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Renate Hammerstingl
Alexander Huppertz
Josy Breuer
Thomas Balzer
Anthony Blakeborough
Rick Carter
Lluis Castells Fusté
Gertraud Heinz-Peer
Werner Judmaier
Michael Laniado
Riccardo M. Manfredi
Didier G. Mathieu
Dieter Müller
Koenraad Mortelè
Peter Reimer
Maximilian F. Reiser
Philip J. Robinson
Kohkan Shamsi
Michael Strotzer
Matthias Taupitz
Bernd Tombach
Gianluca Valeri
Bernhard E. van Beers
Thomas J. Vogl
For the European EOB-study group

Diagnostic efficacy of gadoxetic acid (Primovist)-enhanced MRI and spiral CT for a therapeutic strategy: comparison with intraoperative and histopathologic findings in focal liver lesions

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R. Hammerstingl (✉)
Institute of Diagnostic and Interventional Radiology,
Johann Wolfgang Goethe-University,
ZRAD, Haus 23 C, Theodor Stern Kai 7,
60590 Frankfurt am Main, Germany
e-mail: hammerstingl@em.uni-frankfurt.de
Tel.: +49-69-630187296
Fax: +49-69-630183683

A. Huppertz
Imaging Science Institute,
Charitè - Siemens,
Robert-Koch-Platz 7,
10115 Berlin, Germany
e-mail: Alexander.Huppertz@siemens.com

J. Breuer · T. Balzer
Gobal Clinical Development Diagnostics,
Bayer Schering Pharma AG,
Muellerstr. 178,
13342 Berlin, Germany
e-mail: Josy.Breuer@bayerhealthcare.com
e-mail: Thomas_1.Balzer@bayerheathcare.com

Abstract A multicenter study has been employed to evaluate the diagnostic efficacy of magnetic resonance imaging (MRI) using the new liver-specific contrast agent gadoxetic acid (Gd-EOB-DTPA, Primovist), as opposed to contrast-enhanced biphasic spiral computed tomography (CT), in the diagnosis of focal liver lesions, compared with a standard of reference (SOR). One hundred and sixty-nine patients with hepatic lesions eligible for surgery underwent Gd-EOB-DTPA-enhanced MRI as well as CT within 6 weeks. Pathologic evaluation of the liver specimen combined with intraoperative ultrasound established the SOR. Data sets were evaluated on-site (14 investigators) and off-site (three independent blinded readers). Gd-EOB-DTPA was well tolerated. Three hundred and two lesions were detected in 131 patients valid for analysis by SOR. The frequency of correctly detected lesions was significantly higher on Gd-EOB-DTPA-enhanced MRI compared with CT in the clinical evaluation [10.44%; 95% confidence interval (CI): 4.88, 16.0]. In the blinded reading there was a trend towards Gd-EOB-DTPA-enhanced MRI, not reaching statistical significance (2.14%; 95% CI: −4.32, 8.6). However, the highest rate of correctly detected lesions with a diameter below 1 cm was achieved by Gd-EOB-DTPA-enhanced MRI. Differential diagnosis was superior for Gd-EOB-DTPA-enhanced MRI (82.1%) versus CT (71.0%). A change in surgical therapy was documented in 19 of 131 patients (14.5%) post Gd-EOB-DTPA-enhanced MRI. Gd-EOB-DTPA-enhanced MRI was superior in the diagnosis and therapeutic management of focal liver lesions compared with CT.

Keywords Magnetic resonance imaging · Computed tomography · Focal liver lesions · Liver-specific · Hepatobiliary · Gadoxetic acid-enhanced MRI · Therapeutic strategy

Introduction

The last 10 years have seen dramatic changes in the therapeutic approach of focal liver malignancies. This has been due to the increasing possibilities of surgical procedures, such as atypical liver resection and liver transplantation [1, 2] and the proliferation of new minimal invasive modalities including percutaneous ablative therapies. Imaging modalities, therefore, have to provide an exact diagnosis to enable optimal medical management for each patient.

Accurate identification of the number, size, location, and differential diagnosis of hepatic lesions is required for the final therapeutic decision. Contrast-enhanced ultrasound, computed tomography during arterial portography (CTAP), contrast-enhanced biphasic spiral computed tomography (CT), and magnetic resonance imaging (MRI), have been successfully used for the planning of a therapeutic strategy.

Contrast-enhanced ultrasound (US) [46, 48] improved the reliability of US in the assessment of liver tumors with a good conspicuity. CTAP is particularly effective for identifying small hepatic lesions [3, 4] with the drawback of a high rate of false-positive findings [5, 6]. Contrast-enhanced CT is a relatively non-invasive, widely available, and standardized method for the hepatic work-up [7–11]. Liver MRI is an upcoming alternative as a primary imaging technique due to the implementation of fast imaging

A. Blakeborough
Department of Radiology,
Royal Hallamshire Hospital,
Glossop Road,
Sheffield, S10 2JF, UK
e-mail: Tony.Blakeborough@csuh.nhs.uk

R. Carter
Bayer Health Care Ltd.,
The Brow, Burgess Hill,
West Sussex RH15 9NE, UK
e-mail: Rcarter@schering.co.uk

L. C. Fusté
Liver Unit, Department of
Internal Medicine,
Hospital Vall d`Hebròn,
Paseo Vall d`Hebròn, 119-129,
08035 Barcelona, Spain
e-mail: llcastells@vhebron.net

G. Heinz-Peer
Allg. Krankenhaus der Stadt Wien,
Universitätsklinik für Radiodiagnostik,
Waehringer Guertel 18-20,
1097 Wien, Germany
e-mail: Gertraud.Heinz-Peer@rad.akh.magwien.gv

W. Judmaier
Department of Magnetic Resonance
Imaging and Spectroscopy,
University Hospital Innsbruck,
Anichstr. 35,
6020 Innsbruck, Austria
e-mail: Werner.Judmaier@uibk.ac.at

M. Laniado
Institute for Diagnostic Radiology,
Universitätsklinikum Carl Gustav
Carus, Technische Universität Dresden,
Fetscherstr. 74,
01307 Dresden, Germany
e-mail: Michael.Laniado@mailbox.tu-dresden.de

R. M. Manfredi
Department of Radiology, Policlinico,
University of Verona,
P. le L.A. Scuro 10, 37134 Verona, Italy
e-mail: rmanfredi@univr.it

D. G. Mathieu
Centre d'Imagerie,
1 bd de la République,
13100 Aix en Provence, France
e-mail: profdm@wanadoo.fr

K. Mortelè
Department of Radiology (L1),
Brigham and Women's Hospital,
75 Francis Street,
Boston, MA 02115, USA
e-mail: kmortele@partners.org

D. Müller
Department of Radiology,
Georg-August Universität,
Robert-Koch-Str. 40,
37075 Göttingen, Germany
e-mail: dmuel@med.uni-goettingen.de

P. Reimer
Department of Radiology,
Klinikum Karlsruhe,
Moltkestr. 90,
76133 Karlsruhe, Germany
e-mail: Peter.Reimer@Klinikum-Karlsruhe.com

M. F. Reiser
Institute of Clinical Radiology,
Ludwig-Maximilians-University
Munich - Klinikum Grosshadern,
Marchioninistr. 15,
81377 Munich, Germany
e-mail: M.Reiser@med.uni-muenchen.de

P. J. Robinson
Department of Clinical Radiology,
St James's University Hospital,
Beckett Street,
Leeds LS9 7TF, UK
e-mail: PhilipJRobinson@compuserve.com

K. Shamsi
Corporate Clinical Operations,
Berlex Laboratories Inc.,
P.O. Box 1000,
340 Changebridge Road,
Montville, NJ 07045-1000, USA
e-mail: Kohkan_Shamsi@berlex.com

M. Strotzer
Department of Diagnostic Radiology,
University Hospital,
Franz-Josef-Strauss Allee 11,
93042 Regensburg, Germany
e-mail: Michael.Strotzer@klinik.uni-regensburg.de

M. Taupitz
Department of Radiology,
Universitätsklinikum Charitè,
Med. Fakultät der
Humboldt-Universität,
Schumannstr. 20-21,
10098 Berlin, Germany
e-mail: Matthias.Taupitz@charite.de

B. Tombach
Institute of Clinical Radiology,
Westfälische Wilhelms
Universität Münster,
Albert-Schweitzer-Str. 33,
48129 Münster, Germany
e-mail: Tombach@uni-muenster.de

G. Valeri
Department of Radiology,
University of Ancona,
Regional Hospital Torette,
Via Conca, Torette,
60020 Ancona, Italy
e-mail: g.valeri@ao-umbertoprimo.marche.it

B. E. van Beers
Department of Radiology,
Université Catholique de Louvain,
St-Luc University Hospital,
Avenue Hippocrate 10,
1200 Brussels, Belgium
e-mail: Vanbeers@rdgn.ucl.ac.be

T. J. Vogl
Institute of Diagnostic and
Interventional Radiology,
Johann Wolfgang Goethe-University,
ZRAD Haus 23 C, Theodor Stern Kai 7,
60590 Frankfurt am Main, Germany
e-mail: t.vogl@em.uni-frankfurt.de

techniques and the use of nonspecific, extracellular contrast agents [12, 13]. This technique has shown to be almost equal to CT regarding detection of lesions, but differential diagnosis of tumors is improved due to the ability of dynamic MRI studies [14, 45]. Liver-specific MRI contrast agents such as superparamagnetic iron oxide particles or hepatobiliary agents demonstrate an increased detection rate compared with CT [15–17, 44, 47]. The new liver-specific hepatobiliary contrast agent, gadoxetic acid, offers both the potential of dynamic as well as liver-specific static hepatocyte MRI with accurate delineation and classification as well as characterization of liver tumors [18, 19].

The purpose of this study was to compare hepatic lesion detection and differential diagnosis intraindividually using gadoxetic acid-enhanced MRI versus CT in patients with focal lesions proven by a standard of reference (SOR) and to identify changes in therapeutic management.

Materials and methods

The study was designed as a prospective, multicenter, open-label, within-patient comparison of the diagnostic performance of gadoxetic acid-enhanced MRI and CT in terms of detection and differential diagnosis of focal liver lesions with a corresponding blinded reading. The study was approved by a central ethics committee and the local ethics committee at each study center. All patients gave their written informed consent.

Patients with a age of at least 18 years, known or suspected focal liver lesions, who had been scheduled for CT, and liver surgery were included in the study. Exclusion criteria were previous injection of gadoxetic acid, any other investigational product (within 30 days prior to study entry), other contrast material within 24 h prior to or after administration of the study medication, and injection of any liver-specific agent within 2 weeks prior to the study. Also excluded were pregnant or lactating women, clinically unstable patients, patients scheduled for biopsy or liver surgery within 24 h post-administration of the study medication or patients with a known anaphylactoid or anaphylactic reaction to any other drug.

Patients

A total of 162 patients received gadoxetic acid, of which 31 were excluded from the efficacy analysis due to a missing valid SOR for the whole liver (26 patients) and major protocol deviations (five patients). Thus, the data from the remaining 131 patients (78 male, 53 female; with a mean age of 58 years, range 21—82 years, and a mean weight of 73 kg) were available for efficacy and included in the MRI evaluation. Due to a deviation from the study protocol, three patients had no valuable CT and therefore 128 patients were included in the CT evaluation.

Out of those patients valid for efficacy, two patients had no lesions according to the SOR. Accordingly the analysis regarding the sensitivity in lesion detection were based on 129 patients for MRI and 126 patients for CT.

The evaluation of false positive lesions, however, was performed on all patients included in the efficacy analysis.

Biphasic contrast-enhanced spiral CT

CT was acquired within 6 weeks before or after MRI and was performed during the arterial (25–35 s following contrast injection) and portal venous phase (45–70 s after contrast). A volume of 100–200 ml nonionic contrast material was administered via an antecubital vein with a flow velocity of 3–5 ml/s. The scans were obtained with 100–150 kV and 180–300 mAs using a slice thickness of 5–8 mm with a pitch of 1–2.

MRI

All centers had high-field-strength (1.0–1.5 Tesla) MRI systems and used a phased array surface coil covering the whole liver. Before contrast material administration, patients were imaged with a T2-weighted fast spin-echo (FSE)/ turbo spin-echo (TSE) sequence [≥3,000/90-120 (repetition time in ms/echo time in ms), matrix 192–256×256, slice thickness 5–8 mm, gap 0–2 mm], and a T1-weighted gradient recalled echo (GRE) sequence with chemically-selective fat suppression (FS) and without FS (100–200/ 4–8; flip angle, 70–80°) using a matrix of 160–192×256, slice thickness of 5–8 mm, gap 0–2 mm. Immediately after contrast material administration, dynamic imaging in the arterial, portal venous and equilibrium phase was performed using the T1-weighted GRE sequence without FS. Twenty minutes postinjection, the T1-weighted sequence with FS and the T2-weighted FSE/TSE sequence were repeated. For all sequences, field of view was adjusted as small as possible to include the abdomen only but not to exceed 400 mm.

Liver-specific MRI contrast agent

Gadoxetic acid (SH L 569 B, Gd-EOB-DTPA, Primovist), a liver-specific hepatocyte-directed MRI contrast agent, was obtained from Bayer Schering Pharma AG, Berlin, Germany [20, 21, 43]. All patients received 0.025 mmol/kg body weight (BW) dose of a 0.25 mol/l gadoxetic acid solution administered at a speed of about 2 ml/s through an IV line placed in the cubital vein and flushed with 30 ml of 0.9% saline.

Safety evaluation

Patients were observed for adverse events (AE) from the moment of inclusion in the study until 24 h after injection of the MRI contrast agent. All untoward medical occurrences, including local reactions at the injection site, were registered whether or not there was a potential relationship to the study medication. Vital signs (blood pressure, heart rate) were monitored at baseline, immediately before MRI, 5 min post injection, immediately after MRI, 2–4 h and 20–28 h post injection. Clinical laboratory tests (hematological, coagulation, clinical chemistry tests and urinalysis) were performed immediately before MRI, 2–4 h as well as 20–28 h post injection and evaluated for clinically significant changes.

Efficacy evaluation

The primary efficacy parameter, lesion detection included the number, size, and segmental localization of lesions in the liver. Gd-EOB-DTPA MRI, and CT were evaluated separately. In the overall evaluation, Gd-EOB-DTPA MRI was compared with CT.

As a secondary variable, the performance of Gd-EOB-DTPA MRI and CT in the differential diagnosis of focal liver lesions was evaluated. This diagnosis was based on the lesion morphology, enhancement pattern, evaluation of dynamic parameters and tumor-vascular differentiation of the individual lesion. Lesion classification aimed at differentiating between benign, malignant or not assessable lesions. Lesion characterization referred to the specific lesion type.

Image evaluation was performed as an on-site assessment by one clinical investigator in each center. Separately an off-site assessment by three experienced and independent abdominal radiologists (M.L., D.G.M., P.J.R.), who were not involved in the clinical investigation and fully blinded to all patient-related information, was obtained. The blinded reading was performed in a core lab for digital image management.

Standard of reference (SOR)

The SOR was defined as the combination of histopathology for the resected part of the liver and intraoperative (IO) US for the non-resected segments. Surgical specimens were clearly marked at their borders by the surgeon at the time of the operation to enable an overview of the anatomical details and segmental distribution for pathologic evaluation. The resected specimens were sectioned by the pathologist in the same orientation (axial) and in the same slice thickness as for MRI and CT (5–8 mm). In rare cases for which IOUS was not available for non-resected liver segments, an additional diagnostic procedure (CT, MRI, US) was carried out within the 3-month review period and was accepted as the SOR.

Correlation of Imaging with the SOR

The on-site investigators, the three blinded readers, the surgeons and the pathologists documented all lesions according to Couinaud's system of liver anatomy [22] by drawing liver maps. These maps consisted of eight transverse sections representing the cross-sectional anatomy of the entire liver. Each lesion was documented as accurately as possible according to size and segmental localization using one section of the liver map. For each individual lesion the imaging maps were compared with the map of the SOR by an independent radiologist to verify the same location of the lesion in all the modalities (i.e., lesion tracking).

Change in surgical therapy

The planned surgical procedure was given at three different timepoints by the clinical investigators: before the MR imaging procedure, before contrast application on the basis of the unenhanced MR images and the Gd-EOB-DTPA MRI. The potential planned procedures were liver transplantation, hemihepatectomy, segmentectomy and atypical segmentectomy. The planned therapy was compared with the surgical procedure finally performed.

Statistical analysis

The primary objective of the study was to calculate the sensitivity in lesion detection. Only lesions with the same location in the imaging procedure and the SOR were considered to be correctly detected. The alternative hypothesis tested in this study was that the sensitivity of a first (Gd-EOB-DTPA MRI) and a second test procedure (CT) positively differs verified by the SOR. The comparison of two test procedures, was then based upon differences between sensitivities of the two test procedures in the individual patient (paired differences). An adjusted χ^2 test, which takes into account the clustered nature of the data [23], i.e., multiple diagnostic observations within the same patient, was used for hypothesis testing at a 5% significant level for various comparisons.

The diagnostic efficacy in the blinded reading was assessed by the concept of an "average blinded reader" [24] using an adjusted χ^2 test for any testing of differences between the two image modalities. By this concept, the correlations between different readers in the same modality, the correlation between the same reader in different

Table 1 Sensitivity of lesion detection for Gd-EOB-DTPA MRI and spiral CT

Diagnostic procedure	Reader	n[a]	Sensitivity (%)	95% CI
Gd-EOB-DTPA MRI	**Average reader**	**129**	**72.74**	**67.57, 77.91**
	Reader 1	129	79.47	73.92, 85.02
	Reader 2	129	68.54	62.77, 74.31
	Reader 3	129	70.20	64.06, 76.34
Bi-phasic enhanced spiral CT	**Average reader**	**126**	**70.59**	**64.96, 76.23**
	Reader 1	126	76.09	70.37, 81.82
	Reader 2	126	70.71	64.25, 77.16
	Reader 3	126	64.98	58.71, 71.26

[a]Total number of patients with at least one SOR lesion

modalities and the correlation between different readers in different modalities were taken into account. In addition, the results of the single readers are displayed.

Since the majority of therapeutic options in the presence of focal liver lesions require information on a segmental level, an evaluation on this level was performed by assessing the involvement of liver segments by focal liver lesions. Sensitivity and specificity for "segment affected/not affected by lesion" were estimated in the common way:

$$\text{sensitivity} = \frac{\text{number of true positive segments}}{(\text{number of true positive segments} + \text{number of false negative segments})}$$

$$\text{specificity} = \frac{\text{number of true negative segments}}{(\text{number of true negative segments} + \text{number of false positive segments})}$$

As secondary efficacy variables, differential diagnosis of Gd-EOB-MRI and CT was evaluated and was compared with the SOR procedure in both the on-site and the off-site evaluation.

Results

Safety of Gd-EOB-DTPA

There were no clinically relevant changes in hemodynamic or laboratory parameters due to the contrast agent. No deaths or any AEs leading to the discontinuation of the study were reported. Of the 162 patients, who received the Gd-EOB-DTPA injection, a total of 11 (6.8%) patients reported a total of 21 AEs. These AEs were assessed as: one definitely related, five probably, seven possibly, one unlikely and seven not related to the study drug. The most frequently reported AEs of definite, possible or probable relationship to the contrast agent were nausea, vasodilatation, headache, taste perversion, and injection site pain (HARTS terms).

Table 2 Difference of sensitivity in lesion detection between Gd-EOB-DTPA MRI and CT

Reader	Procedure 1	Procedure 2	Difference[a] (%)	95% CI
Average reader	Gd-EOB-DTPA MRI	Spiral CT	2.36	−1.61, 6.33
Reader 1	Gd-EOB-DTPA MRI	Spiral CT	3.70	−0.97, 8.37
Reader 2	Gd-EOB-DTPA MRI	Spiral CT	−2.36	−8.06, 3.35
Reader 3	Gd-EOB-DTPA MRI	Spiral CT	5.72	−0.23, 11.68

[a]Difference in sensitivity between the two procedures (i.e., 1 minus 2)

Patients

In 131 patients a total of 302 lesions were verified by SOR. A histopathologic specimen was available in 112 patients. IOUS covering the nonresected liver segments was performed in 17 patients. In the remaining two patients for whom IOUS could not be applied to the whole liver, a follow-up examination was performed. SOR revealed 215 malignant, 80 benign lesions, and seven lesions were not to be classified. Histopathology revealed metastases (n=172), HCC (n=31) and CCC (n=12), as well as liver cysts (n=41), hemangiomas (n=18), FNH (n=7), and other

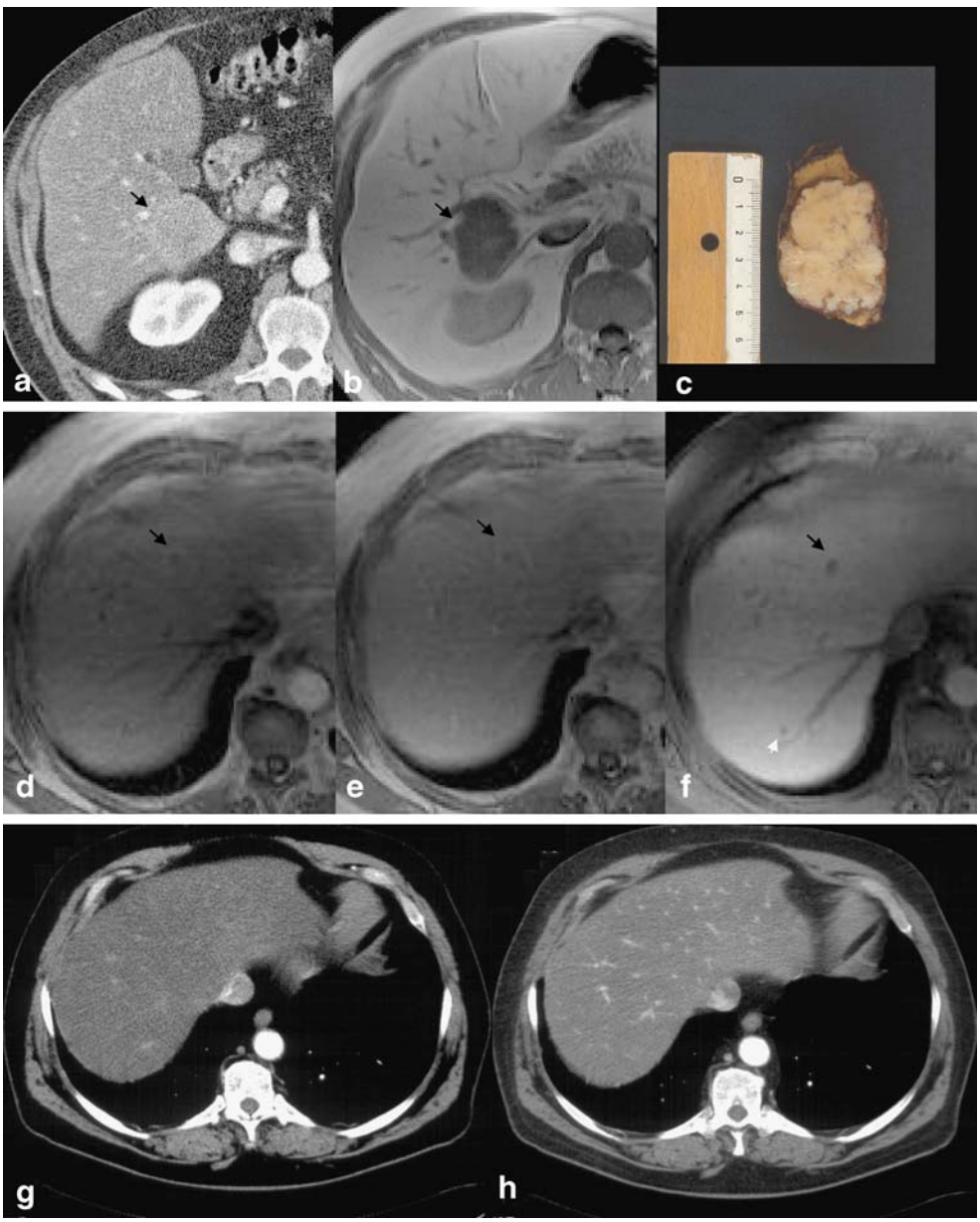

Fig. 1 Colorectal metastasis. A 63-year-old male patient with colon cancer in his medical history. One liver metastasis was known in the right lobe. Imaging procedure was to identify any additional lesions. Depiction of the known liver metastasis in the right liver lobe in venous phase imaging of spiral CT (**a**) and T1-weighted delayed liver imaging (Gd-EOB-DTPA MRI) (**b**) as well as liver specimen (**c**). Suspected tiny liver metastasis in the right liver lobe (segment 8/4A) using T1-weighted MR imaging in the arterial phase (**d**). Dynamic imaging revealed a rim enhancement as a sign of malignancy in the venous phase (**e**). Delayed liver-specific fat-saturated T1-weighted imaging (Gd-EOB-DTPA MRI) documented the lesion with an irregular margin and no uptake of contrast material (**f**). Tiny spot in the right liver lobe (*white arrow*) was depicted as a small vessel taking images cranial and caudal of the presented scan into consideration. CT in both arterial (**g**) and venous phases (**h**) showed no evidence of the lesion. The histopathologic evaluation revealed a metastasis in this location

Table 3 Analysis regarding lesion size in the blinded reading. Correctly matched lesions in the per-protocol set using Gd-EOB-DTPA MRI (n=302) and CT (n=297)

Examination	Number of lesions	Reader 1		Reader 2		Reader 3	
		<1 cm	≥1 cm	<1 cm	≥1 cm	<1 cm	≥1 cm
Gd-EOB-DTPA MRI	Matched	35	205	17	190	23	189
	Not matched	33	29	51	44	45	45
Spiral CT	Matched	25	201	20	190	15	178
	Not matched	42	29	47	40	52	52

benign lesions (adenomas, hydatid cysts, abscesses) (n=14).

Efficacy in the imaging evaluation

In the *analysis for correct lesion detection and localization* the clinical study revealed sensitivities of 77.1% [simultaneous 95% confidence interval (CI): 70.91, 83.3] for CT and 87.42% (simultaneous 95% CI: 83.17, 91.66) for Gd-EOB-DTPA MRI. The difference between CT and EOB-MRI was significant (10.44%; simultaneous 95% CI: 4.88, 16.0). In the blinded reading, more lesion were correctly detected by Gd-EOB-DTPA, however, the difference between Gd-EOB-DTPA MRI and CT did not reach statistical significance (Tables 1, 2).

When individual lesions were evaluated, for correct detection of lesions smaller than 1 cm, Gd-EOB-DTPA MRI (42/68 lesions) was clearly superior to CT (25/67 lesions) (Fig. 1). A greater number of small lesions were detected in Gd-EOB-DTPA MRI than in CT (Table 3).

The number of patients with false positive lesions was higher in Gd-EOB-DTPA MRI compared with CT in the clinical evaluation and in one blinded reader, whereas in the two other blinded readers Gd-EOB-DTPA MRI was more accurate (Table 4).

On the *segmental level*, a total of 1,029 (MRI) or 1,008 (CT) liver segments were evaluated by the SOR. Gd-EOB-DTPA MRI in the clinical study had superior sensitivity and specificity of 88.7% and 90.1%, respectively, when compared with CT, which had a a lower sensitivity of 80.7% and a specificity of 88.5%. The data of the blinded read showed comparable data (Table 5).

In the analysis regarding *differential diagnosis*, Gd-EOB-DTPA also improved the number of lesions that were correctly detected, localized and classified or characterized compared with CT with statistical significance (Fig. 2). These results were confirmed in the blinded reading (Table 6).

Change in surgical therapy

In 22 of the 131 patients (16.8%), the planning of the surgical procedure was changed following MRI.

In nine patients (6.8%), the change was performed in unenhanced MRI and in 13 additional patients in Gd-EOB-DTPA MRI. All changements in therapy planning documented in unenhanced MRI were confirmed by Gd-EOB-DTPA MRI.

In eight of the nine patients with changes at unenhanced MRI the surgical procedure was rarely modified in accordance with the MR imaging findings. In five patients, additional segments were resected and in three patients additional lesions excluding the possibility of resection were detected and no resection was performed. In one patient, revealing no possibilty for resection due to a larger extend of the lesions, the surgical procedure planned at baseline was nevertheless performed.

In 11 of 13 patients with changes in therapy post Gd-EOB-DTPA MRI, the surgical procedure was finally modified in accordance with the MR imaging findings. In seven patients, additional segments were resected and in four patients additional lesions excluding the possibility of resection were detected and no resection was performed.

In one patient with the diagnosis of additional lesions in Gd-EOB-DTPA MRI, no resection was performed due to lymph node metastases in the ligamentum hepatoduodenale. In one patient planned for segmentectomy of segments 7 and 8 with the additional finding of an FNH in segment 4b, the lesion was confirmed by IOUS and intraoperative biopsy, the segment was not resected and the surgical procedure therefore not modified in comparison to the planning at baseline.

Table 4 Comparison of clinical study and blinded reading regarding false positive lesions. Patients (per-protocol set) having MRI (n=131) and CT (n=128) with false-positive lesions

Examination	Clinical study	Reader 1	Reader 2	Reader 3
Gd-EOB-DTPA MRI	43 (32.8%)	64 (48.9%)	33 (25.2%)	45 (34.4%)
Spiral CT	38 (29.9%)	68 (53.1%)	41 (32%)	33 (25.8%)

Table 5 Segment-based analysis regarding involvement of liver segments by liver lesions in the blinded reading. Percentage of affected segments for Gd-EOB-DTPA MRI (n=1,029) and CT (n=1,008)

Examination		Reader 1	Reader 2	Reader 3
Gd-EOB-DTPA MRI	Sensitivity	79.94%	78.53%	68.93%
	Specificity	82.07%	86.37%	86.52%
Spiral CT	Sensitivity	83.05%	76.44%	57.47%
	Specificity	78.48%	83.33%	87.73%

Discussion

The optimum imaging strategy prior to any therapy should ideally provide diagnostic information with high sensitivity but also with a low false-positive rate. Lesion characterization is particularly important because of the high prevalence of benign liver lesions [25]. In our study, the new liver-specific contrast agent, gadoxetic acid, was compared with biphasic helical CT in the diagnosis of focal liver lesions for an effective therapeutic strategy.

Although much research has been conducted to assess the use of liver-specific MRI in the detection of focal liver lesions, to our knowledge few studies to date have assessed MRI performance with a large sample of patients with

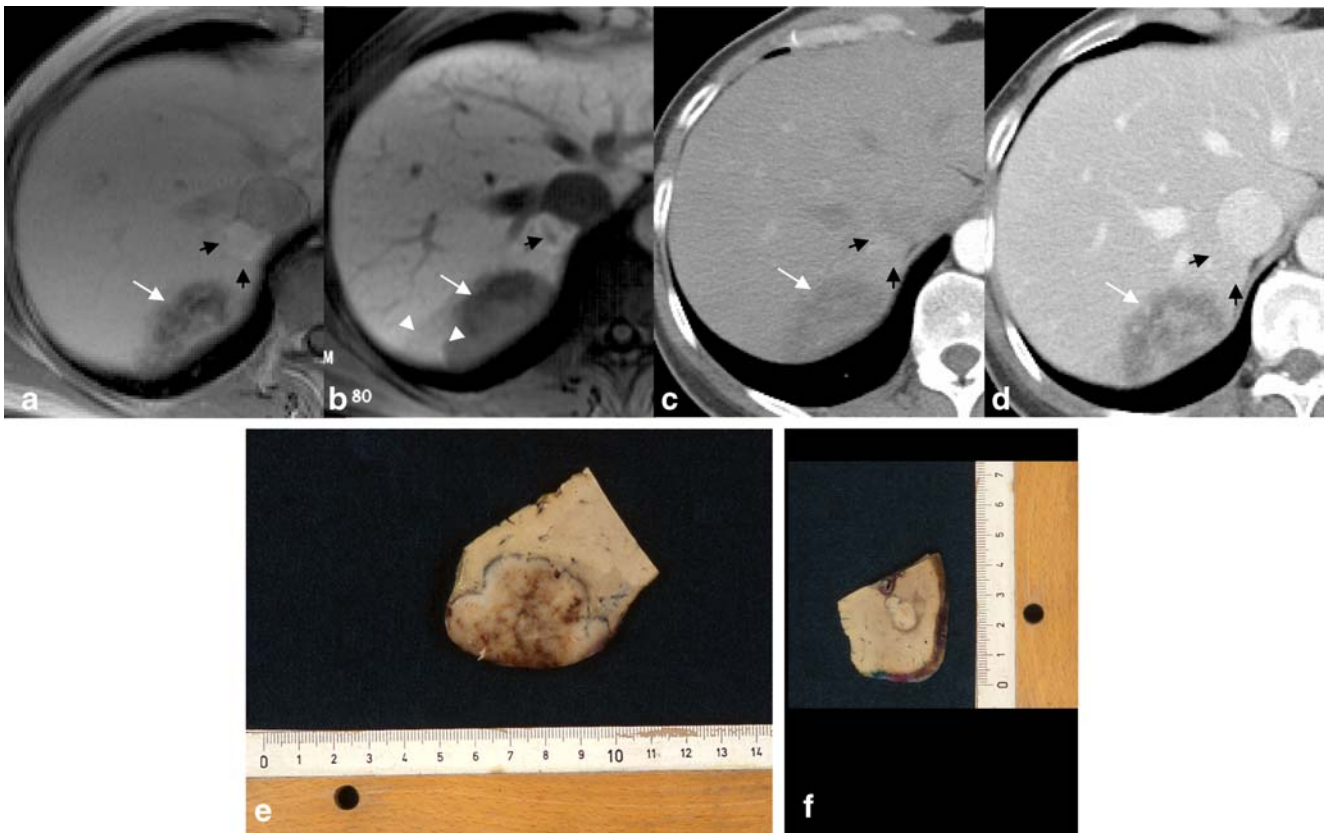

Fig. 2 Metastasis and FNH in the same patient. A female patient suffering from breast cancer, with suspected liver lesions in the right liver lobe. **a** Delineation of a lesion in the right liver lobe (segment 7) revealing irregular boundary and inhomogeneous enhancement suspicious for a malignant lesion using early phase of the dynamic GD-EOB-DTPA MRI protocol. Please note an additional smaller hypervascularized lesion (*black arrows*) with homogenous early uptake. **b** Using delayed GD-EOB-DTPA MRI (fat saturated T1-weighted sequence) no enhancement was documented in the large lesion as a sign of liver metastasis (*white arrow*). Vascular defect in terms of a triangular sign was clearly documented (*arrowheads*). A small lesion was visualized in addition to the one with uptake of the contrast material characteristic for a benign lesion; in this case a FNH (*black arrows*). The fat-suppressed protocol defined the inner scar of this tiny FNH better than the conventional protocol (**a**). CT depicted the large lesion (*white arrow*) with identical diagnostic information using arterial (**c**) and venous (**d**) phase-imaging. The tiny FNH (*black arrows*) and its inner structures were not so clearly visualized compared with liver-specific EOB-MRI. Specimen confirmed the diagnosis of metastasis (**e**) and FNH (**f**)

Table 6 Analysis on patient level regarding differential diagnosis: clinical study and blinded reading. Sensitivity for classification and characterization of matched lesions in the per protocol set

	Clinical study		Blinded reading					
			Reader 1		Reader 2		Reader 3	
	No. of patients with any difference	No. of patients with EOB-MRI>CT	No. of patients with any difference	No. of patients with EOB-MRI>CT	No. of patients with any difference	No. of patients with EOB-MRI>CT	No. of patients with any difference	No. of patients with EOB-MRI>CT
Classification		P=0.0058	42	27(64.8%), P=0.6033, n.s.	48	24(50%), P=0.7569, n.s.	73	54(74%), P=0.0003
Characterization		P=0.0241	48	26(54.2%), P=0.4230, n.s.	51	29(56.9%), P=0.6054, n.s.	62	48(77.4%), P=0.0006

histopathologically confirmed lesion diagnoses. Sensitivities and specificities are considered mainly on the basis of lesion counting without any SOR. Our study used a very rigorous analysis, including tracking and matching of detected lesions in each modality to verify each single lesion. The highest possible SOR—histopathology and/or IOUS—was obtained to prove the presence of each individual lesion and its localization. Consequently, the results with regard to sensitivities and specificities were expected to be numerically lower when compared with the published studies.

Our results for accuracy in diagnosis of biphasic helical CT are well comparable with published clinical studies with a large sample of patients (more than 50) [26, 27]. Kamel et al. [28] found sensitivities between 69 and 71%, and specificities between 86 and 91% in a blinded reading evaluation. Compared with our segment-based evaluation, they used a less accurate lesion tracking procedure based on the liver lobes. In a multicenter study using contrast-enhanced MRI, sensitivity values were documented to a percentage between 69.3% and 79.9% [15] in an off-site reading using a modified tracking procedure. The interpretation of these obvious differences in numerical values should take the strictly preselected patient population in our study into consideration. Patients were only included if already scheduled for surgery, revealing a reduced likelihood to detect additional lesions. Concerning the data of our study, the clinical results were numerically higher when compared with the blinded reader results. The main reason might be that the on-site investigators had knowledge of patient-related information.

In general, the number of false-positive lesions was relatively high for all modalities. One reason—a limitation of our study—is the availability of histopathology for lesion detection in only 205 of the 302 SOR proven lesions. Proof of remaining lesions results from IOUS, which was used as second best possible SOR when resected specimens were not available. However, in the literature the published rates for sensitivity of IOUS range from 80 to 98% [29–31]. Mainly subcapsular lesions and small cysts are often missed, which are excellently delineated using MRI. Nevertheless, the aim of our trial was to show the results for the entire liver of patients, as this is the only method to reflect the true disease status of a patient and not to encounter only malignant lesions. Our study results revealed a statistically significant increase in sensitivity for lesion detection in both the clinical evaluation and the blinded reading after Gd-EOB-DTPA. Even the standard of care—spiral CT—was worse compared with MRI by detecting more false positive lesions.

In the analysis for lesion delineation a high number of lesions smaller than 1 cm were additionally correctly detected and localized by Gd-EOB-DTPA MRI compared with CT in the clinical as well in the blinded read. This is relevant as the size of liver lesions is an important prognostic factor in malignant liver disease. In patients with metastatic colorectal cancer, IOUS documented only 50% of all liver metastases smaller than 1 cm [35].

With the introduction of multidetector-row CT, increased detection rates—especially of small lesions—have been reported in the literature using thinner sections for scanning [32], although an overall effective slice thickness of 5 mm—as used in our CT series—offered to be the best compromise for diagnostic imaging of focal liver lesions with additional information due to thinner sections in special cases [33, 34].

Furthermore, classification and characterization of Gd-EOB-DTPA MRI versus CT was evaluated. A superiority of Gd-EOB-DTPA MRI was observed in the on-site and off-site readings, and was rated as statistically significant in the clinical study compared with CT. The diagnostic capability to differentiate between malignant and benign lesions was improved using Gd-EOB-DTPA MRI compared with CT.

Dynamic imaging represents an obligatory tool for the characterization of focal liver lesions in MRI [36, 37]. Gd-EOB-DTPA is a hepatocyte-specific contrast agent, which has the transient, less intense blood pool properties of an extracellular contrast agent using early scanning and dynamic features [38, 39] for differential diagnosis of liver tumors. As a second effect it has the prolonged T1-shortening effect on liver parenchyma as well as hepatocyte-selective enhancement of liver tumors [40–42]. To prove the effectiveness of this new liver-specific compound for differential diagnosis of liver tumors in a more general

population as well in underlying severe liver cirrhosis, additional studies will have to be performed with a special focus on histopathological correlation.

In this highly preselected collective, a change in surgical therapy was documented in 14.5% of the patients, which is an important finding and can be considered as an increase in the accuracy of a preoperative planning of liver resection. One limitation of our data is that the information about the surgical procedure was given by the radiologist and not by the surgeon, but all the investigators taking part in this study were highly experienced abdominal radiologists with close relation to their respective surgical departments.

In conclusion, the results of the present study indicate that MRI using the new liver-specific hepatobiliary compound, gadoxetic acid, is safe. The detection rate is comparable with CT, with a higher rate of detected small lesions and a distinctly lower rate of false positive results. Additional information for differential diagnosis is achieved using gadoxetic acid-enhanced perfusion and hepatocyte-specific MR-imaging for the characterization of malignant versus benign liver lesions and classification according to lesion type. Gadoxetic acid-enhanced MRI is superior to CT in the overall analysis for the therapeutic approach in liver-imaging regarding lesion detection, localization, delineation, differential diagnosis, and management of patients.

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