Preliminary Experience with Intracellular Manganese Ions as Contrast Agents in the Human Myocardium.

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Background. Animal experiments have shown that intracellular manganese (Mn) ions (Mn^{2+}) may be promising contrast agents for imaging (MnMRI) of normal and ischemic myocardium (1-4). Cardiomyocytes accumulate paramagnetic Mn^{2+} by entry via slow calcium (Ca^{2+}) channels (1,3) and by transient trapping in mitochondria. Binding to intracellular proteins enhances relaxivity of Mn^{2+} strongly (4) and improves further signal intensity in T_1 weighted images. The aim of the present study was to examine whether MnMRI may be applied for imaging of human myocardium.

Method. 3 groups (n=5) of human volunteers (20-29 years) received respectively 5, 10 and 15 µmol/kg of MnDPDP (Mn-dipyridoxyl-diphosphate, Teslascan™, Amersham Health) by 30 min infusion out-of-magnet. R_1 was measured before and 30 min and 1, 2, 4, 8 and 24 hours following infusion. MR-examinations were performed at 1.5 T (Siemens Magnetom Symphony) with use of a thorax surface coil. R_1 was measured in a single short-axis slice of left ventricular myocardium using an inversion recovery (IR) turbo-FLASH sequence with varying TI. Myocardial R_1 in s^{-1} was calculated as the mean value from 16 sectors, and ΔR_1 was calculated as the difference between control and postinfusion.

Results. No participant experienced adverse effects during infusion of MnDPDP. Figure 1 shows images before and 30 min after infusion of 5 µmol/kg. Myocardial R_1 rose from 0.96 s^{-1} to 1.35 s^{-1}, and was parallelled by a marked enhancement of signal intensity and an improved demarcation of the left ventricular wall.

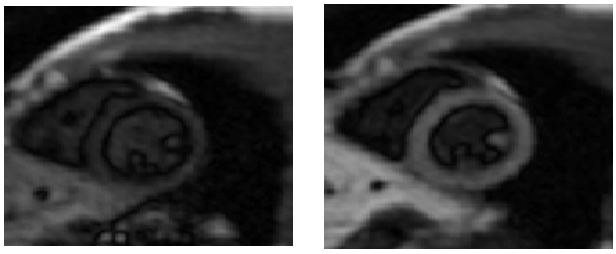

Figure 1. Short-axis images before and after MnDPDP.

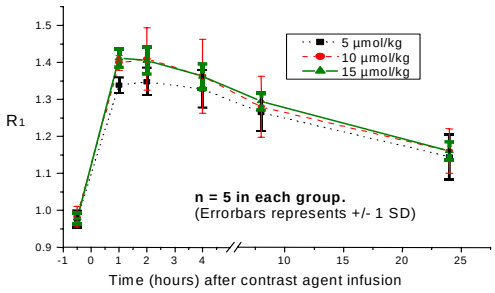

Figure 2. Myocardial R_1 in all groups

Mean control R_1 was 0.98 s^{-1} (SD=0.02 s^{-1}). Individual ΔR_1 values varied between 0.33 and 0.45 s^{-1}. As indicated in Figure 2, ΔR_1 values (s^{-1}) after 1-2 hours were 0.36 (SD=0.02), 0.43 (SD=0.03), and 0.43 (SD=0.01) in the three groups. There was a tendency to higher ΔR_1 with an increase in dose from 5 to 10 µmol/kg, but not from 10 to 15 µmol/kg. R_1 remained elevated before slowly declining after 2 hours. Still after 24 hours R_1 was higher than control. R_1 analysis from intraventricular blood revealed a control value of 0.65 s^{-1} and a mean value 1 hour postinfusion of 0.68 s^{-1}.

Discussion. A main result was the first time documentation that MnMRI may be applied to imaging of the human myocardium. Thus a close to 45 % rise in R_1 and an imaging window of 2-4 hours were observed. However promising, kinetics and dynamics of MnMRI are complex with many factors to consider and exploit. Among these are: the formulation of contrast media for Mn^{2+} release; the dose and duration of infusion or injection; plasma protein binding and low extracellular Mn^{2+}; the major uptake of protein-bound Mn^{2+} in liver; the influence of sympathetic tone; and finally, the more exquisite uptake of Mn^{2+} in cardiomyocytes and other excitable cells. As shown in the present study, a 30 min infusion of the preferably slow Mn^{2+} releaser MnDPDP raised R_1 effectively, but an apparent saturation occurred when the dose was raised above 5-10 µmol/kg. Whether the documented rise in R_1 can be further enhanced with MnDPDP or with other Mn^{2+} releasers remains to be seen.

References

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