Manganese-Enhanced Magnetic Resonance In Vivo Imaging of Rat Myocardium Using FLASH: Comparative Study of Contrast at 2.35T and 7T

M. Bruvold[1], T. Pavlin[1], H. Brurok[1], P. Jynge[1], J. G. Seland[1]

[1]Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway

Background:

The interest in Manganese Enhanced MRI (MEMRI) has been growing in recent years due to the unique property of Mn^{2+} to act as an intracellular contrast agent [1]. The uptake of Mn^{2+}, which occurs through Ca^{2+} channels, can reveal important information on the viability and activity of cells. MEMRI has been used in human brain MRI studies [2] and in cardiac MRI to enhance the contrast of myocardium tissue [3]. One of the biggest obstacles for human MEMRI studies is Mn^{2+} toxicity. Therefore, most of the basic research and development in MEMRI has been done on small rodents.

A great advantage of small animal studies has been the ability to perform very high field MRI studies, offering increased sensitivity and resolution (due to increase in SNR). However, to increase specificity of MR, it is essential to optimize the contrast as well as SNR. While the contrast in MEMRI is generated by increased T_1-relaxivity due to the uptake of paramagnetic Mn^{2+}, little is known about the effect of T_1 dispersion on the contrast in MEMRI (most research in MEMRI has been done between 1T and 3T [1,2,3]). In this study we compare the contrast generated in rat myocardium using MEMRI at two different field strengths. The ultimate goal is to determine the optimal field strength for small animal studies using MEMRI.

Material and Methods:

Wistar male rats were anesthetized with isoflurane and the femoral vein was catheterized for infusion of 40 µmol/kg $MnCl_2$ over 20 min. MRI was performed using ECG-gated FLASH sequence [4] (*TE* 1.9 ms, BW 69 kHz, FOV 45x45 mm^2, matrix size 128x128, slice 1.5 mm, NA=10) at 7T and 2.35T (Bruker Biospec, Germany) with a volume coil as the transmitter and a surface rat-head coil as the receiver (Rapid Biomedical GmbH, Germany). The RF homogeneity profile of the receiver coil was found to be satisfactory for our study. Respiration and temperature were monitored during the experiment. The repetition time, *TR*, was defined by the period between R-peaks in the cardiac cycle (135-145 ms) and one line of k-space was acquired each heart beat in the late diastole. Scans with flip angles varying between 10 and 90 degrees were performed before and 30 min after manganese infusion.

Results and Discussion:

One of the main challenges in cardiac MRI of small animals is the fast heart rate, which necessitates the use of fast pulse sequences, such as FLASH. The contrast in FLASH is primarily a function of TR/T_1 ratio and the flip-angle θ[4,5]. The *TR* delay time is fixed by the period of the animal cardiac cycle, while the effective T_1 depends on the intrinsic T_1 of tissue, the uptake of Mn^{2+} contrast agent, and the main magnetic field strength. The TR/T_1 ratio is therefore completely determined by experimental conditions and will lead to a specific choice for the flip-angle, depending on whether proton-density or T_1-weighted contrast is preferred. Figure 1 shows MR signal strength as a function of the flip-angle. As expected, the Ernst angle (i.e., angle at highest intensity) increases for post-Mn data because of the increased T_1-relaxivity. To achieve best T_1 contrast, we chose to acquire images with a 60 degrees flip angle.

Figure 2 compares myocardial contrast at 7T and 2.35T for a range of flip-angles. Each point on the two curves is a ratio between post- and pre-Mn mean signal intensities in a region of interest within the myocardium. Note that there is on average a 10% improvement in contrast at 7T compared to 2.35T for flip-angles between 40 and 90 degrees. This is also evident from the axial images of rat myocardium (Figure 3a at 2.35T and Figure3b at 7T), which were obtained by subtracting pre-Mn from post-Mn MR images, using a 60 degree flip angle.

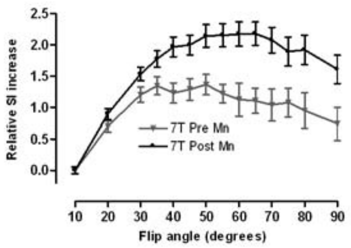

Figure 1

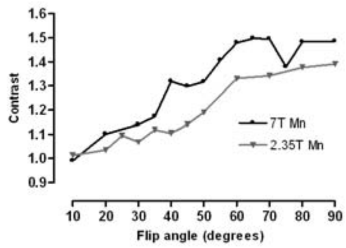

Figure 2

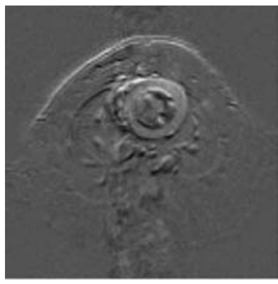

Figure 3a

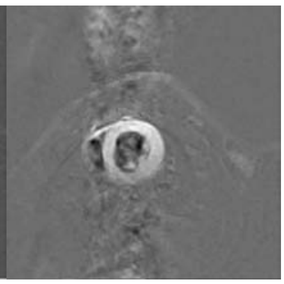

Figure 3b

Conclusion: The results presented show that an increased contrast is expected when MEMRI is performed at higher field strengths. Combined with the increase in SNR and the reduction in potential toxic Mn^{2+} dose to achieve sufficient contrast, MEMRI at high field has the capacity to become a valuable tool in molecular imaging of myocardial viability.

References:

[1] Koretsky AP and Silva AC. *NMR Biomed*, **17**(8), 527-31, (2004)
[2] Silva AC, Lee JH, Aoki I and Koretsky AP. *NMR Biomed*, **17**(8), 532-43, (2004).
[3] Wendland MR. *NMR Biomed*, **17**(8), 581-594, (2004).
[4] Frahm J, Haase A and Matthaei D. *Magn Reson Med*, **3**, 321-327, (1986).
[5] Haacke EM *et al.* "Magnetic Resonance Imaging. Physical Principles and Sequence Design" John Wiley & Sons (1999)