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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.

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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 µmol/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: MnCl₂ doses were 25, 50 and 100 µmol/kg bw, respectively and promoting agent: ascorbic acid doses were 50, 100 and 200 µmol/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

MnCl₂ 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 MnCl₂ intake. At a manganese dose of 50 µmol/kg bw with ascorbic acid and at a dose 100 µmol/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 µmol/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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Objective: Evaluation of the diagnostic performance of oral manganese as a new contrast medium in liver MR imaging in patients with liver metastases.

Method and Materials: Fifteen patients with known liver metastases were examined with MRI at 1.5 and 3 T before and 3 h after oral administration of Mn contrast agent diluted in 400 mL of water. MRI included T_1 -weighted FLASH breathhold sequences in coronal and transversal planes. At 1.5 T, contiguous 5 mm slices and at 3 T 3 mm slices were made. Additionally, a T_2 -weighted true-FISP sequence was performed to recognize liver cysts and hemangiomas. Contrast between liver tissue and metastases was determined on the pre- and post-Mn contrast scans. The homogeneity of liver enhancement was evaluated. In addition, the number of detected liver metastases and bowel and bile duct opacification was evaluated.

Results: There were no side-effects after the intake of oral Mn contrast agent. The mean liver metastases contrast improved at 1.5 and 3 T by factors of 2.1 and 1.5, respectively. Higher liver metastases contrast increased the number of detected liver metastases by more than 50% at both 1.5 and 3 T. In patients with a history of chemotherapy, liver enhancement was inhomogeneous, probably owing to disturbance of the portal circulation; nonetheless, this did not influence the improved metastases detection. In addition, bowel opacification was improved in all patients and excretion of contrast medium through the bile allowed visualization of the hepatic duct, gallbladder and choledochal duct on T_1 -weighted images in all patients.

Conclusions: This pilot study shows that oral Mn contrast medium is a simple and promising contrast agent, which results in improved visualization of liver metastases by a selective increase in the liver signal and also bowel and bile duct opacification is obtained using this contrast agent.

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First use of intra-articular carbon dioxide for MR arthrography; a feasibility study

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Rationale and Objective: Although the use of CO₂ for intra-articular conventional arthrography is feasible, it is hardly used because there are no advantages over the use of air. In MRI, direct arthrography is performed by using dilute Gd-DTPA. However, this intra-articular use lacks FDA approval and gadolinium compounds are expensive in comparison with CO₂. We decided to evaluate its feasibility for direct MR arthrography.

Materials and Methods: For the animal experiment, a pig weighting 15 kg was used. After baseline imaging and MRI-guided puncture of the knee joints, 12 cm³ of CO₂ was injected intra-articularly. A 1.5 T system (Magnetom Sonata, Siemens Medical Solutions, Erlangen, Germany) was used. MR images were acquired using sagittal T_1 -weighted 3D spoiled gradient-echo (TR/TE 40/10 ms slice thickness 2.5 mm) and T_1 -weighted (TR/TE 500/12 ms, slice thickness 4 mm) and T_2 /proton density-weighted (TR/TE 1740/11/80 ms, slice thickness 4 mm) spin-echo sequences.

Results: CO₂ resulted in loss of signal and hardly caused susceptibility artifacts. Owing to its bright appearance with most MR sequences, articular cartilage was sharply delineated on the CO₂ MR arthrograms. Also, structures with low signal intensity such as cruciates and menisci were well visualized. Only tiny susceptibility artifacts occurred.

Discussion: As is known, CO₂ is a cheap agent suitable for direct intra-articular injection and ready for clinical use. As in CO₂ MR angiography (1), CO₂ replaces the H-spins present, resulting in signal loss without inducing significant susceptibility artifacts.

Although this new kind of direct MR arthrography especially improves the delineation of structures with high signals in various sequences such

as cartilage and bone, structures with relatively low signals such as menisci and cruciates are also well visualized. This is also true during the use of the driven equilibrium sequences used for visualization of cartilage (2).

Owing to the high contrast, CO₂ MR arthrography might visualize smaller lesions and ruptures better than diagnostic methods applied so far (3).

In conclusion, direct CO₂ MR arthrography is new, feasible and possibly helpful in cartilage imaging.

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Noninvasive hyperpolarized helium-3 imaging studies in rats under spontaneous breathing conditions using a retrospective radial cine imaging technique

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Rationale and Objectives: Helium-3 ventilation imaging studies in rats are usually performed using tracheotomy or intubation approaches combined with assisted ventilation using respirator devices (1,2). These approaches are not appropriate for longitudinal ventilation studies or for precise assessment of subtle patho-physiological lung function changes. In this work, we developed and applied a fully noninvasive imaging protocol based on retrospective radial cine imaging under spontaneous animal breathing conditions.

Methods: MRI experiments were performed on a 2 T magnet in Lyon. A home-built spin-exchange apparatus was used to polarize 1.2 L of helium-3 to around 20%. Male Sprague-Dawley rats were anesthetized by intraperitoneal injection of sodium pentobarbital. A home-made mask was placed on the animal head. For the imaging protocol, a plastic bag containing 30 mL of hyperpolarized helium-3 gas was screwed on to the mask. The projection-reconstruction sequence was triggered 2 s later. The imaging parameters were 128 acquired samples, 200 radial directions per image, $TR = 10$ ms, $TE = 40$ μ s, $FOV = 80$ mm, flip angle 3°. The total acquisition time was 20 s. Retrospective cine ventilation image reconstructions were based on the NMR signal variations induced by the animal breathing.

Results: Figure 1 shows the time evolution of the helium-3 NMR signal intensity in the animal lungs following every RF pulse. This signal evolution curve was obtained by plotting the magnitude of the signal in the center of the k -space after each RF pulse. The signal amplitude oscillation corresponds to the animal breathing cycle with maxima and minima corresponding to the end-inspiration and end-expiration phase, respectively. The decrease in the maximum signal intensities is due to helium-3 T_1 relaxation and RF depolarization. In most of the acquisitions, the breathing pattern was very regular and suitable for retrospective cine imaging. Typically, cine images were reconstructed using a 200 ms image window. Figure 2(a) represents the ventilation image obtained during the animal maximum lung inflation and corresponding to the dashed box in Fig. 1. Figure 2(b) shows the lung