How to determine the optimal flip angle for each patient in hepatobiliary-phase easily and quickly during Gd-EOB-DTPA-MRI examination? Recommends using imaging findings of cirrhotic liver as the indicator.

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Aims and objectives

Porpuse

This study aim to the followings on Gadolinium-ethoxybenzyl-diethylenetriamine-pentaacetic-acid (Gd-EOB-DTPA) examination.

- To investigate for the difference of T1 value of between liver and cirrhosis liver, corresponding to the imaging findings.
- To determine the optimal fillip angle in Hepatobiliary-phase for each patient using the imaging findings.
- To propose how to select the optimal fillip angle quickly and easily during the examination.

Background and introduction

From the point of view of the pharmacological action of the clinical patient.

Gd-EOB-DTPA is taken into normal functioning liver cell, and the intensity of liver tissue changes to the high intensity by T1-shortening effect. On the other hand, liver tumors don't take in Gd-EOB-DTPA. Therefore, liver tumors are imaged as a low intensity region in Hepatobiliary-phase (HP) [1]. The uptake of Gd-EOB-DTPA into hepatic cell depends on liver function of each patient. The uptake of patient with liver dysfunction is less than that in normal patients. In particular, the uptake in patients with liver cirrhosis (LC) is only a very little. In HP, the liver tissue of LC patients becomes the comparatively high T1 value [2].

From the point of view of the scanning parameters for Hepatobiliary-phase.

In HP, 3D-gradient-echo (3D-GRE) T1-weighted sequence is commonly used. In that case, repetition time (TR) and echo time (TE) are set to the minimum limit of MRI machine to obtain the short imaging time and T1-contrast [1]. Under the circumstances, the flip angle (FA) is the most important factor to improve the contrast between liver tissue and tumor. The optimal FA in 3D-GRE is varied according to T1 value of the imaging target. Recently, the imaging using 3D-GRE with the high FA has been recommended to HP [3,4]. However, T1 value of liver tissue is not equivalent between normal patients and LC patients. Therefore, the difference of the optimal FA to detect the liver tumor for each patient in HP should be suggested. However, the evidence for indicator of the optimal FA had not been yet proven.
**The necessity of the real-time and simple indicator for the optimal flip angle.**

As mentioned, LC patients are categorized into Child-Pugh classification. The difference of T1-LT is confirmed between normal, Child-Pugh A and Child-Pugh B, C [2]. Child-Pugh classification might be the indicator for the optimal FA based on the former reports. Though, Child-Pugh classification requires the detailed biochemical data, and the imaging data to assess the ascites. And, the confirmation of them requires a time-consuming and an expertise. Furthermore, the operator needs the medical chart to confirm them during the examination.

On the other hand, many of LC patients possess the typical imaging findings [5]. And, the operator can confirm them immediately during Gd-EOB-DTPA examination. So, the imaging findings also might be the indicator for the optimal FA.

**The aims.**

The aims of this study are to investigate for the difference of T1-LT normal and cirrhotic liver tissue, corresponding to the imaging findings. And, to determine the optimal FA in HP using the imaging findings. In addition, to propose how to select the optimal FA quickly and easily in HP.
Methods and materials

Measurement of T1 value of liver tissue in clinical patient.

Between July 2010 and July 2012, 32 patients underwent Gd-EOB-DTPA-enhanced-examination using 1.5 Tesla MRI, and was measured T1-LT in HP after 20 min from injection. Gd-EOB-DTPA was injected 0.025µmol/kg [1]. T1-LT was measured by fast-spin-echo (FSE) sequence with the different TR [6]. This method was a simple measurement method. The measurement was performed under the breath holding. TR-combination was 400 msec and 200 msec in HP. The other settings were shown in Table 1. Region of interest (ROI) was set on the liver tissue to obtain signal-intensity (SI). Then, T1 value was calculated using an obtained SI (Fig. 1). The ROIs were set on avoiding the fatty liver part and blood vessel. There was no patient with the overall fatty liver. The diameter of ROI was 1cm. And, The biochemical data, the clinical factor of hepatitis virus and LC were researched about the subject patients.

\[ T1 = -\frac{TR_a}{\ln (SI_a - SI_b/SI_b)} \]

\[ SI_a : \text{Signal intensity at TR}_a \]
\[ SI_b : \text{Signal intensity at TR}_b \]
\[ 2TR_a = TR_b \]

Fig. 1: Mathematical formula of T1 value measurement by fast-spin-echo (FSE) sequence.

References: Radiology, Otaru Municipal Hospital - Otaru City/JP

Grouping by imaging data and Comparing T1 value of liver tissue

Patients were classified into two groups. One group was normal image group, and the other group was LC image group. Patients classified into LC image group had one or more the following the image findings: Irregularity of liver surface, Splenomegaly (on axial image, the major axis > 10 cm or the minor axis > 6 cm), Expanding of hepatic portal (main trunk > 1.5 cm) (Fig. 2-4). The imaging findings were picked up by retrospectively observation in the Gd-EOB-DTPA protocol imaging. About the irregularity of liver surface, the radiology reports by 26-years experienced certified radiologist were used as a reference.

T1-LT and biochemical data were compared between normal image group and LC image group using Mann-Whitney U-test (# < 0.05).
Defining the optimal flip angle by the phantom study.

On the basis of obtained clinical T1-LT data, the phantom study was performed. The self-made phantoms were produced by diluting Gd-EOB-DTPA. The phantoms possessed two liver tissue phantoms and liver tumor phantom, and were constituted of the followings phantoms: simulated T1-LT of normal image group, simulated T1-LT of LC image group, and simulated the liver tumor. T1 value of each liver tissue phantom was adjusted to approximately clinical T1-LT data. And, T1 value of liver tumor phantom was adjusted to approximately 1000 msec [7]. The Shape of the phantoms was a bottle-shaped, placed in a box and filled with water (Fig. 5).

**Fig. 5**: The detail of the phantom.

*References*: Radiology, Otaru Municipal Hospital - Otaru City/JP
Fig. 6: The string of ROI on the phantom.

References: Radiology, Otaru Municipal Hospital - Otaru City/JP

The phantoms were imaged with 10-25 degrees FA using 3D-fast-field-echo (FFE)-sequence. The sequence was the one which TR was set to 4.8 msec. The other parameters were shown in Table 3. FFE-sequence was the spoiled-GRE-sequence, and was commonly used for HP. FA was changed to every 1 degree. All parameters excepting FA were set to the same for all FA. For each FA, the following were measured and calculated: Signal-intensity (SI) of each phantom, Signal-noise-to ratio (SNR) (Fig. 7) [8], Contrast-noise-to ratio (CNR) (Fig. 8) [9]. SNR and CNR were calculated between the liver tissue phantoms and liver tumor phantom.
Fig. 7: Mathematical formula of Signal-to-noise ratio (SNR).

\[ \text{SNR} = \frac{SI(x)}{SD_b} \]

\( SI(x) \) : Signal intensity of the phantom  
\( SD_b \) : Standard deviation of signal intensity of background

References: Radiology, Otaru Municipal Hospital - Otaru City/JP

Fig. 8: Mathematical formula of Contrast-to-noise ratio (CNR).

\[ \text{CNR} = \left( \frac{\pi}{2} \right)^2 \frac{1}{SI_a - SI_b} / SI_b \]

\( SI_a, SI_b \) : Signal intensity of the subject phantom  
\( SI_b \) : Signal intensity of background

References: Radiology, Otaru Municipal Hospital - Otaru City/JP

The scattering of CNR-measured value was expected. For this reason, using statistical analysis software, the approximate curve of 2-4 order were fitted to CNR-measured value, and the most suitable model was selected using as a reference the following coefficient: the coefficient of determination (R2, Adjusted-R2) and Akaike's-Information-Criterion (AIC) [10]. And, the optimal FA was defined as indicating the maximum CNR in the most suitable model.

Clinical LC patient was imaged by the optimal flip angle.

Thereafter, clinical LC patient were examined with changing FA. FA was set to the followings: 15 degrees, the optimal FA for normal image group, or LC image group. The setting of 15 degrees was the conventional setting for HP. For each FA, root-mean-square (RMS)-CNR was calculated (Fig. 9) [11]. The target patient was male, and diagnosed with multiple liver metastasis of colon cancer. In imaging findings, Splenomegaly and Expanding of hepatic portal were observed.
Fig. 9: Mathematical formula of root-mean-square-CNR (RMS-CNR).

References: Radiology, Otaru Municipal Hospital - Otaru City/JP
Table 1: Table 1 The scan setting of fast-spin-echo (FSE) sequence.

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR (msec)</th>
<th>TE (msec)</th>
<th>ETL</th>
<th>Echo space (msec)</th>
<th>Slice th (mm)</th>
<th>Mtx</th>
<th>FOV (cm×cm)</th>
<th>Flip angle (degree)</th>
<th>Speeder plug</th>
<th>NEX</th>
<th>Band width (Hz/px)</th>
<th>Coil</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSE</td>
<td>200/400</td>
<td>10</td>
<td>4</td>
<td>10</td>
<td>10</td>
<td>96×128</td>
<td>30 × 37</td>
<td>90</td>
<td>1.7</td>
<td>3</td>
<td>±195</td>
<td>4ch Torso SPEEDER</td>
</tr>
</tbody>
</table>

Table 2: Protocol of Gd-EOB-DTPA-examination.

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR (ms)</th>
<th>TE (ms)</th>
<th>FOV (cm)</th>
<th>Matrix</th>
<th>Slice th / Gap (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axial T1WI in–out of phase</td>
<td>FE 2D</td>
<td>181</td>
<td>2.7 / 5</td>
<td>30 × 37</td>
<td>144 × 352</td>
</tr>
<tr>
<td>T1WI 3D (Dynamic)</td>
<td>FFE 3D</td>
<td>4.8</td>
<td>1.9</td>
<td>32 × 43</td>
<td>144 × 256</td>
</tr>
<tr>
<td>Axial Heavy T2WI</td>
<td>FASE 2D</td>
<td>20000</td>
<td>100</td>
<td>30 × 37</td>
<td>192 × 320</td>
</tr>
<tr>
<td>Axial T2WI</td>
<td>FSE 2D</td>
<td>3000</td>
<td>90</td>
<td>30 × 37</td>
<td>160 × 320</td>
</tr>
<tr>
<td>DWI</td>
<td>SE–EPI</td>
<td>8600</td>
<td>100</td>
<td>30 × 37</td>
<td>272 × 128</td>
</tr>
<tr>
<td>T1WI 3D (Hepatobiliary phase)</td>
<td>FFE 3D</td>
<td>4.8</td>
<td>1.9</td>
<td>32 × 43</td>
<td>144 × 256</td>
</tr>
</tbody>
</table>

FE: Field echo, FFE: Fast field echo, FASE: Fast advanced spin echo, FSE: Fast–spin echo
SE–EPI: Spin echo echo planer imaging, DWI: Diffusion weighted image
**Fig. 2:** Typical image of Irregularity of liver surface.

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**Fig. 3:** Typical image of Splenomegaly.

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**Fig. 4:** Typical image of Expanding of main hepatic portal.

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<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR (msec)</th>
<th>TE (msec)</th>
<th>flip angle (degrees)</th>
<th>FOV (cm)</th>
<th>Matrix</th>
<th>Slice th / Gap (mm)</th>
<th>Band width (Hz/pix)</th>
<th>NEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFE 3D</td>
<td>4.8</td>
<td>1.9</td>
<td>10 − 30</td>
<td>25 × 25</td>
<td>128 × 128</td>
<td>5.0</td>
<td>±445Hz</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 3:** The Scan setting of 3D fast-field-echo (FFE) sequence for phantom study.
Results

**Measuring T1 value of liver tissue in clinical patient.**

The result of grouping and the research of patient data were shown in Table 4. And, The image findings in case of LC on image was shown in Table 5. Male were 19 cases and female were 13 cases. The mean age was 68.9±12.5 age. 15 patients were diagnosed with the liver dysfunction on biochemical data. Furthermore, 6 patients of them were diagnosed with liver cirrhosis. Child-Pugh B and C was each one case and the rest was Child-Pugh A. T1-LT was measured in all patient without incident.

**Classification by image data and Comparing T1 value of liver tissue.**

7 patients were classified into LC image group. 6 cases of them had hepatitis virus. T1-LT and biochemical was shown in Table 6.

In regard to median of T1-LT, normal image group was 226.1 msec and LC image group was 323.7 msec. T1-LT of LC image group was higher than that of normal image group. T1-LT had a statistically significant difference between groups (Fig. 10). In biochemical data, there was an overall difference, and the data was unfavorable value in LC image group patients. Further, a statistically significant difference was observed in few items.
Fig. 10: Comparison of T1 value of liver tissue in hepatobiliary phase by the image data classification. There was a significant difference (* P < 0.05).

References: Radiology, Otaru Municipal Hospital - Otaru City/JP

Defining the optimal flip angle by the phantom study.

The detail of self-made phantoms was shown in Table 7. T1 value of phantoms was the following: Normal image group phantom was 234.5 msec, LC image group phantom was 346.1 msec, and liver tumor phantom was 988.9 msec.
Table 7: The detail of phantom: Concentration, T1 and T2 value.

<table>
<thead>
<tr>
<th>Simulating</th>
<th>Gd–EOB–DTPA (mol/l)</th>
<th>T1 value (ms)</th>
<th>T2 value (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal on image</td>
<td>$0.63 \times 10^{-3}$</td>
<td>234.5</td>
<td>114.0</td>
</tr>
<tr>
<td>LC on image</td>
<td>$0.42 \times 10^{-3}$</td>
<td>346.1</td>
<td>137.0</td>
</tr>
<tr>
<td>Tumor</td>
<td>$0.15 \times 10^{-3}$</td>
<td>988.9</td>
<td>178.5</td>
</tr>
</tbody>
</table>

**Signal-intensity.**

The relationship between SI and FA was shown (Fig. 11). In normal image group phantom, SI was the maximum at 13-14 degrees. Then, SI decreased gradually. In the other phantoms, SI decreased according to increase of FA.

**Fig. 11:** The Relationship between Signal-intensity and flip angle.

**References:** Radiology, Otaru Municipal Hospital - Otaru City/JP
**Signal-to-noise ratio.**

The relationship between SNR and FA was shown (Fig. 12). In normal image group phantom, SNR was the maximum at FA was 22-23 degrees. In LC image group phantom, SNR didn't change up to about 20 degrees. Then, SI decreased gradually.

![Graph showing the relationship between Signal-to-noise ratio and flip angle.](image)

**Fig. 12:** The Relationship between Signal-noise-to ratio and flip angle.

**References:** Radiology, Otaru Municipal Hospital - Otaru City/JP

**Contrast-to-noise ratio.**

$R^2$, Adjusted-$R^2$ and AIC of the approximate curve were shown in Table 8. And, the scatter charts of CNR with the best model were shown (Fig. 13, 14).
Table 8: The coefficient of the approximate curve

<table>
<thead>
<tr>
<th>Order</th>
<th>R²</th>
<th>Adjusted R²</th>
<th>AIC</th>
<th>R²</th>
<th>Adjusted R²</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.83</td>
<td>0.81</td>
<td>87.0</td>
<td>0.85</td>
<td>0.83</td>
<td>58.8</td>
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<tr>
<td>3</td>
<td>0.84</td>
<td>0.83</td>
<td>85.0</td>
<td>0.87</td>
<td>0.84</td>
<td>60.4</td>
</tr>
<tr>
<td>4</td>
<td>0.89</td>
<td>0.87</td>
<td>85.0</td>
<td>0.87</td>
<td>0.84</td>
<td>62.6</td>
</tr>
</tbody>
</table>

In normal image group phantom, the approximate curve of 4-order was the most suitable. And, CNR was the maximum at about 24 degrees FA.

Fig. 13: The Relationship between Contrast-noise-to ratio and flip angle. In normal image group. With 4-order approximate curve.

References: Radiology, Otaru Municipal Hospital - Otaru City/JP
In LC image group phantom, the approximate curve of 2-order was the most suitable. And, CNR was the maximum at about 18 degrees the FA.

**Fig. 14**: The Relationship between Contrast-noise-to ratio and flip angle. In LC image group. With 2-order approximate curve.

**References**: Radiology, Otaru Municipal Hospital - Otaru City/JP

Clinical LC patient was imaged by the optimal flip angle.

The images of each FA were shown (Fig. 15-17). RMS-CNR between tumor and liver was the maximum at 18 degrees, and the minimum was at 21 degrees (Fig. 18).
Fig. 18: RMS-CNR at each flip angle. The minimum at 21 degrees.

References: Radiology, Otaru Municipal Hospos tal - Otaru City/JP
Table 4: The result of grouping and the research of patient data: Diagnosis, Hepatitis virus, Liver dysfunction, Child pugh classification.

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### Table 5: The Image findings in case of liver cirrhosis on image.

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<table>
<thead>
<tr>
<th>Classification</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Hepatitis virus</th>
<th>Imaging findings</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Irregularity of</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>liver surface</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Splenomegaly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expanding of</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>hepatic portal</td>
</tr>
<tr>
<td>LC on image</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>53 M</td>
<td>53</td>
<td>M</td>
<td>Chronic hepatitis Type B,C</td>
<td>C,B</td>
<td></td>
</tr>
<tr>
<td>64 F</td>
<td>64</td>
<td>F</td>
<td>Chronic hepatitis Type B</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>70 M</td>
<td>70</td>
<td>M</td>
<td>Hepatocellular carcinoma</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>60 M</td>
<td>60</td>
<td>M</td>
<td>Hepatocellular carcinoma</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>74 M</td>
<td>74</td>
<td>M</td>
<td>Hepatocellular carcinoma</td>
<td>C</td>
<td>+</td>
</tr>
<tr>
<td>76 M</td>
<td>76</td>
<td>M</td>
<td>Hepatocellular carcinoma</td>
<td>C</td>
<td>+</td>
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<tr>
<td>57 F</td>
<td>57</td>
<td>F</td>
<td>Liver metastases</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

### Table 6: Comparison of T1 value and biochemical data.

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<table>
<thead>
<tr>
<th>Group</th>
<th>Normal on image</th>
<th>LC on image</th>
<th>Mann-Whitney test [α=0.05]</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>25 (M:14,F:11)</td>
<td>7 (M:5,F:2)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>70.0±13.4</td>
<td>64.9±8.8</td>
<td></td>
</tr>
</tbody>
</table>
| Median value of T1 value in hepatobiliary phase (ms) | 226.1          | 323.7       | * P=0.007
| Albumin (g/dL)         | 3.97±0.41       | 3.75±0.76   | P=0.660
| Total bilirubin (mg/dL)| 0.76±0.36       | 0.79±0.47   | P=0.917
| AST (IUL/L)            | 24.36±8.39      | 39.29±18.28 | * P=0.017
| ALT (IU/L)             | 19.20±11.21     | 31.71±19.44 | P=0.110
| Prothrombin activation (%) | 100.75±24.02 | 76.85±16.25 | P=0.079
| Platelet count (×10⁴/μL) | 21.06±7.76    | 13.27±7.03  | * P=0.027
**Fig. 10:** Comparison of T1 value of liver tissue in hepatobiliary phase by the image data classification. There was a significant difference (* P < 0.05).

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### Table 7: The detail of phantom: Concentration, T1 and T2 value.

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<table>
<thead>
<tr>
<th></th>
<th>Gd–EOB–DTPA (mol/l)</th>
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<th>T2 value (ms)</th>
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<tr>
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<td>114.0</td>
</tr>
<tr>
<td>LC on image</td>
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<td>346.1</td>
<td>137.0</td>
</tr>
<tr>
<td>Tumor</td>
<td>0.15 × 10^{-3}</td>
<td>988.9</td>
<td>178.5</td>
</tr>
</tbody>
</table>

### Table 8: The coefficient of the approximate curve.

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<table>
<thead>
<tr>
<th>Order</th>
<th>Normal on image - tumor model</th>
<th>Liver cirrhosis on image - tumor model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R^2</td>
<td>Adjusted R^2</td>
</tr>
<tr>
<td>2</td>
<td>0.83</td>
<td>0.81</td>
</tr>
<tr>
<td>3</td>
<td>0.84</td>
<td>0.82</td>
</tr>
<tr>
<td>4</td>
<td>0.89</td>
<td>0.87</td>
</tr>
</tbody>
</table>
**Fig. 15:** The image of liver cirrhosis patient. Flip angle = 15 degrees.

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Fig. 16: The image of liver cirrhosis patient. Flip angle = 18 degrees.

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Fig. 17: The image of liver cirrhosis patient. Flip angle = 21 degrees.

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Conclusion

This study demonstrated the followings.

- The imaging findings of liver cirrhosis reflect the liver function and the uptake of Gd-EOB-DTPA into liver cell.
- The optimal flip angle was 21 degrees in the normal liver functioning patients, and 18 degrees in the liver cirrhosis patients possessing abnormal imaging findings. (In phantom study and 3D-GRE that TR = 4.8msec)
- By using the imaging findings as the indicator, the operators can be selected the optimal flip angle for the Hepatobiliary phase quickly and easily, for each patient.

Consideration

The classification by imaging findings of LC.

In this study, the patients were classified into the two groups by imaging findings. Between normal image group and LC image group, the difference of T1-LT and biochemical data was observed. It suggested that LC imaging findings (Irregularity of liver surface, Splenomegaly, Expanding of hepatic portal) surely reflected the liver function and the uptake of Gd-EOB-DTPA into hepatic cell. Therefore, the possibility that the imaging findings can be the indicator for the optimal FA in HP was shown.

The usefulness of imaging findings as the indicator.

The operator can confirm the imaging findings quickly and easily during the examination. And, the operator does not need any devices to confirm the imaging findings, excepting MRI machine. The imaging findings as the indicator are useful also for the inexperienced operator, because clear criteria have been set for the imaging findings. Provided that the evaluation of the Irregularity of liver surface needs a little expertise.

The optimal FA for each group.

In the self-making phantom study, T1 values of each phantom were obtained exceedingly similar values of clinical case. In 3D-GRE that TR was set to 4.8msec, the optimal FA was 21 degrees in normal image phantom, and 18 degrees in LC image phantom.
In normal image group phantom, the obvious improvement of CNR was confirmed at the optimal FA that compared to the 15 degrees of conventional use.

Contrariwise, the obvious improvement was not confirmed in LC image group phantom. The value of CNR was overall lower than that normal image group. The reason is that the patients with LC cannot obtain the adequate T1-shortening effect by contrast agent. Therefore, the contrast between liver tissue and tumor becomes weak in HP. And, the value of CNR is about the half value of normal image group (Fig. 13, 14). In addition, the high FA setting degraded CNR.

**The consideration about the evaluation using SI, SNR, CNR.**

In GRE sequence, SI becomes the highest at the Ernst angle for each substance. The difference of SI between liver tissue and tumor, will be the maximum at about the Ernst angle of the liver tissue phantoms. However, in view of contrast, the evaluation involving the background noise was required. Because, the weak low intensity lesion cannot be detected in the noisy image. Therefore, the evaluation by SNR and CNR is essential to evaluate the optimal FA. In particular, CNR is the most important. And, to obtain the high CNR, SNR of both of the subject must be high.

The approximate curve was fitted to the scattered CNR-measured value. The most suitable model was obtained by the evaluation of each coefficient (R2, Adjusted-R2, AIC). The most suitable model was extremely useful for accurately evaluating the overall trend of CNR for each phantom.

In normal image group phantom, CNR was the maximum at 21 degrees. However, SNR was the maximum at about 23 degrees. And, SNR of the liver tumor phantom was continued decreasing. Probably, that angle (21 degrees) was FA which SNR of liver tissue phantom was high. And, SNR of tumor phantom was not too low (Fig. 12, 13).

In LC image group phantom, SNR was continued decreasing according to increase of FA. Therefore, CNR decreased rapidly according to increase of FA.

**Clinical LC patient was imaged by the optimal flip angle.**

In clinical LC patient imaging, RMS-CNR was the highest at 18 degrees, and the lowest at 21 degrees. This result shows that FA should be accurately selected for each patient, and the high FA that is generally recommended must not be used for LC patient (Fig. 18). Because the contrast between liver tissue and tumor deteriorate more.
Limitation and Perspective.

The patients were classified into two groups by possessing one or more imaging findings of LC. Therefore, the detailed severity of LC was not evaluated in this study.

The classification by the number of imaging findings the patient possessing, might be able to provide the detailed T1-LT for each patient. And therefore, the FA that is more suitable for each patient might be able to be proposed.
Fig. 12: The Relationship between Signal-noise-to ratio and flip angle.

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Fig. 13: The Relationship between Contrast-noise-to ratio and flip angle. In normal image group. With 4-order approximate curve.

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**Fig. 14:** The Relationship between Contrast-noise-to ratio and flip angle. In LC image group. With 2-order approximate curve.

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**Fig. 18:** RMS-CNR at each flip angle. The minimum at 21 degrees.

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