI

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INTRODUCTION

The aim of this study to investigate the potential of integrated cardiac MRI (CMR) protocols for better assessment and diagnosis of coronary artery disease (CAD), especially for acute coronary syndrome (ACS). CMR has become an essential utility in evaluating various stable cardiovascular diseases, including established CAD. T₂-weighted MRI, myocardial perfusion, delayed enhancement, and more recently, cine imaging, have been applied to appraise myocardium status of CAD. However, its role in ACS is less known. Our goal is to characterize myocardium after ischemic injury with integrated cellular and functional MRI, in search of potential application of ACS assessment in emergency room setting.

METHODS

BN inbred rats were subjected to either 30-min transient left descending artery (LDA) occlusion or permanent LDA ligation. Cardiac functions were monitored longitudinally up to 1 month after LDA occlusion.

Micro-meter sized iron oxide (MPIO) particles (3 mg/kg) were used to label immune cells *in vivo* by direct intravenous administration and the migration of the labeled cells, mainly macrophages, to the injured hearts are tracked over time with T₂^{*}-weighted MRI. Cine MRI was used to access global systolic functions, whereas tagging MRI followed by strain analysis is used to assess regional ventricular wall motion abnormality. Real-time first-pass dynamic contrast with Gd-based contrast agent (Ominiscan, 0.05 or 0.075 mmol/kg) was used to access myocardial perfusion. Real-time free-breathing dynamic imaging, with 8 ms frame rate and equivalent 10-sec retrospective reconstructed temporal resolution, was achieved with Bruker ParaVision Intragate for respiration motion and cardiac cycle deconvolution. Delayed enhancement (DE) with Gd was used to evaluate myocardial viability and scarring. All *in vivo* MRI is acquired with Bruker 7-Tesla Avance III instrument with 156 μm in-plan resolution; whereas *ex vivo* MR microscopy (MRM) is performed with Bruker 11.7-Tesla system with 46-μm isotropic resolution.

RESULTS AND DISCUSSION

Immediately after transient ischemic-reperfusion injury (Fig.1), the local myocardial blood flow was greatly reduced (Fig. 1E, G) in the affected myocardium, with delayed wash-in kinetics (Fig. 1F), even though the full myocardial perfusion has been fully restored. The affected myocardium also showed significantly retarded regional wall motion and regional strain (Fig. 1A). The myocardial perfusion was fully restored in the affected myocardium 16-hr post-ischemia, with normal wash-in kinetics (Fig1, I-N). Although most of the cardiac function has regained, the regional wall motion was not fully recovered (Fig. 1H), with areas showing decreased strain. Tagging with local strain analysis might be sensitive in determining injured myocardium after re-vascularization. At this early time, however, inflammation has already set in, and macrophages have already infiltrated around and near the ischemic site (Fig. 2). On the other hand, shortly after permanent ischemia (Fig. 3), myocardial perfusion defects are much more severe and spread through much larger areas. Chronic myocardial infarction (MI) can be visualized as hyperintensity with MRI (Fig. 4A, D). Although myocardial perfusion in the surrounding areas showed recovery in chronic MI, the regional wall motion and strains still remained compromised (Fig. 4).

CONCLUSION

Our data indicate that integrated CMR with tagging and perfusion to assess perfusion and regional wall motion simultaneously might be valuable for better assessment of myocardial status after MI, and can better assist early evaluation of ACS. In addition, inflammation and macrophages may play a role in ischemia-reperfusion injury.

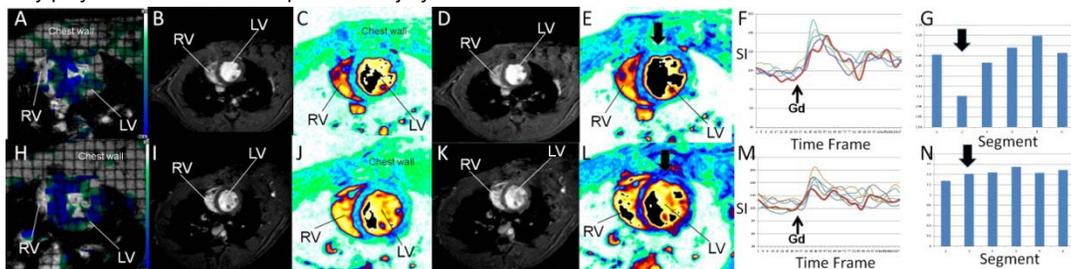


Figure1 Regional ventricular wall motion with tagging MRI and first-pass dynamic myocardial perfusion immediately (top panels, A-G) or 16-hr (lower panels, H-N) after transient LDA occlusion. (A, H) Circumferential strain (Ecc) by tagging MRI; (B, I) pre-contrast imaging; (D, K) post-Gd imaging; (C, J) partially enlarged colored images of B & I; (E, L) partially enlarged colored images of D & K; (F, M) temporal signal changes of different heart regions, showing red as the effected anterior wall; The onset of Gd administration is labeled with arrow. (G, N) mean signal of each heart segment, from left to right; 1-anterio-lateral, 2-anterior, 3-anterio-septum, 4-inferior septum, 5-inferior, 6-inferior lateral. The black arrowheads pointing to the effected anterior wall.

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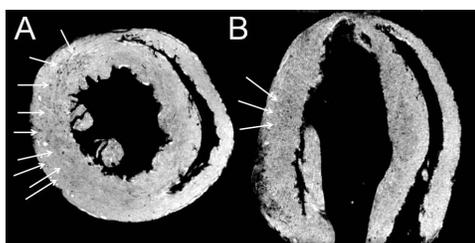


Figure 2 MRM of a heart harvest 1 day after transient ischemic injury and *in vivo* MPIO labeling. (A) short-axis view, (B) long-axis view, with white arrows pointing spots with hypointensity, which are macrophages.

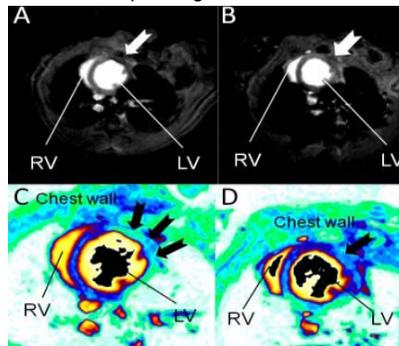


Figure 3 Myocardial perfusion with first-pass dynamic contrast at different time points after permanent LDA ligation: (A, C) immediate, (B, D) 5 days. (A, B) The top panels are original images (C, D) partially enlarged colored images of the top counterparts.

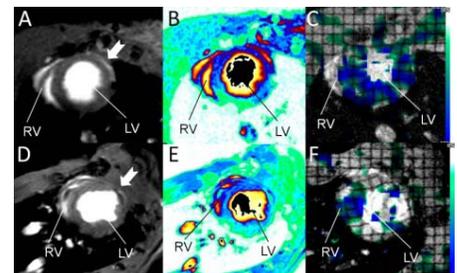


Figure 4 (A, B, D, E) First-pass dynamic myocardial perfusion and (C, F) Circumferential strain (Ecc) by tagging MRI tagging of chronic MI after (A-C) 20 days and (D-F) 26 days.