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following parameters: TR/TE 14.0/5.22 ms, flip angle 30° , 28 partitions, partition thickness 0.5 mm, FOV 80 mm, matrix size 512×512 , voxel size 0.15×0.15 mm, 32 averages. The total imaging time was 60 min. Images were evaluated using a scanner software package (Syngo, Siemens). The SC was outlined and the mean signal was calculated. A second ROI was placed outside the animal contours for noise measurement. The mean signal-to-noise ratio (SNR) and standard deviation (SD) were calculated.

Results: After 2–3 days, a homogeneous enhancement in the SC lasting for 36 h was observed, after which a slow washout started. Uninjured animals displayed a homogeneous SNR of about 18 without and 36 with contrast agent throughout the SC. Proximal to the injury, injured mice showed an SNR comparable to uninjured mice. On moving further distal towards the lesion, the SNR gradually decreased, reaching background levels just at the lesion site.

Conclusion: An *in vivo* method for structural and functional spinal cord imaging in mice using MEMRI was developed. Manganese was readily taken up and transported through the spinal cord although means of uptake and transportation need to be elucidated. Changes in manganese uptake profiles on comparing injured and healthy mice suggest a function-dependent decrease in uptake in the injured mice. The decrease in enhancement proximal to the lesion site may correlate with dying back of axons. The decrease to baseline levels may indicate a near total loss of functional neurons at these levels. Correlation with histology supports this hypothesis.

References

- Demjen D, *et al.* *Nat Med.* 2004; 10: 389–395.
- Aoki I, *et al.* *Neuroimage* 2004; 22: 1046–1059.

CMR 2005: 14.02

Abdominal MRI made easy with orally administered manganese: a liver-specific contrast agent and a bowel marker

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Rationale and Objectives: A first clinical trial of orally administered manganese with and without ascorbic acid as a promoting agent in liver MRI was planned. The objectives of the study were to assess efficacy of the contrast agent in doses up to $100 \mu\text{mol/kg}$ bw, assess whether addition of ascorbic acid (molar ratio 1:2) to the contrast agent improved enhancements in the liver to such a degree that it may be of clinical importance and to assess acute safety.

Methods: Eighteen healthy adult males were enrolled in the trial. The mean age was 25.0 years and mean weight 77.6 kg. Contrast medium: drug: MnCl_2 doses were 25, 50 and $100 \mu\text{mol/kg}$ bw, respectively and promoting agent: ascorbic acid doses were 50, 100 and $200 \mu\text{mol/kg}$ bw, respectively. The trial was designed as a phase I, cross-over trial with two study periods separated by a wash-out period of 4 weeks.

All imaging was performed on a 1.5 T clinical MRI system (Siemens Somatom Vision, Erlangen, Germany). Three pulse sequences in the abdomen were used: (i) T_1 -weighted axial gradient-echo (GE), TR/TE 52.5/4.8 ms, flip angle 80° , thickness 10.0 mm and scan time 20 s; (ii) as for (i) but in the coronal plane; and (iii) T_1 -weighted axial spin-echo (SE), TR/TE 250/12 ms, fat suppression, thickness 10.0 mm, averages 7 and scan time 5 min 39 s. To gather information about contrast passage from ventricle to small intestine, occasionally more pulse sequences were used in the coronal plane, but no quantitative analysis was performed of the bowel distribution of the contrast agent. Phantom vials containing standardized Ni–agarose gels were placed in a fixed position under the patient in the bed and used for signal intensity measurements. Time points for imaging were precontrast and 1, 2.5, 4, 6, 9 and 24 h after

MnCl_2 intake. Safety parameters assessed in the trial were clinical examinations and vital signs including heart rate and blood pressure. Hematology and clinical chemistry were assessed with standard laboratory procedures.

Results: All pulse sequences showed a clear dose–response in the liver. High enhancements in the liver were seen between 2.5 and 6 h after MnCl_2 intake. At a manganese dose of $50 \mu\text{mol/kg}$ bw with ascorbic acid and at a dose $100 \mu\text{mol/kg}$ bw both without and with ascorbic acid, the hepatic enhancements were higher than 100%, GE pulse sequence. Using the volunteers as their own controls, the promoting effect of ascorbic acid was significant at a manganese dose of $100 \mu\text{mol/kg}$ bw. The contrast agent distributed well in the small intestine, delineating intra-abdominal organs well. No serious or unexpected adverse events were encountered. The drug was generally tolerated well except for gastrointestinal adverse events such as loose stool ($n = 12$), nausea (6) and vomiting (1). No significant alteration in hematology or clinical chemistry was seen.

Conclusion: Oral manganese is easy to use and has few side-effects. Besides the liver-specific effect, the agent delineates the intestine.

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Preliminary clinical experience with oral manganese (CMC-001) for liver imaging in daily routine

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Rationale and Objectives: Recently, a new liver specific MR agent has been introduced that is administered orally and only small amounts enter the general circulation. It is the only contrast medium that is delivered to the liver in high doses in the portal vein and very low doses in the hepatic artery. It is taken up by the hepatocytes and excreted together by the bile. We recently received permission from the Danish Health Authorities to use CMC-001 clinically (phase IV). In this paper we evaluate retrospectively our preliminary experience.

Methods: Six patients were studied. All had known liver metastases from colorectal cancers. From midnight the patients were not allowed to drink or eat. Between 8 and 9 a.m. the patients drank CMC-001 dissolved in 400 mL of water and 2 h later the MR examination (1.5 T) took place. The sequences are still being optimized.

Results: In three of the six patients, important new knowledge was obtained. The uptake in the liver was excellent in all patients. There were segmental differences in the uptake in four of the six patients, probably due to early fibrosis induced by chemotherapeutics or decreased portal vein flow due to metastatic compression. There was excellent visualization of the biliary system on the T_1 -weighted images. No contrast medium adverse events were reported.

Conclusion: CMC-001 seems to be useful in the work-up of patients with liver metastases regarding both the liver parenchyma and the biliary tract. Further research is strongly warranted.

Financial disclosure: Thomsen HS. Manganese containing magnetic resonance contrast agent. US Patent 6 015 545, 18 January 2000.

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Oral manganese as contrast medium in detecting liver metastases with MR imaging at 1.5 and 3 T

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