Detection of Focal Inflammation on Myocardial Disorder Using T2 Contrast Agent-based MRI: Comparison to Late-enhanced MRI with T1 contrast agent

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Introduction: Late enhanced-cardiac MRI using T1 contrast agent is known as the current standard of myocardial inflammation diagnosis. However, the poor sensitivity of late enhanced-cardiac MRI has hindered the reaching of a consensus on the clinical practice guidelines for its evaluation and treatment1. In this study, we investigated whether T2 contrast agent-combined CMR (cardiac magnetic resonance) imaging would be feasible and effective for the detection of the inflammation in a rat model of experimental autoimmune myocarditis (EAM) in comparison between T2 and T1 contrast agents, and whether T2 contrast agent-combined CMR imaging could give a guidance where the biopsy samples should be collected.

Materials and Methods: Myocardial inflammation was induced according to the reported induction method of experimental autoimmune myocarditis (EAM)2 in four 7-week-old male Lewis rats. We used home-made magnetic nanoparticles (MNPs) T2 contrast agent that enable the detection of both their fluorescence and magnetic properties in cells and tissues3 and Gd-DTPA (Magnevist®). We performed T2*- and T1-weighted MRI in EAM (n=4) rats before injection of contrast agents, then injected Gd-DTPA (0.2 ml/kg). 40 min after the Gd-DTPA injection, we acquired contrast-enhanced T1-weighted (Gd-enhanced) MR images. After the MR imaging, a bolus of MNPs was injected via tail vein (10 mg Fe/kg), and T2*-weighted (MNP-enhanced)MR image was obtained 24 hr after the injection. MRI measurement was performed using a 4.7 T MRI system (BioSpec 47/40; Bruker, Germany) with dual ECG and respiratory gating (SA Instruments, Stony Brook, NY, USA). T1-weighted MR images were obtained with a black-blood fast low-angle-shot (FLASH) cine sequence (TE/TR = 2.8/8 ms) in the center, upper and lower side of the heart in axial direction. A gradient-echo (FLASH) sequence (TE/TR = 6/130 ms) was used for T2*-weighted imaging. After serial in vivo MR imaging, all hearts were extracted and performed with immunohistochemistry (IHC) staining and fluorescence microscopy imaging.

Results and Discussion: Thickened ventricular walls and pericardial and/or pleural effusion in some instances were noted in the EAM rats. Gd- and MNP-induced contrast patterns in the MR images were not uniformly homogeneous in the myocardium, especially in moderately inflamed hearts. There is small difference in the contrast patterns of Gd- and MNP-enhanced MR images, which could be elucidated from the dominated origins between edema and inflammatory cells, respectively. Some dark spots by negative contrast in MNP-induced MR images were obtained, while there was no significant enhancement in those spots of Gd-enhanced MR images. We obtained H&E- and IHC-stained images from the adjacent sections of same heart, which were compared with T1- and T2*-weighted MR images. The regions with infiltrated monocytes in the IHC-stained and H&E stain images are in good correlation with the positive and negative contrast areas by Gd-DTPA and MNP accumulation in MR images, respectively. These results support the potential of MNP-combined CMR as a valuable tool in the research and clinical applications. Furthermore, we expect that the MNP-contrasted CMR imaging could give us a guide where to take biopsy samples from the heart suspecting myocarditis, which will reduce making an error in diagnosis of human myocarditis.

References

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