Development of new imaging techniques for improved detection and characterization of focal liver lesions using magnetic resonance imaging

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Chapter 3

IMPROVED FOCAL LIVER LESION DETECTION: COMPARISON OF SINGLE SHOT DIFFUSION-WEIGHTED ECHO PLANAR AND SINGLE SHOT T₂W TURBO SPIN ECHO TECHNIQUES.

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ABSTRACT

**Objective:** To compare diffusion-weighted respiratory-triggered Single-Shot Spin-Echo Echo-Planar Imaging (SS SE-EPI) sequence using four b-values (b=0, b=20, b=300, b=800 s/mm²) and Single-Shot T2-weighted Turbo Spin Echo (T2W SS TSE) in patients with focal liver lesions, with special interest in small (<10mm) lesions.

**Methods:** Twenty-four patients underwent routine MRI. The five sequences were compared qualitatively for image quality, lesion conspicuity and artifacts. Quantitative analysis was performed for lesion identification and lesion-to-liver Contrast-to-Noise Ratio. Subgroup analyses were performed for different types of lesions with different sizes. Sequences were compared by rank order statistic (RIDIT) and Kruskal-Wallis.

**Results:** Best image quality (p<0.05) was achieved with T2W TSE and best lesion conspicuity (p<0.05) with T2W TSE for biliary cysts and SE-EPI DWI (b=20s/mm²) for hemangiomas and metastases. Image artifacts were lowest (p<0.05) with T2W TSE. T2W TSE was found to be the best protocol (p<0.05) for identification of biliary cysts and SE-EPI DWI (b=20s/mm²) for hemangiomas and metastases. The lesion-to-liver CNRs were highest on T2W TSE for biliary cysts and SE-EPI DWI for hemangiomas and metastases (p<0.05).

**Conclusion:** This study shows the potential of SS SE-EPI DWI (especially b-value 20s/mm²) as a promising technique for detecting small (<10mm) focal liver lesions.
**INTRODUCTION**

*T*₂-weighted (T2W) fast spin-echo (FSE) sequences are widely applied in the identification of focal liver lesions [1-3]. Although many focal liver lesions can be easily identified on *T*₂-weighted FSE, this mainly applies for lesions larger than 10mm in diameter [4]. Smaller focal liver lesions are more difficult to identify. To enable the detection of small (<10mm) liver lesions, high spatial resolution in combination with high signal-to-noise is needed. This was one of the reasons for the authors to use a respiratory-triggered T2W single shot TSE sequence and was a reason why a multi-shot T2W TSE sequence was less appropriate for this study. A respiratory-triggered multi-shot T2W TSE sequence in patients with irregular breathing may suffer from a significant risk of blurring, degrading the images when compared with a single shot T2W TSE sequence. One reason for decreased identification using T2W TSE is the difficulty to distinguish small focal liver lesions from intrahepatic vessels [5].

Recently, diffusion-weighted imaging techniques for the identification of focal liver lesions have been examined [6, 7]. Using diffusion-weighted Single-Shot Spin-Echo Echo-Planar Imaging (SS SE-EPI DWI), black-blood images of the liver were obtained by applying low b-values, facilitating differentiation between a lesion and vessel [6, 8].

The purpose of this study was to compare qualitatively and quantitatively respiratory-triggered SS SE-EPI DWI sequences with four b-values (b=0, b=20, b=300, b=800 s/mm²) and T2W SS TSE in patients with focal liver lesions, with special focus on small (<10mm) lesions. The potential of SS SE-EPI DWI concerning identification of different types of focal liver lesions (biliary cysts, hemangiomas and metastases) with different sizes (<10mm, 10-20mm, and >20mm) was compared with T2W SS TSE.
MATERIALS AND METHODS

Patients

24 consecutive patients (9 female; 15 male, mean age 59.8 ± 12.8 years) suspected for malignant liver lesions based on available laboratory results ((elevated Carcino-Embryonic Antigen > 3.4 ng/ml for non-smokers, >4.3 ng/ml for smokers, elevated transaminase levels (ALT >41 U/l for male, >31 U/l female patients), elevated alkaline fosfatase >129 U/l, elevated bilirubin (total bilirubin > 1.2 mg/dl)), findings on ultrasonographic (US) or computed tomographic (CT) examination were included in this study.

This prospective study was approved by the hospital ethics committee and written informed consent was obtained from all patients.

Technique

A 1.5T MRI whole-body scanner (Intera, Philips Medical Systems, Best, The Netherlands) with a 4-elements SENSE (SENSitivity Encoding) body phased-array coil was used. The respiratory-triggered T2W SS TSE and respiratory-triggered SS SE-EPI DWI images were acquired using the following parameters:

1) Axial T2W Half-Fourier turbo spin-echo (SS TSE): TR: single shot technique, TE: 60ms, EchoTrain Length (ETL): 85, flip angle: 90°, Number of Signal Averages (NSA):1, Field-of-View (FOV): 375mm, rectangular FOV of 70% (reduction of the number of phase-encodings to 70% (FOV: 375mm x 265mm), matrix 256x256 with 80% scan percentage (matrix: 256x208), half scan factor: 0.59, slice thickness: 6mm, slice gap: 0mm, CLEAR: yes. The acquired voxel size was 1.46mm x 1.84mm x 6mm. Depending on the breathing frequency of each patient, the acquisition time for this sequence ranged from 2 to 3 minutes.
2) Axial fat-suppressed SS SE-EPI DWI sequence with b-values of 0, 20, 300, and 800 s/mm²: TR: single shot technique, TE:49.7ms, flip angle:90°, NSA:4, FOV: 385mm, rectangular FOV of 75%, matrix 160x256 with 80% scan percentage, half scan factor 0.605, slice thickness 7mm, slice gap 0mm, foldover direction AP, EPI-factor 51, SENSE-factor 2 along the in-plane phase-encoded direction. The measured voxel size was 2.41mm x 3.02mm x 7mm. Susceptibility artifacts from bowel loops were partially overcome by giving the patients 0.5l of water just before starting the SS SE-EPI DWI. Depending on the breathing frequency of each patient, the acquisition time for this sequence ranged from 3 to 5 minutes.

**Analysis**

The different types of detected focal liver lesions (biliary cysts, hemangiomas and metastases) are sub-grouped by size (<10mm, 10-20mm, and >20mm) for further analysis.

All examinations were read on a PACS workstation (Agfa, Mortsel, Belgium) allowing the readers to scroll up and down the data set to evaluate whether a suspected lesion could be mistaken for a vascular structure.

Each lesion was detected without bias and once detected the location was recorded by writing down the number of the slice in which a detected lesion was found. Matching was possible by comparing the slice numbers of each sequence of the different readers.

**Qualitative analysis**

Two abdominal radiologists, experienced in interpreting liver MRI in daily clinical practice (5 years and 13 years of experience respectively), independently evaluated all images and subjectively
rated each sequence for overall image quality, lesion conspicuity, and artifacts. To avoid any learning bias, review of each image was done in a randomized, blinded fashion. Overall image quality and lesion conspicuity were based on the following five grading scales: excellent = 1; good = 2; fair = 3; poor = 4; and unacceptable = 5. The presence of artifacts was rated using the following four grading scales: absent = 1; mild = 2; moderate = 3; and severe = 4. The two radiologists did not have any other information about patient history, clinical examination, laboratory results, findings of other imaging techniques, or final diagnosis.

**Quantitative analysis**

*Lesions identification*

Discrepancies of interpretation regarding the presence or absence of a lesion were resolved by means of a consensus reading by the same abdominal radiologists. The number of lesions was recorded in each sequence.

For lesion identification in each image, the lesions on each image were evaluated by comparing them to the reference standard findings including US findings, follow-up CT, and contrast-enhanced MRI (see paragraph reference standard).

For comparison of lesion identification between T2W SS TSE and SS SE-EPI DWI, only the maximum number of discrete lesions identified on one sequence was used to determine the total number of discrete lesions. Lesions not identified with any of the four remaining sequences were rated with the worst score for evaluation of the overall image quality and lesion conspicuity (score “5”) and for evaluation of image artifacts (score “4”) (see paragraph qualitative analysis).
ROIs were placed independently by both readers on the hepatic parenchyma and on all the focal liver lesions. An interval of at least 4 weeks was maintained between consensus reading for lesion identification and ROI placement. The ROIs on liver parenchyma were placed by avoiding intrahepatic vessels and intrahepatic lesions and consisted of at least 100 pixels. These ROIs were always placed in the posterior sector of the right liver lobe to avoid artifacts from the great vessels. For the liver lesions, a ROI was drawn manually to encompass the whole lesion. For heterogeneous lesions, ROIs included entire lesions, without separating components with various signal intensities.

Signal intensities measurements

Signal intensities were measured unaware of the measurements and evaluations performed by the other reader. To minimize any learning bias, we set the intervals of reviewing the five types of imaging protocols—that is, respiratory-triggered T2W SS TSE and SS SE-EPI DWI with b=0, b=20, b=300, and b=800s/mm²—at 2 weeks. Lesion-to-liver Contrast-to-Noise Ratio (CNR) was calculated using the following equation:

$$\text{lesion-to-liver CNR} = \frac{[SI_{\text{lesion}}] - [SI_{\text{liver}}]}{SD_{\text{liver}}}$$

where $[SI_{\text{lesion}}]$ is the average signal intensity of the lesions and $[SI_{\text{liver}}]$ is the average signal intensity of the liver. $SD_{\text{liver}}$ is the standard deviation of the signal intensity within the ROIs. Lesions which were not visible on a given pulse sequence (using only the studied T2W SS TSE sequence and the SS SE-EPI DWI sequence with b-values b=0, 20, 300, 800s/mm²) were rated with CNR = 0.
**Reference standard**

For biliary cysts and hemangiomas, the diagnosis was based on typical findings on US, CT, or MRI. Typical lesion characteristics had to be present on at least two of the three imaging modalities.

For evaluating liver metastases, in patients eligible for surgery, intraoperative US findings during surgery and histopathologic findings were used as reference standard. In all other patients the final diagnosis was established by independent reading of all available imaging examinations (retrospective and prospective analysis) of all available imaging studies (US, CT, and MRI) by two radiologists, and follow-up imaging were used. MRI included T2W SS TSE, T2W SS TSE with fat saturation, inversion recovery T1W gradient echo, in and out phase imaging, and fat saturated T1W 3D gradient-echo imaging before the injection of gadolinium BOPTA, during the arterial, portal-venous and late venous phase and during the delayed phase (one to one-and-a-half hour after the injection of gadolinium BOPTA). Findings at SS SE-EPI DWI were not taken into account. No consensus reading was needed for this final evaluation as no differences existed in the evaluation of the images between both readers. To differentiate between a focal liver lesion and an artifact, all patients had a follow-up CT or MRI examination at least 6 months after the SS SE-EPI DWI.

**Statistical Analysis**

1) The five imaging protocols were compared for image quality, lesion conspicuity, artifacts and lesion identification by RIDIT analysis [9].

In addition subgroup analyses concerning lesion conspicuity were performed for different types of lesions (biliary cysts, hemangiomas, and metastases) and lesions <10mm.
2) The five imaging protocols were compared for lesion identification by RIDIT analysis. In addition subgroup analyses were performed for different types of lesions (biliary cysts, hemangiomas, and metastases) and different sizes (<10mm, 10-20mm, >20mm).

3) The five imaging protocols were compared for lesion-to-liver CNR by Kruskal-Wallis test (http://www2.chass.ncsu.edu/garson/pa765/statnote.htm). In addition subgroup analyses were performed for different types of lesions (biliary cysts, hemangiomas, and metastases) and different sizes (<10mm, 10-20mm, >20mm).

RIDIT analysis was originally developed by Bross for the analysis of ordinal data [9]. RIDIT analysis calculates one aggregate score that is the probability of a higher/lower score in the distribution under investigation (e.g. image quality of T2W images) relative to an common reference distribution (e.g. image quality of all images irrespective the technique). [9-12]. The null hypothesis is an a priori RIDIT of 0.5, which implies a fifty-fifty distribution. The RIDITs were all subtracted by 0.5 to have the mean at zero and multiplied by (-1) to have positive values for the promising results.

The more positive the RIDIT the better the result, the more negative the worse the result is for the considered imaging protocol. A RIDIT of zero means that the distribution of values of the criterion under consideration in the subgroup (e.g. T2W), is not different from the distribution of values in the reference population (all techniques). A difference was considered statistical significant with p<0.05.

For RIDIT analysis Microsoft Excel 2000 (version 5.0, Washington, USA) was used and for Kruskall-Wallis test, SPSS 12.0. (Windows, SPSS, Chicago, IL).
RIDIT-analysis is not a readily available function in Excel but the authors programmed it themselves and is available from them upon request.

As well known the “best” gold standard for lesion detection is intra-operative ultrasound with resection and histopathologic analysis. Because of inoperable disease or because of detection of merely benign liver lesions this gold standard could not be performed in many cases. So the authors could not study the sensitivity nor the specificity. As a consequence ROC analysis could not be performed.

RESULTS

129 hepatic masses (36 biliary cysts, 53 hemangiomas, 40 metastases) were identified.

Biliary cysts and hemangiomas

53 hepatic lesions in 8 patients were hemangiomas and of 36 lesions in 18 patients were biliary cyst. The diameter of hemangiomas and biliary cysts measured on the MR images ranged from 4 to 72mm (mean diameter: 14.5mm ± SD: 10.3mm) and from 3 to 29mm (mean diameter: 15.0mm ± SD: 9.0mm) respectively.

Liver metastases

Forty lesions in 14 patients were colorectal liver metastases; 5 of these liver metastases were diagnosed by intraoperative US findings during surgery and histopathology findings. Diagnosis of the remaining 35 was determined based on all available imaging examinations and follow up imaging after at least 6 months. The diameter of the liver metastases ranged from 4 to 26mm (mean diameter: 10.9mm ± SD: 6.2 mm).
Qualitative analysis

Image quality

Figure 1a shows significantly \( p=2.7 \times 10^{-11} \) better overall image quality for T2W SS TSE compared with all SS SE-EPI DWI sequences. SS SE-EPI DWI with \( b=20 \text{s/mm}^2 \) \( p=2.4 \times 10^{-8} \) was significantly the best SS SE-EPI DWI sequence.

Lesion conspicuity

For all types of lesions, a significantly \( p=1.02 \times 10^{-89} \) better lesion conspicuity was obtained with SS SE-EPI DWI with \( b=20 \text{s/mm}^2 \) (Figure 1b).

A significantly \( p=4.5 \times 10^{-12} \) better lesion conspicuity was obtained with T2W SS TSE for biliary cysts and with SS SE-EPI DWI with \( b=20 \text{s/mm}^2 \) for hemangiomas \( p=1.3 \times 10^{-85} \) and metastases \( p=3.0 \times 10^{-102} \) (Figure 1c).
**Figure 1b.** Comparison of lesion conspicuity for all lesions (biliary cysts, hemangiomas and metastases).

**Figure 1c.** Comparison of lesion conspicuity for each type of lesions (biliary cysts (1), hemangiomas (2) or metastases (3)).

A significantly ($p=3.2\times10^{-16}$) better lesion conspicuity was obtained with T2W SS TSE for biliary cysts $<$10mm and with SS SE-EPI DWI with $b=20s/mm^2$ for hemangiomas ($p=1.7\times10^{-92}$) and metastases $<$10mm ($p=2.4\times10^{-105}$) (Figure 1d).
Figure 1d. Comparison of lesion conspicuity for each type of lesions (biliary cysts (1), hemangiomas (2) or metastases (3)) < 10 mm.

The usefulness of the coinciding black-blood effect for the identification of focal liver lesions in the vicinity of the intrahepatic vasculature is shown in figure 2.

Lesions identification

Table 1 shows the number of lesions identified on T2W SS TSE and SS SE-EPI DWI with respectively b-values of 0, 20, 300, 800s/mm². A substantial part of the focal liver lesions included were <10mm in diameter. This is important for an accurate comparison of the studied sequences for the purpose of lesion identification. Four additional small (<10mm) liver metastases were identified by SS SE-EPI DWI with b=20s/mm² compared with (the second best imaging sequence being) T2W SS TSE. Two of those additionally detected small liver metastases (<10mm) were resected during surgery with histopathologic proof; the other two additionally detected small liver metastases showed increase in diameter during follow-up studies and were also detected on the additionally performed MRI sequences after IV injection of Gd-BOPTA.
Figure 2. On T2W SS TSE (axial plane; fig.2a) and SS SE-EPI DWI with $b=0\text{s/mm}^2$ (axial plane; fig.2b), the attention is drawn on two small hyperintense nodules (white arrow and white arrowhead). These hyperintensities are hard to differentiate from the surrounding intrahepatic vessels. When evaluating the SS SE-EPI DWI images (mainly $b=20\text{s/mm}^2$ (axial plane; fig.2c) and $b=300\text{s/mm}^2$ (axial plane; fig.2d), these nodules are clearly displayed as hyperintense nodules, contrasting with the surrounding intrahepatic vessels which show a strong signal intensity decrease. On the SS SE-EPI DWI image with $b=800\text{s/mm}^2$ (axial plane; fig.2e), a low signal-to-noise hampers the evaluation of the liver. Hepatic segmentectomy confirmed the presence of two small liver metastases in this hepatic region.
The increased detection of small lesions with the SS SE-EPI DWI sequence was thus not accompanied by an increase of false positives. T2W SS TSE and SS SE-EPI DWI with \( b=20\text{s/mm}^2 \) identified the same number of biliary cysts and hemangiomas.

### Table 1. Comparison of the number of identified lesions on each technique

<table>
<thead>
<tr>
<th>Lesion size</th>
<th>Lesions identified</th>
<th>T2W SS TSE</th>
<th>b=0</th>
<th>b=20</th>
<th>b=300</th>
<th>b=800</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary cysts</td>
<td>36</td>
<td>36</td>
<td>34</td>
<td>36</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>&lt;10mm</td>
<td>13</td>
<td>13</td>
<td>11</td>
<td>13</td>
<td>9</td>
<td>9</td>
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<tr>
<td>10-20mm</td>
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<td>11</td>
<td>11</td>
<td>11</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>&gt;20mm</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Hemangiomas</td>
<td>53</td>
<td>53</td>
<td>51</td>
<td>53</td>
<td>49</td>
<td>47</td>
</tr>
<tr>
<td>&lt;10mm</td>
<td>20</td>
<td>20</td>
<td>18</td>
<td>20</td>
<td>17</td>
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</tr>
<tr>
<td>10-20mm</td>
<td>28</td>
<td>28</td>
<td>28</td>
<td>28</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>&gt;20mm</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Metastases</td>
<td>40</td>
<td>36</td>
<td>32</td>
<td>40</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>&lt;10mm</td>
<td>24</td>
<td>20</td>
<td>17</td>
<td>24</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>10-20mm</td>
<td>12</td>
<td>12</td>
<td>11</td>
<td>12</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>&gt;20mm</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

T2W SS TSE = respiratory triggered T2W single-shot TSE images; \( b=0 \) = SS SE-EPI DWI images without MPG; \( b=20 \) = SS SE-EPI DWI images with MPG (\( b=20\text{s/mm}^2 \)); \( b=300 \) = SS SE-EPI DWI images with MPG (\( b=300\text{s/mm}^2 \)); \( b=800 \) = SS SE-EPI DWI images with MPG (\( b=800\text{s/mm}^2 \)).

**Artifacts**

Image artifacts were significantly \((p=1.4\times10^{-44})\) less noted in T2W SS TSE when compared with SS SE-EPI DWI (Figure 3).

**Quantitative analysis**

The mean lesion-to-liver CNR among biliary cysts, hemangiomas, and metastases in liver for T2W SS TSE and SS SE-EPI DWI images with \( b=0\text{s/mm}^2 \) and \( b=20\text{s/mm}^2 \) are summarized in
table 2. Comparison with SS SE-EPI DWI with $b=300$ s/mm$^2$ and $b=800$ s/mm$^2$ was difficult because of hampered visualization of several liver lesions due to suboptimal signal-to-noise and more pronounced artifacts.

![Artifacts](image)

**Figure 3.** Comparison of image artifacts.

For all biliary cysts, the highest lesion-to-liver CNR was found on T2W SS TSE compared to SS SE-EPI DWI images with $b=0$ s/mm$^2$ and $b=20$ s/mm$^2$ ($z=11.63$ and $z=11.46$ respectively). For all hemangiomas, the mean lesion-to-liver CNR was highest on SS SE-EPI DWI with $b$-value of 20 s/mm$^2$ compared to T2W SS TSE and SS SE-EPI DWI with $b=0$ s/mm ($z=14.22$ and $z=14.35$ respectively).

For all metastases, the mean lesion-to-liver CNR was highest on SS SE-EPI DWI with $b$-value of 20 s/mm$^2$ compared to T2W SS TSE and SS SE-EPI DWI images with $b=0$ s/mm ($z=11.17$ and $z=11.82$ respectively).

For biliary cysts <10mm, significant differences in lesion-to-liver CNR were seen between SS SE-EPI DWI with $b$-value of 20 s/mm$^2$ and T2W SS TSE ($z=6.28$) and between SS SE-EPI DWI
with b-value of 0s/mm² and 20s/mm² (z=6.56). In this evaluation, T2W SS TSE showed the highest lesion-to-liver CNR.

**Table 2. Comparison of mean lesion-to-liver CNR**

<table>
<thead>
<tr>
<th>Mean lesion-to-liver CNR</th>
<th>T2W SS TSE</th>
<th>b=0</th>
<th>b=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNR</td>
<td>CNR</td>
<td>SD</td>
<td>CNR</td>
</tr>
<tr>
<td>Biliary cysts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10mm</td>
<td>13.2</td>
<td>1.4</td>
<td>3.5</td>
</tr>
<tr>
<td>10-20mm</td>
<td>20.3</td>
<td>0.3</td>
<td>8.4</td>
</tr>
<tr>
<td>&gt;20mm</td>
<td>30.7</td>
<td>0.2</td>
<td>19.3</td>
</tr>
<tr>
<td>Total weighted mean</td>
<td>21.2</td>
<td>0.7</td>
<td>10.7</td>
</tr>
<tr>
<td>Hemangiomas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10mm</td>
<td>6.2</td>
<td>0.7</td>
<td>6.1</td>
</tr>
<tr>
<td>10-20mm</td>
<td>15.6</td>
<td>1.2</td>
<td>11.7</td>
</tr>
<tr>
<td>&gt;20mm</td>
<td>10.2</td>
<td>0.3</td>
<td>13</td>
</tr>
<tr>
<td>Total weighted mean</td>
<td>11.5</td>
<td>0.9</td>
<td>9.9</td>
</tr>
<tr>
<td>Metastases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10mm</td>
<td>8.8</td>
<td>0.7</td>
<td>8.5</td>
</tr>
<tr>
<td>10-20mm</td>
<td>8.9</td>
<td>0.6</td>
<td>8.8</td>
</tr>
<tr>
<td>&gt;20mm</td>
<td>10</td>
<td>0.3</td>
<td>9.7</td>
</tr>
<tr>
<td>Total weighted mean</td>
<td>9.7</td>
<td>0.6</td>
<td>8.8</td>
</tr>
</tbody>
</table>

Total weighted mean was calculated with absolute values of the different AppCNRs. T2W SS TSE = respiratory triggered T2W single-shot TSE images; b=0 = SS SE-EPI DWI images without MPG; b=20 = SS SE-EPI DWI images with MPG (b=20s/mm²). CNR : Contrast-to-Noise Ratio ; SD : Standard Deviation. The shaded parts in the table indicate the best results concerning the lesion-to-liver CNR when comparing the presented imaging sequences.

For hemangiomas <10mm, significant differences in lesion-to-liver CNR were seen between SS SE-EPI DWI with b-value of 20s/mm² and T2W SS TSE (z=8.44) and between SS SE-EPI DWI with b-value of 0s/mm² and 20s/mm² (z=8.68). In this evaluation, SS SE-EPI DWI ( b=20s/mm²) showed the highest lesion-to-liver CNR.
For metastases <10mm, significant differences in lesion-to-liver CNR were seen between SS SE-EPI DWI with b-value of 20s/mm² and T2W SS TSE (z=8.08) and between SS SE-EPI DWI with b-value of 0s/mm² and 20s/mm² (z=8.81). In this evaluation, SS SE-EPI DWI (b=20s/mm²) showed the highest lesion-to-liver CNR.

**DISCUSSION**

A significantly (p<0.05) better overall image quality for T2W SS TSE was found compared with SS SE-EPI DWI, followed by SS SE-EPI DWI with b=20s/mm² and b=0s/mm². When comparing the imaging protocols, better lesion conspicuity was obtained with T2W SS TSE for biliary cysts and with SS SE-EPI DWI with b=20s/mm² for hemangiomas and metastases. Comparing the imaging protocols for lesions <10mm, better lesion conspicuity was obtained with T2W SS TSE for biliary cysts and with SS SE-EPI DWI with b=20s/mm² for hemangiomas and metastases.

For diffusion-weighted imaging, SS SE-EPI DWI with b=20s/mm² shows the best results for identification of focal liver lesions and lesion-to-liver CNR, especially for small (<10mm) focal liver lesions. Overall, SS SE-EPI DWI with b=300s/mm² and even more with b=800s/mm² is not accurate in this study for the identification of focal liver lesions. The presence of artifacts is explained by a severe chemical shift due to a rather low band width in the phase-encoding direction of EPI sequences, and infolding which can be found on locations determined by the SENSE-factor [13] and RFOV. Susceptibility artifacts of the lungs and surrounding air filled bowel loops hampered the evaluation in those lesions which were located at the periphery of the liver and in the subphrenic hepatic areas [14].
The application of diffusion-weighted EPI for liver lesion identification and characterization is still not widely used. Mostly, emphasis has been on calculation of parameters such as true diffusion, perfusion factor and apparent diffusion coefficient [15-19]. However, new interest has risen for the potential of diffusion-weighted EPI in the identification of focal liver lesions [6, 8]. To our knowledge, this is the first study using diffusion-weighted imaging for the identification of small (<10 mm) liver lesions. The use of the black-blood effect for facilitating identification of liver lesions has been described previously [8]. This coinciding black-blood effect mainly when using a b-value b=20s/mm² was useful in this study for identifying lesions <10mm in diameter. The identification of small (<10mm) focal liver lesions was a main purpose of this study.

In a review article by Morana G et al. [4] the clinical relevance of small lesion detection is discussed. Morana G et al. state when performing non-invasive imaging techniques like US, CT and MRI (even when using intravenous contrast agents) focal liver lesions mostly are only detected down to a diameter of 10mm. However, they showed when performing cadaver studies, when dealing with a primary colorectal carcinoma, on average at least one liver metastasis <10mm in diameter is missed for each detected liver metastasis having a diameter above 10mm. The detection of even the smallest liver lesions thus is clinically important.

In the presented SS SE-EPI DWI sequence, the main importance of parallel imaging was the shortening of the echo-train, thus reducing blurring effects [20].

Absence of the confusing bright signals from the intrahepatic vessels in this study facilitated identification of focal liver lesions, particularly of small (<10mm) liver metastases situated against
intrahepatic vessels. No false positive results were observed in this study.

As the “best” gold standard for lesion detection – being intra-operative ultrasound with resection and histopathologic correlation - could not be performed in many cases reading of all available imaging examinations (retrospective and prospective analysis of all available imaging studies ((US, CT, Magnetic Resonance Imaging (MRI)) and follow-up imaging were used as a reference. Regarding the above explanation sensitivity, specificity and accuracy cannot be calculated.

The RIDIT analysis is a powerful and elegant method in quantifying the different imaging techniques based on the visual scoring of the images as is commonly done in clinical practice by radiologists.

Table 1 gives the lesion count which are given to illustrate the number of detected lesions. Since a detection means a CNR it is our variable of interest. Consequently, Kruskal-Wallis tests are calculated on these CNR values that reveal a statistical significant difference along the technique. CNR was measured with different techniques (T2W, b=0, b=20, b=300, b=800). We consider these techniques as independent from each other. For these reasons, the Kruskal-Wallis test was used. Comparing contrasts with Kruskal-Wallis produces z-scores which indicate significance.

A potential limitation could be the use of the presented T2W TSE sequence as a comparison for the diffusion-weighted SS SE-EPI DWI sequence. The authors preferred to use a respiratory triggered SS TSE rather than a breath-holding TSE to avoid cross-talk artifacts, to increase SNR and for patient comport. The NSA was 1 in the acquired T2W SS TSE sequence. Increasing the number of signal averages might increase the intrinsic contrast of a TSE sequence but
also increases the risk of irregular breathing and movement of the patient. These movements may decrease image quality and might increase the false-positive detection of focal liver lesions. The comparison of the presented diffusion-weighted SS SE-EPI DWI sequence with a dedicated MRI sequence in combination with the use of superparamagnetic iron oxide (SPIO) could be a useful study to further evaluate the performance of SS SE-EPI DWI in the identification of focal liver lesions.

In this study, SS SE-EPI DWI was not examined for the accuracy of characterizing the different focal liver lesions. Further study needs to be done regarding the potential of SS SE-EPI DWI to characterize different focal liver lesions.

After consensus reading, ROI placements were performed by the same two radiologists. This could have had an influence of the ROI placement on the identified focal liver lesions. The drawing of the different ROIs was however performed independently by two radiologists with a time interval of 4 weeks, resulting in independent signal intensity measurements.

The retrospective and prospective analysis of all available imaging studies was performed by the same two abdominal radiologists for establishment of the reference standard for the identification of focal liver lesions. This could have had a bias on the identification of the focal liver lesions. The purpose of this evaluation was however to optimize the reference standard for lesion identification. Therefore both retrospective and prospective analyses of all available images were preferred.

In conclusion, this preliminary study shows the potential of SS SE-EPI DWI especially using b-value 20s/mm$^2$ as a promising technique for the identification of small (<10mm) focal liver lesions. Further studies are necessary to support these results and to further
SS SE-EPI and T2W TSE

optimize this sequence. The authors have already noticed a potential improvement for lesion identification and lesion conspicuity when using a b-value 10s/mm² instead of b-value 20s/mm² and are now studying the effect of multiple low b-values to further improve the identification of small focal liver lesions. This study shows that SS SE-EPI DWI (especially b-value 20s/mm²) has advantages over T2W SS TSE imaging for the identification of small (<10mm) focal liver lesions.
REFERENCES


