The hepatocellular carcinoma to liver parenchyma contrast on Gd-EOB-DTPA enhanced MRI: Is measured signal intensity available for quantitative evaluation?

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Purpose

Gd-EOB-DTPA is a contrast medium with T1-shortening effects, and some researchers have assessed liver function and contrast of the tumorous and non-tumorous areas using signal intensity on T1-weighted imaging with Gd-EOB-DTPA\textsuperscript{1-6}. However, quantitative comparison of signal intensity in images of pre- and post-contrast enhancement did not show any straightforward relationship, as the window level and width of MRI differs with every image. This means that signal intensity on T1-weighted GRE imaging may vary depending on the pulse sequence designed by different MRI system manufacturers. We therefore cannot directly compare signal intensities alone using ROIs of hepatic parenchyma. On the other hand, T1 relaxation time is an absolute value, and it can be measured by the Look-Locker sequence\textsuperscript{7,8}.

The purpose of this study was to investigate the precision of hepatocellular carcinoma (HCC) to liver parenchyma contrast based on measured signal intensity (SI) using calculated T1-value (absolute value).
Methods and Materials

Materials

Eighteen patients with 20 hypervascular HCCs, who underwent 3-T MRI (Achieva, Philips Healthcare) using a cardiac 32ch coil, were enrolled in this study (15 males and 3 females, age mean 67.5 ranging 50-85).

The pathological diagnosis of HCC was made based on surgically resected specimens in 5 of the 20 HCCs. In 3 HCCs, the specimens were obtained by ultrasound-guided needle core biopsy. The remaining 12 HCCs were proven from image findings of enhanced US, CT and MRI.

MR Imaging

Patients underwent MR imaging on a clinically available 3-T system (Achieva; Philips Medical System, Netherlands). For signal reception, a cardiac 32ch coil was used and covered the whole liver in all examinations. For all patients, enhanced T1-weighted (T1w), fat-saturated, 3D high-resolution examination (eTHRIVE) images were taken before (pre-contrast) and 20min after Gd-EOB-DTPA administration (post-contrast). Fat-suppressed T1-weighted GRE images with eTHRIVE sequence were acquired using the following parameters: repetition time, 3.5 ms; echo time, 1.7 ms; flip angle, 10º; field of view, 350 × 280 mm; matrix, 320 × 250, zip; thickness, 1.5 mm; acquisition time, 18.5 sec; acceleration factor, 1.9. For all patients, Look-Locker sequences (single slice multiphase imaging using gradient-echo sequence with inversion recovery pulse: repetition time, 12 ms; echo time, 1.7 ms; flip angle, 7º; field of view, 420 × 285 mm; matrix, 112 × 66, 256zip; thickness, 10 mm; acquisition time, 1 phase = 145 ms, 31 phases; acceleration factor, 2) were obtained before (pre-contrast) and at 18 min after Gd-EOB-DTPA administration (post-contrast). The sequence was obtained as only one axial slice at the level of the porta hepatis.

Gd-EOB-DTPA (Primovist®; Bayer Schering Pharma AG, Berlin, Germany) was used as a hepatocytic contrast agent. All patients received 0.025 mmol/kg body weight of Gd-EOB-DTPA administered at 2 ml/s through an intravenous line placed in a cubital or cephalic vein and flushed with 35 ml of 0.9% saline at the same speed.

Imaging analysis

SI measurements

For SI measurements of the liver, a region of interest (ROI) with less than 50 pixels pixels was drawn manually in the liver on 3D T1-TFE images obtained before and 20 min after Gd-EOB-DTPA administration. Liver SI measurement was evaluated using a pixel-wise technique. Four ROIs were sparsely placed in both lobes of liver parenchyma,
without focal hepatic lesions, major branches of the portal or hepatic veins, or imaging artifacts. For reproducible ROIs before and after Gd-EOB-DTPA administration, every effort was made to place ROIs at the same positions in the liver of each patient. Mean SI measurements for the four ROIs were considered as the representative liver SI measurements for the liver. The ROI for each HCC was positioned over a homogeneous area, avoiding areas of necrosis and hemorrhage as much as possible (Fig1).

**T1 value**

The Philips Research Integrated Development Environment (PRIDE) T1 fitting tool (Philips Healthcare, Best, Netherlands) was employed for measurement of T1 relaxation time using data from the Look-Locker sequence. PRIDE software can depict T1 relaxation time on a pixel-by-pixel basis in a color distribution map (T1 mapping).

For T1 relaxation time assessment of the liver, a region of interest (ROI) with less than 50 pixels pixels was drawn manually in the liver on T1 mapping images obtained before and 18 min after Gd-EOB-DTPA administration. Liver T1 relaxation time was evaluated using a pixel-wise technique. Four ROIs were sparsely placed in both lobes of liver parenchyma, without focal hepatic lesions, major branches of the portal or hepatic veins, or imaging artifacts. For reproducible ROIs before and after Gd-EOB-DTPA administration, every effort was made to place ROIs at the same positions in the liver of each patient. Mean T1 relaxation time for the four ROIs were considered as the representative T1 relaxation time for the liver. The ROI for each HCC was positioned over a homogeneous area, avoiding areas of necrosis and hemorrhage as much as possible (Fig2).

In addition, one quantitative parameter of the tumorous lesion to the surrounding non-tumorous area on the unenhanced images (pre-contrast EOB ratio) and those on the enhanced images (post-contrast EOB ratio) at each time was calculated and compared using the following formula:

The relative SI measurements ratios = SI measurements of HCC / SI measurements of the liver

The relative T1 values ratios = T1 value of HCC / T1 value of the liver

**Numerical analysis**

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**Liver parenchyma: Correlation between the mean SI and the mean T1 values**

**HCC:#Correlation between the SI and the T1 values**

**HCC-liver contrast : Correlation between the ratio of the SI and the T1 value**
Pearson's product moment correlation coefficient was used for statistical analysis, respectively pre-contrast and post-contrast.
Fig. 1: A 56 year-old man with HCC on S7 (arrow). 3D T1-TFE image acquired 20 min after EOB injection. Four ROIs with less than 50 pixels were sparsely placed in both lobes of liver parenchyma. Major vessel structures were avoided for ROI of liver parenchyma. The ROI for HCC was positioned as accurately as possible. Mean SI measurements of the liver post-contrast, at 20 min, was 794.4. SI measurement of the HCC on post-contrast, at 20 min, was 579.5. The relative SI measurement ratio of HCC/liver was 0.73.

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Fig. 2: A 56 year-old man with HCC on S7 (arrow). T1 map acquired 18 min after EOB injection. Four ROIs with less than 50 pixels were sparsely placed in both lobes of liver parenchyma. Major vessel structures were avoided for ROI of liver parenchyma. The ROI for HCC was positioned as accurately as possible. Mean T1 values of the liver on post-contrast, at 18 min, was 433.3 milliseconds. T1 value of the HCC post-contrast, at 18 min, was 827.1 milliseconds. The relative T1 value ratio of HCC/liver was 1.91.

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## Liver parenchyma: Correlation between the mean SI and the mean T1 values

The mean SI measurement and mean T1 value of liver parenchyma was 846.1±187.6 and 914.7±85.9 milliseconds at pre-contrast and 694.3±224.7 and 466.5±91.5 milliseconds at post-contrast, respectively (Table 1). The coefficient of determination between SI and T1 value contrast of liver was 0.0079 (P=0.7258) at pre-contrast and 0.0883 (P=0.2312) at post-contrast (Fig. 3, Fig. 4). There was no significant correlation between SI and T1 value of liver parenchyma (Table 2).

## HCC: Correlation between the SI and the T1 values

The mean SI measurement and mean T1 value of liver parenchyma was 812.2±217.8 and 1196.9±196.8 milliseconds at pre-contrast and 493.4±189.8 and 887.0±169.4 milliseconds at post-contrast, respectively (Table 3). The coefficient of determination between the SI and T1 value contrast of HCC was 0.0742 (P=0.2453) at pre-contrast and was 0.1896 (P=0.0550) at post-contrast (Fig. 5, Fig. 6). There was no significant correlation between SI and T1 value of HCC (Table 4).

## HCC-liver contrast : Correlation between the SI ratio and the T1 value

SI and T1 value contrast of HCC / liver was 0.92±0.14 and 1.32±0.29 at pre-contrast, and 0.65±0.17 and 2.00±0.62 at post-contrast, respectively (Table 5). The coefficient of determination between SI and T1 value contrast of HCC/ liver was 0.4367 (P=0.0055) at pre-contrast and was 0.2182 (P=0.0379) at post-contrast (Fig 5, Fig 6). There was no significant correlation between SI and T1 value contrast of HCC / liver (Table 6).

### Summary of results

Our data showed that there was no significant correlation between the SI and T1 value of HCC, the SI and T1 value of liver parenchyma, or between SI and T1 value contrast of HCC / liver, respectively. Due to the usage of a calculated T1 value (absolute value), quantitative comparison of signal intensity in each image before and after contrast enhancement does not show any straightforward relationships. This is because the signal intensity of MR imaging depends on the gain of radiofrequency amplifier, thus it may vary considerably each time. Therefore, the signal intensity is not absolute like the CT value. We cannot directly compare the signal intensities alone using ROIs in hepatic parenchyma and HCC.
Table 1: Mean SI of the liver and mean T1-values of the liver obtained on pre-contrast and post-contrast after injection of Gd-EOB-DTPA

<table>
<thead>
<tr>
<th></th>
<th>pre-contrast</th>
<th>post-contrast</th>
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<tbody>
<tr>
<td>SI</td>
<td>846.1±187.6</td>
<td>694.3±224.7</td>
</tr>
<tr>
<td>T1value (msec)</td>
<td>914.7±85.9</td>
<td>466.5±91.5</td>
</tr>
</tbody>
</table>

Fig. 3: Mean SI of the liver and mean T1-values of the liver obtained on pre-contrast and post-contrast after injection of Gd-EOB-DTPA

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**Fig. 4:** Scatter plot of the correlation between the mean SI of the liver and the mean T1 values of the liver, post-contrast

<table>
<thead>
<tr>
<th></th>
<th>pre-contrast</th>
<th>post-contrast</th>
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</thead>
<tbody>
<tr>
<td>Coefficient of determination</td>
<td>0.0079</td>
<td>0.0883</td>
</tr>
<tr>
<td>P value</td>
<td>0.7258</td>
<td>0.2312</td>
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</table>

**Table 2:** Results of Pearson's product moment correlation coefficient, between the mean SI of the liver and the mean T1 values of the liver on pre-contrast and post-contrast.

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Table 3: Mean SI of the HCC and mean T1 values of the HCC obtained on pre-contrast and post-contrast after injection of Gd-EOB-DTPA

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>SI</td>
<td>812.2 ± 217.8</td>
<td>493.4 ± 189.8</td>
</tr>
<tr>
<td>T1 value (msec)</td>
<td>1196.9 ± 196.8</td>
<td>887.0 ± 169.4</td>
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Fig. 5: Scatter plot of the correlation between SI of HCC and T1 values of the HCC on pre-contrast

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**Fig. 6:** Scatter plot of the correlation between SI of HCC and T1 values of the HCC on post-contrast

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<tr>
<td>P value</td>
<td>0.2453</td>
<td>0.0550</td>
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**Table 4:** Results of Pearson's product moment correlation coefficient between the mean SI of the HCC and the mean T1 values of the HCC on pre-contast and post-contast

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Table 5: Mean HCC / liver SI ratio and mean HCC / liver T1 value ratio obtained on pre-contrast and post-contrast after injection of Gd-EOB-DTPA

<table>
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<tr>
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<tbody>
<tr>
<td>HCC/ liver SI ratio</td>
<td>0.92±0.14</td>
<td>0.65±0.17</td>
</tr>
<tr>
<td>HCC/ liver T1 value ratio</td>
<td>1.32±0.29</td>
<td>2.00±0.62</td>
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Fig. 7: Scatter plot of the correlation between the HCC / liver SI ratio and the HCC / liver T1 value ratio on pre-contrast

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**Fig. 8:** Scatter plot of the correlation between the HCC / liver SI ratio and the HCC / liver T1 value ratio on post-contrast

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<tr>
<td><strong>P value</strong></td>
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<td>0.0379</td>
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**Table 6:** Results of Pearson's product moment correlation coefficient, between HCC / liver SI ratio and HCC / liver T1 value ratio on pre-contrast and post-contrast.

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Conclusion

Our data showed that there was no significant correlation between SI and T1 value contrast of HCC / liver. In conclusion, SI ratio of HCC / liver on Gd-EOB-DTPA may not be suitable for quantitative analysis.
References


