Synopsis
A new citrate-coated, iron-oxide-based blood pool contrast medium (very small superparamagnetic iron oxide particles, VSOP-C184) was investigated in rats to determine its potential for MRI of liver tumors. In these experiments VSOP-C184 was compared with a low-molecular-weight Gd-based agent (Multihance) in T1-weighted dynamic MRI and with a conventional SPIO (Resovist) using T2*- and T2-weighted sequences. In dynamic T1-weighted MRI, VSOP-C184 (45 and 60 µmol Fe/kg) has the same liver-tumor CNR as Multihance (100 µmol Gd/kg). On delayed T2*- and T2-weighted sequences, VSOP-C184 (15 µmol Fe/kg) has the same effect as Resovist (15 µmol Fe/kg).

Introduction
VSOP-C184 is an iron-oxide-based superparamagnetic MR contrast medium (SPIO) that can be applied as a bolus. Based on its blood pool properties and strong T1-shortening effect, VSOP-C184 was primarily developed for MRA (1-3) and successfully tested in a clinical phase I trial (up to 75 µmol Fe/kg). The present experimental study was performed to determine whether VSOP-C184 is also suitable for liver imaging, the classical indication for SPIO. To this end, VSOP-C184 was compared with a SPIO preparation already approved for clinical use. In addition, VSOP-C184 was compared with a low-molecular-weight Gd-based contrast medium in terms of its signal-enhancing effect in liver imaging.

Material and methods
Contrast medium: The citrate-stabilized iron oxide preparation VSOP-C184 (Ferropharm GmbH, Teltow, Germany) was investigated. The particles have a total diameter of 8.6 nm with a core size of 4 nm. R1 and R2 relaxivities at 0.94 T in water are 20.1 and 37.1 l/(mmol*s), respectively. This preparation was compared with Resovist (Schering AG, Berlin, Germany) and Multihance (Bracco, Milano, Italy).

Subjects and dosages: A total of 32 WAG rats were examined by MRI 3–4 weeks after implantation of CC531 colon cancer into the liver. VSOP-C184 was administered at doses of 15, 45, and 60 µmol Fe/kg, Resovist at 15 µmol Fe/kg, and Multihance at 25, 50, and 100 µmol Gd/kg (intraindividual comparison of VSOP-C184 and Multihance).

MR imaging: Magnetom Vision 1.5 T (Siemens AG, Erlangen, Germany), extremity coil, T1w 3D-GRE precontrast and up to 2.5 min postcontrast, every 6 s, as well as after 7 and 90 min; T1w SE, precontrast, 9 and 92 min postcontrast; T2*w 2D-GRE, precontrast, 17 and 96 min postcontrast; T2w TSE, precontrast, 20 and 98 min postcontrast.

Analysis: Signal intensities of the liver, tumor, and background were determined by means of ROI measurements and signal-difference-to-noise ratios (CNR) calculated for all sequences and time points. Wilcoxon and Mann-Whitney tests were applied for statistical analysis (p < .05).

Results
In dynamic T1-weighted MRI, VSOP-C184 produced an increase in positive liver-tumor CNR with doses of 45 and 60 µmol Fe/kg yielding values equivalent to Multihance at 100 µmol Gd/kg and significantly higher values than Multihance at 50 and 25 µmol Gd/kg and Resovist at 15 µmol Fe/kg. On static T2*- and T2-weighted sequences, there was an increase in negative liver-tumor CNR with VSOP-C184 at 15 µmol Fe/kg being comparable to Resovist at 15 µmol Fe/kg. Higher doses of VSOP-C184 did not lead to a further increase in CNR using these sequences.

Conclusion
VSOP-C184 is an MRI contrast agent that produces a high contrast of liver tumors on MRI using both T1- and T2-weighted sequences. The contrast values on either sequence are comparable with those of purely T1 and T2 contrast media, respectively. VSOP-C184 thus allows for the combined T1-weighted dynamic and T2-weighted static MRI of liver tumors.

References
3) Taupitz et al, Radiology 2002; 222: 120-126