Usefulness of breath-hold inversion recovery-prepared T1-weighted two-dimensional gradient echo sequence for detection of hepatocellular carcinoma in Gd-EOB-DTPA-enhanced MR imaging

Author(s)
Ohno, Tsuyoshi

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Usefulness of breath-hold inversion recovery-prepared T1-weighted two-dimensional gradient echo sequence for detection of hepatocellular carcinoma in Gd-EOB-DTPA-enhanced MR imaging

Tsuyoshi Ohno *, Hiroyoshi Isoda, Akihiro Furuta, Shigeki Arizono, Rikiya Yamashita, Ayako ono, Kaori Togashi

Department of Diagnostic Imaging and Nuclear Medicine, Kyoto University Graduate School of Medicine, 54 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan

**Abstract**

The aim is to evaluate the diagnostic performance and the added value of breath-hold inversion recovery-prepared T1-weighted two-dimensional gradient echo (IR-2D-GRE) sequence for detection of hepatocellular carcinoma (HCC) in patients with insufficient liver parenchymal enhancement during the hepatobiliary phase (HBP) of Gd-EOB-DTPA-enhanced magnetic resonance imaging (MRI). Seventeen patients with a quantitative liver-to-spleen contrast ratio of \( \leq 1.5 \) on HBP images and 36 HCCs were included. Liver-to-lesion contrast ratios on HBP images obtained with IR-2D-GRE sequence were significantly higher than those with three-dimensional gradient echo sequence. The addition of IR-2D-GRE sequence during HBP of Gd-EOB-DTPA-enhanced MRI yielded higher diagnostic accuracy and improved sensitivity.

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1. Introduction

Gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) (Bayer Schering Pharma AG, Berlin, Germany) has been widely used as a hepatocyte-specific magnetic resonance (MR) contrast agent that offers both dynamic imaging and static liver-specific imaging (i.e., hepatobiliary phase, HBP) with accurate delineation, classification, and characterization [1,2]. The addition of HBP images has improved the per-lesion sensitivity for the diagnosis of hepatocellular carcinoma (HCC) [3,4]. HBP images are also useful for distinguishing HCCs from arterioporal shunts when the hypervascular pseudolesions are round or oval and difficult to be differentiated from HCCs [5]. Accurate identification of the number, size, location, and differential diagnosis of hepatic lesions is clinically important to guide the therapeutic decision [2,6,7]. Sufficient enhancement of the liver parenchyma in HBP is required to obtain enough liver-to-lesion contrast ratios and accurately detect lesions. However, accurate diagnosis of hepatic lesions is occasionally challenging, particularly, in patients with hepatic damage because of decreased or heterogeneous enhancement of the liver parenchyma [8–10].

Some methods were reported to improve liver-to-lesion contrast ratios on HBP images. One was using inversion recovery-prepared gradient echo (IR-GRE) sequence [11]. HBP images obtained with IR-GRE sequence are expected to improve the detection of hepatic lesions in patients with insufficient liver parenchymal enhancement. To the best of our knowledge, there has been no report on the usefulness of IR-GRE sequence during Gd-EOB-DTPA-enhanced magnetic resonance imaging (MRI) for the detection of HCC in patients with insufficient liver parenchymal enhancement. The aim of this study was to evaluate the diagnostic performance and the added value of breath-hold (BH) inversion recovery-prepared T1-weighted two-dimensional gradient echo (IR-2D-GRE) sequence during HBP of Gd-EOB-DTPA-enhanced MRI for such purpose.

2. Materials and methods

2.1. Patients

This retrospective study was performed in accordance with the Declaration of Helsinki. Local ethics committee approval was granted, and written informed consent was waived. From January 2013 to March 2015, 191 patients suspected as suffering from liver cirrhosis underwent Gd-EOB-DTPA-enhanced MRI at 3 T using both T1-weighted three-dimensional gradient echo (3D-GRE) and IR-2D-GRE sequences in HBP for evaluation of HCC at our institution. The suspicion of suffering from liver cirrhosis was based on morphological changes on MRI and on blood test data (i.e., aspartate aminotransferase-to-platelet ratio index).

Among these patients, 174 were excluded because of the following criteria: duplicate MRI examinations in the same patient (n = 40); quantitative liver-to-spleen contrast ratio of > 1.5 (sufficient liver...
parenchymal enhancement) during HBP imaging with 3D-GRE sequence (n = 117); patients with portal venous tumor thrombus (n = 2); patients with no HCC or those with more than 10 lesions (n = 14); and unknown final diagnosis because of loss of follow-up (n = 1). The medical and imaging records of the remaining patients were retrospectively reviewed. Viable liver lesions that were treated before with local treatment, like transarterial chemoembolization and radiofrequency ablation, were carefully excluded.

A total of 17 patients, including 11 men and 6 women, aged 57–80 years (mean, 70.4 years), were included in the study. The analysis included 36 liver nodules measuring 5–24 mm in diameter (mean, 13 mm) (Fig. 1). Of 17 patients, 6 had solitary lesion, 6 had two lesions, and 1 had six lesions. All patients had chronic liver disease caused by alcohol abuse (n = 5), viral hepatitis type B (n = 1), and viral hepatitis type C (n = 11). The follow-up interval was 4–28 months (mean, 17.8 months).

2.2. Standard of reference

The presence or absence of HCC was decided by consensus of two radiologists, with 25 and 9 years of experience in abdominal imaging, respectively, and who did not perform the image analysis.

The diagnosis of HCC was based on histopathological confirmation following surgical resection (n = 7) or biopsy (n = 1) or on characteristic contrast-enhanced multiphase multidetector computed tomography (MDCT) and/or MRI findings, based on the recommendations of the American Association for the Study of Liver Disease, and/or elevated tumor markers (e.g., α-fetoprotein and protein induced by vitamin K absence II) and follow-up image studies (n = 28) (Table 1).

2.3. MRI technique

All MRI examinations were performed at 3 T using a commercially available MR system (Magnetom Skyra; Siemens Medical Solutions, Erlangen, Germany). MR images on BH T1-weighted image (T1WI) gradient echo sequence with dual echo of in-phases and opposed-phases were acquired before administration of Gd-EOB-DTPA. Dynamic T1-weighted 3D-GRE images in the axial plane were obtained using volumetric interpolated BH examination sequence with chemically selective fat saturation. HBP images in the axial plane were obtained using T1-weighted 3D-GRE sequence with chemically selective fat saturation and BH IR-2D-GRE sequence. Images from the initial T1-weighted 3D-GRE sequence were acquired before administration of contrast agent.

A bolus of Gd-EOB-DTPA (Bayer Schering Pharma AG, Berlin, Germany) at 25 μmol/kg body weight was administered at a rate of 2 ml/s using a power injector (Sonic Shot, Nemoto Kyorindo, Tokyo, Japan) through the antecubital vein, followed by flushing with 20 ml of sterile saline. After a bolus injection of Gd-EOB-DTPA with fixed delay, the following three dynamic phases were acquired: arterial (delay time 25 s), portal venous (65 s), and late (110 s) phases. Then, HBP images were obtained with 3D-GRE and IR-2D-GRE sequences after 20–25 min of contrast agent injection. For IR-2D-GRE sequence, three different inversion times (TIs) were adopted (500 ms, 700 ms, and 900 ms) and acquisition time for each IR-2D-GRE sequence was 17–21 s. Between the dynamic phase and HBP, two imaging data were acquired with respiration triggering using prospective acquisition correction method: fat-saturated T2-weighted (T2WI) MRI turbo spin-echo sequence and diffusion-weighted image (DWI) using a single-shot spin-echo planar imaging sequence in the axial plane. The imaging parameters are summarized in Table 2.

Fig. 1. Flowchart of patient enrollment. 3D-GRE: three-dimensional gradient echo; IR-2D-GRE: inversion recovery-prepared T1-weighted 2D gradient echo; Q-LSC: quantitative liver-to-spleen contrast ratio.
of the liver [9]. In patients whose anterior lobe was resected, ROIs were placed on the middle of the spleen and on the other remaining lobe of the liver in the same axial image. ROIs were drawn three times on each position and the mean SI values were adopted. ROIs in the liver and spleen parenchyma were at least 20 mm² and located on a homogenous portion devoid of vessels and prominent artifacts. The quantitative liver-to-spleen contrast ratio on HBP images with 3D-GRE sequence was calculated by the formula, quantitative liver-to-spleen contrast ratio = \( S_I_{\text{liver}} / S_I_{\text{spleen}} \). For quantitative analysis, the liver-to-lesion contrast ratios on HBP images from the 3D-GRE and IR-2D-GRE sequences were calculated. ROIs were drawn three times on each position and the mean SI values were adopted. ROIs in the liver parenchyma were at least 20 mm² and located on a homogenous portion of the liver devoid of vessels and prominent artifacts. ROIs in the lesions were at least 10 mm² and located throughout the lesions. Because the standard deviation (SD) of the background noise could not be used to calculate the image contrast-to-noise ratio due to using the parallel imaging technique, we calculated SD of signal values in the ROIs in the liver parenchyma and in the lesions as noise [15]. The liver-to-lesion contrast ratio was calculated with the formula,

\[
liver-to-lesion\ contrast\ ratio = \frac{S_I_{\text{liver}} - S_I_{\text{lesion}}}{\sqrt{SD\ liver^2 + SD\ lesion^2}}
\]

### 2.4. Imaging analysis

Three image sets were created, namely, set A (precontrast T1WI, fat-saturated T2WI, DWI, Gd-EOB-DTPA-enhanced dynamic study, and 3D-GRE sequence HBP images), set B (precontrast T1WI, fat-saturated T2WI, DWI, Gd-EOB-DTPA-enhanced dynamic study, and IR-2D-GRE sequence HBP images), and set C (precontrast T1WI, fat-saturated T2WI, DWI, Gd-EOB-DTPA-enhanced dynamic study, and both 3D-GRE and IR-2D-GRE sequence HBP images).

Two radiologists, both with 13 years of experience in abdominal imaging, independently and randomly reviewed the three sets of MRIs. These two observers were not the same radiologists who determined the presence or absence of HCC on the basis of radiological and pathological findings. They knew that the patients were at risk for HCC, but they were blinded to all other information, including the number, size, and location of the lesions. To minimize any learning bias, we scheduled a 4-week interval between the first and second interpretation sessions and a 6-week interval between the second and third interpretation sessions. Each observer recorded the presence of and segmental location of lesions and assigned a possibility of HCC for each lesion using the following five-point confidence rating scale: 1 = definitely not HCC; 2 = probably not HCC; 3 = equivocal; 4 = probably HCC; and 5 = definitely HCC. Sensitivity calculations were based on those lesions that were graded a confidence rating of 4 or 5. The observers subjectively diagnosed HCC referenced on following criteria [5,12–14]. Lesions graded a confidence rating of 5 showed hyperenhancement in the arterial phase and washout in the late phase and low intensity in HBP. Lesions graded a confidence rating of 4 showed (a) hyperenhancement in the arterial phase and no washout in the late phase, as well as low intensity in HBP; (b) no hyperenhancement in the arterial phase and washout in the late phase, as well as low intensity in HBP with one or more ancillary features favoring an HCC diagnosis (high intensity on T2WI, high intensity on high-b DWI, intratumoral fat, capsular enhancement on portal venous phase or late phase images); and (c) hyperenhancement in the arterial phase and iso-to-high intensity in the late phase, as well as high intensity in HBP with one or more ancillary features. The observers carefully distinguished arterioperitonal shunts from HCCs considering the presence or absence of ancillary imaging features that prefer HCCs and the signal intensity (SI) on HBP images that were useful for distinguishing HCCs from hypervascular pseudolesions [5]. A third radiologist, with 9 years of experience in abdominal imaging, correlated the scored lesions with the reference standards on lesion size and location.

For the quantitative liver-to-spleen contrast ratio on HBP images with 3D-GRE sequence, the largest possible regions of interest (ROIs) in the same axial image were manually drawn by one radiologist on the middle of the spleen and almost on the center of the anterior lobe of the liver [9]. In patients whose anterior lobe was resected, ROIs were placed on the middle of the spleen and on the other remaining lobe of the liver in the same axial image. ROIs were drawn three times on each position and the mean SI values were adopted. ROIs in the liver and spleen parenchyma were at least 20 mm² and located on a homogenous portion devoid of vessels and prominent artifacts. The quantitative liver-to-spleen contrast ratio on HBP images with 3D-GRE sequence was calculated by the formula, quantitative liver-to-spleen contrast ratio = \( S_I_{\text{liver}} / S_I_{\text{spleen}} \). For quantitative analysis, the liver-to-lesion contrast ratios on HBP images from the 3D-GRE and IR-2D-GRE sequences were calculated. ROIs were drawn three times on each position and the mean SI values were adopted. ROIs in the liver parenchyma were at least 20 mm² and located on a homogenous portion of the liver devoid of vessels and prominent artifacts. ROIs in the lesions were at least 10 mm² and located throughout the lesions. Because the standard deviation (SD) of the background noise could not be used to calculate the image contrast-to-noise ratio due to using the parallel imaging technique, we calculated SD of signal values in the ROIs in the liver parenchyma and in the lesions as noise [15]. The liver-to-lesion contrast ratio was calculated with the formula,

\[
liver-to-lesion\ contrast\ ratio = \frac{S_I_{\text{liver}} - S_I_{\text{lesion}}}{\sqrt{SD\ liver^2 + SD\ lesion^2}}
\]

### 2.5. Statistical analysis

Jackknife alternative free-response receiver operating characteristics (JAFROC) curves for each observer and each image set were calculated using Jackknife FROC software (JAFROC, version 4.1; http://www.devchakraborty.com). The diagnostic accuracy of each imaging set and observer was determined by figure of merit (FOM), defined as the probability that a true-positive lesion was rated higher than the highest-rated false-positive lesion on normal images [16].

The interobserver agreement for the evaluation of the three imaging sets was analyzed with the kappa statistic. The agreement in terms of kappa values was as follows: <0.20 = poor; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.80 = good; and 0.81–1.0 = excellent. The sensitivity and positive predictive value (PPV) for each image set were then calculated. The sensitivity values of the three sets were compared using McNemar’s test. The liver-to-lesion contrast ratio of each sequence was compared using Wilcoxon signed-rank test.

Statistical analyses of the kappa statistic, McNemar’s test, and Wilcoxon signed-rank test were performed using the MedCalc Statistical Software (version 12.4.0.0, MedCalc Software, Ostend, Belgium). For all analyses, \( P < .05 \) was considered to be statistically significant. For multiple comparisons, Bonferroni correction was applied to assess
possible significance, with \( P < .025 \) (0.05/2) and \( < .008 \) (0.05/6) indicating a significant difference.

3. Results

The JAFROC FOM observer-averaged values of image sets B and C had a tendency to be better than that of image set A for the detection of HCC, though there was no significant difference (Table 3).

The sensitivity and PPV for the detection of lesions for each observer and image set are summarized in Table 4. The sensitivity of image sets B and C were higher than that of set A for each observer; the difference between sets A and C was significant. Interobserver agreement was moderate to good (0.417–0.628). The number of false-positive lesions in image sets B and C was equal or increased by only one from that in image set A for each observer. The PPV of image set C was slightly decreased from that of image set A.

Among the 36 lesions, both observers failed to detect 2 lesions on HBP images with 3D-GRE sequence that were clearly visualized on HBP images with IR-2D-GRE sequence (Fig. 2). There were 8 other true lesions that either of the two observers found on HBP images with IR-2D-GRE sequence (Fig. 3). Conversely, there were 3 HCCs that were better visualized on HBP images with 3D-GRE sequence than on HBP images with IR-2D-GRE sequence for the two observers. These lesions were small hepatic HCCs. With combined 3D-GRE/IR-2D-GRE sequence, 5 other true lesions were detected by both or either of the two observers.

The mean liver-to-lesion contrast ratios on HBP images obtained with IR-2D-GRE sequence at varying TIs were significantly higher than those obtained with 3D-GRE sequence. There was no significant difference among mean liver-to-lesion contrast ratios obtained with IR-2D-GRE sequence at varying TIs. These results are summarized in Fig. 4.

4. Discussion

For detecting hepatic lesions, Gd-EOB-DTPA-enhanced MRI has higher sensitivity and specificity than dynamic CT and MRI with conventional extracellular contrast agents [2,6,17]. In patients with chronic liver damage, adding HBP images to dynamic images enabled subtle abnormalities depicted at other sequences to be better appreciated and improved the diagnosis of HCC [3,4]. Another reported benefit of HBP images was differentiation of hypervascular HCCs from hypervascular pseudolesions, such as focal alterations in perfusion due to arterioporal shunts [18]. However, because the uptake of Gd-EOB-DTPA into hepatocytes is thought to be related to hepatocyte function, detection of hepatic lesions is occasionally difficult because of poor liver-to-lesion contrast ratio. Asbach et al. reported that respiratory-triggered inversion recovery-prepared 3D-GRE (IR-3D-GRE) images improved liver-to-lesion contrast ratios in HBP compared with those with usual BH 3D-GRE images [11]. We hypothesized that HBP images acquired with IR-GRE sequence would improve T1 contrast and yield better liver-to-lesion contrast ratios, hence better diagnostic performance for detection of HCC in patients with insufficient liver parenchymal enhancement. To the best of our knowledge, this was the first study that assessed the usefulness of such imaging technique.

In the current study, each mean liver-to-lesion contrast ratio acquired with IR-2D-GRE of three different TIs was significantly higher than those acquired with 3D-GRE sequence in patients with insufficient liver parenchymal enhancement. This may be due to inversion recovery preparation, which may have improved T1-weighted sequence contrast. In addition, by waiting to examine the signal amplitude from two different tissues until one of the decay curves was nearly zero, the percentage difference between the two signals will be very large [21].

In visual assessment, image set B showed a tendency of better diagnostic performance and increased number of detected HCCs than image set A, although image set B had a disadvantage of larger slice thickness of HBP. These results may have resulted because improvement of liver-to-lesion contrast ratios had a greater influence than high spatial resolution on HCC detection in patients with insufficient liver parenchymal enhancement during HBP. Improved liver-to-lesion contrast ratios by IR-GRE sequence may have enabled detection of HCCs that were obscure on the usual 3D-GRE sequence HBP images. Tran et al. reported that liver-to-lesion contrast ratio on HBP images was improved using respiratory-triggered IR-3D-GRE sequence compared with that using the usual BH 3D-GRE sequence, but they concluded that BH 3D-GRE sequence detected larger number of hepatic lesions [22]. In contrast, our study showed the advantage and utility of IR-GRE sequence for detection of HCCs. This difference may be due to differences in study population; there may have been patients in our study who had insufficient liver parenchymal enhancement, although this was not stated. Conversely, there were some HCCs detected on usual 3D-GRE sequence HBP images that were difficult to detect on IR-2D-GRE sequence. This may have resulted from the higher spatial resolution of 3D-GRE sequence. Small HCCs may be difficult to detect by IR-2D-GRE sequence alone.

In this study, we also assessed the additional benefit of IR-2D-GRE. We found that there was significantly higher sensitivity for combined 3D-GRE/IR-2D-GRE than for 3D-GRE alone. Both observers detected significantly more HCCs on combined 3D-GRE/IR-2D-GRE sequence than those on the 3D-GRE sequence. Due to improved liver-to-lesion contrast ratios, one or the other of the two observers could detect 10 lesions on IR-2D-GRE sequence HBP images that were not visualized on usual 3D-GRE sequence. Three lesions were better visualized on 3D-GRE sequence.

Table 4

Table 4 Sensitivity and PPV of each set in detection of 36 HCCs

<table>
<thead>
<tr>
<th>Imaging sets</th>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Kappa value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set A</td>
<td>47.2 (17)</td>
<td>44.4 (16)</td>
<td>0.436</td>
</tr>
<tr>
<td>Set B</td>
<td>61.1 (22)</td>
<td>55.6 (20)</td>
<td>0.417</td>
</tr>
<tr>
<td>Set C</td>
<td>72.2 (26)</td>
<td>66.7 (24)</td>
<td>0.628</td>
</tr>
<tr>
<td>PPV (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set A</td>
<td>94.4 (1)</td>
<td>94.1 (1)</td>
<td></td>
</tr>
<tr>
<td>Set B</td>
<td>91.7 (2)</td>
<td>95.2 (1)</td>
<td></td>
</tr>
<tr>
<td>Set C</td>
<td>92.9 (2)</td>
<td>92.3 (2)</td>
<td></td>
</tr>
</tbody>
</table>

a Numbers in parentheses represent the number of true-positive lesions.

b \( P \) values are the difference between sets A and B and sets A and C, respectively.

Bonferroni correction was applied and \( P < .025 \) (0.05/2) indicated a significant difference.

cMcNemar’s test revealed a significant difference between sets A and C.

A quantitative liver-to-spleen contrast ratio score of \( \geq 1.5 \) may render the detection of HCCs difficult because of poor liver-to-lesion contrast ratio. Asbach et al. reported that respiratory-triggered inversion recovery-prepared 3D-GRE (IR-3D-GRE) images improved liver-to-lesion contrast ratios in HBP compared with those with usual BH 3D-GRE images [11]. We hypothesized that HBP images acquired with IR-GRE sequence would improve T1 contrast and yield better liver-to-lesion contrast ratios, hence better diagnostic performance for detection of HCC in patients with insufficient liver parenchymal enhancement. To the best of our knowledge, this was the first study that assessed the usefulness of such imaging technique.

Table 3

Table 3 Diagnostic performance presented as FOM for detection of HCC

<table>
<thead>
<tr>
<th></th>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>JAFROC FOM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Set A</td>
<td>0.715</td>
<td>0.703</td>
<td>0.709</td>
</tr>
<tr>
<td>Set B</td>
<td>0.766</td>
<td>0.760</td>
<td>0.763</td>
</tr>
<tr>
<td>Set C</td>
<td>0.801</td>
<td>0.758</td>
<td>0.779</td>
</tr>
<tr>
<td>PPV</td>
<td>0.0273/0.0461</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The differences between sets A and B and between sets A and C were not significant.

a \( P \) values were the difference between sets A and B and between sets A and C, respectively. Bonferroni correction was applied and \( P < .025 \) (0.05/2) indicated a significant difference.

b \( P \) values are the difference between sets A and B and sets A and C, respectively.

Bonferroni correction was applied and \( P < .025 \) (0.05/2) indicated a significant difference.

cMcNemar’s test revealed a significant difference between sets A and C.
sequence HBP images than on IR-2D-GRE sequence. IR-2D-GRE sequence HBP images made it difficult to detect the signal from small lesions. Therefore, combined use of IR-2D-GRE sequence HBP images with 3D-GRE sequence HBP images provided higher sensitivity than 3D-GRE sequence HBP images alone for the detection of HCCs. Regarding PPV, we did not find a specific tendency.

Ahn et al. reported that mean sensitivities of Gd-EOB-DTPA-enhanced MRI for diagnosis of HCC were in the range 80–90% regardless of the sequence used.

Fig. 2. Histopathologically proven well differentiated HCC in a 61-year-old woman with hepatitis C cirrhosis (Child–Pugh A). (a) Arterial phase of EOB-DTPA-enhanced MRI shows a hypervascular mass (arrow) with delayed washout (not shown). (b) In HBP, the mass is unclear because of poor liver-to-lesion contrast on an image acquired with usual 3D-GRE sequence. However, on images acquired with IR-2D-GRE sequence of TI=500 ms (c), 700 ms (d), and 900 ms (e), the mass is more clearly visible as hypointense lesion (arrows). In this case, the lesion is most clearly visible on an image of TI=500 ms. Both observers failed to detect this lesion in set A (HBP images with 3D-GRE sequence) but could detected in sets B (HBP images with IR-2D-GRE sequence) and C (HBP images with both 3D-GRE and IR-2D-GRE sequence).

Fig. 3. HCC diagnosed based on characteristic imaging findings on contrast-enhanced multiphase MDCT and MRI and follow-up image studies in a 78-year-old man with clinically alcoholic liver cirrhosis (Child–Pugh B). (a) Arterial phase of EOB-DTPA-enhanced MRI shows a hypervascular mass (arrow). (b) In HBP, the mass is unclear because of poor liver-to-lesion contrast on an image acquired with usual 3D-GRE sequence. (c) On an image acquired with IR-2D-GRE sequence (TI=500 ms), the mass is visible as hypointense lesion (arrow). In this case, the lesion is most clearly visible on an image of TI=500 ms. The liver-to-lesion contrast ratios on HBP images using 3D-GRE and IR-2D-GRE sequence are 1.24 and 4.28, respectively.
of the presence or absence of HBP images [3]. Sensitivities in this study were much lower than the previous report. This difference may be due to differences in study population. Ahn et al. included HCCs that ranged from 0.4 to 11 cm (mean, 2.8 cm) in diameter. However, in our study, the diameters of HCCs were ranged from 0.5 to 2.4 cm (mean, 1.3 cm) that were much smaller than the previous report. In addition, there may have been few patients in their study who had insufficient liver parenchymal enhancement on HBP images, although this was not stated. These factors may have affected on the lower sensitivities in our study.

In our study, inversion recovery recovery pulses of TI = 500 ms, 700 ms, and 900 ms were used. It is difficult to estimate the optimal TI before MR examination because T1 values of liver parenchyma with chronic liver damage varied according to the degree of hepatic function, fibrosis, and fat or iron deposition [23]. T1 values of HCC may also vary depending on the degree of degeneration, hemorrhage, and uptake of Gd-EOB-DTPA. In respiratory-triggered sequence, prolonged time is required to obtain HBP images with multiple TIs. On the other hand, with BH IR-GRE sequence, acquisition of HBP images with different TIs is possible within a few minutes, making this seemingly acceptable for clinical use. Whether HBP images of all three different TIs would be needed was controversial. However, they may all be useful based on our results of significant differences in mean liver-to-lesion contrast ratio between 3D-GRE sequence images and each IR-2D-GRE sequence images at different TIs. A number of different and suitable TIs needed should be examined in the future studies.

Our study has several limitations. First, this was a retrospective study with a small sample size; therefore, the data may have been influenced by selection and verification biases. Because this was a pilot study, further prospective studies with larger sample sizes are needed. Second, not all HCCs were histopathologically diagnosed. However, two experienced abdominal radiologists carefully read and reviewed all clinical information and follow-up study. Moreover, we were sure that widely accepted and image-based diagnoses with clinical follow-up evaluations were adequate for the diagnosis of hypervascular HCC. Third, patients with Child–Pugh class C were not enrolled in our study because they are usually not candidates for therapeutic intervention and have less opportunity to undergo Gd-EOB-DTPA-enhanced MRI than patients in the other two classes. Fourth, we did not compare HBP images obtained with IR-2D-GRE sequence with those obtained by 3D-GRE sequence of higher flip angle (FA). Haradome et al. reported that increasing FA during the hepatocyte phase of EOB-enhanced MRI increased liver-to-lesion contrast ratio and improved the detection of focal liver lesions [24]. However, the main purpose of this study was to evaluate the usefulness of IR-2D-GRE HBP images. Further study is needed to compare HCC detection by the “IR method” with that of “high FA method”.

In conclusion, the addition of IR-2D-GRE sequence during HBP of Gd-EOB-DTPA-enhanced MRI yielded higher diagnostic accuracy and improved liver-to-lesion contrast ratio than using conventional MRI obtained with 3D-GRE sequence in diagnosis of HCCs in patients with insufficient liver parenchymal enhancement.

References

lar carcinoma in gadoxetic acid-enhanced MRI and diffusion-weighted MRI with
resolution T1-weighted MR imaging of liver and biliary tract during uptake phase
[13] Willatt JM, Hussain HK, Adusumilli S, Marrero JA. MR Imaging of hepatocellular carcino-
signal intensity at gadoxetic acid-enhanced MR Imaging—correlation with molecular
3.0 T vs. 1.5 T: preliminary experience in healthy volunteers. J Magn Reson Imaging
[16] Chakraborty DP. Analysis of location specific observer performance data: validated
extensions of the jackknife free-response (JAFROC) method. Acad Radiol 2006;
13(10):1187–53.
comparison of gadoxetate disodium-enhanced MR imaging and 64-section multide-
tector CT in the Detection of hepatocellular carcinoma in patients with cirrhosis. Ra-
diology 2010;256(3):806–16.
magnetic resonance imaging for differentiating small hepatocellular carcinomas (<
or = 2 cm in diameter) from arterial enhancing pseudolesions: special emphasis
[19] Onishi H, Theisen D, Dietrich O, Reiser MF, Zech CJ. Hepatic steatosis: effect on hepa-
tocyte enhancement with gadoxetate disodium-enhanced liver MR imaging. J Magn
the hepatocyte phase of Gd-EOB-DTPA-enhanced MR imaging: is it possible to
[22] Tran PV, Jhaveri KS. Comparison of high spatial resolution respiratory triggered in-
version recovery-prepared spoiled gradient echo sequence with standard
breathhold T1 sequence MRI of the liver using gadoxetic acid. J Magn Reson Imaging
function using T1 mapping on Gd-EOB-DTPA-enhanced magnetic resonance imag-
Gadoxetic acid disodium-enhanced hepatocyte phase MRI: can increasing the flip
132–9.