Quantitative evaluation of focal liver lesions with T1 mapping using a phase-sensitive inversion recovery sequence on gadoxetic acid-enhanced MRI

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Purpose: To determine the usefulness of T1 values measured using a phase-sensitive inversion recovery (PSIR) sequence for the diagnosis of focal liver lesions.

Method: The study enrolled 87 patients who underwent gadoxetic acid-enhanced magnetic resonance imaging (MRI) for assessment of 38 hepatocellular carcinomas, 33 hepatic hemangiomas, 30 metastatic liver tumors, and 14 hepatic cysts. PSIR was performed before and 15 min after contrast agent administration, and then the respective T1 values were measured and the T1 reduction rate was calculated. Wilcoxon matched-pairs signed-rank test was used to compare T1 values pre- and post-contrast administration in each tumor. The Kruskal-Wallis test and Dunn’s post-hoc test were used to compare T1 values among all tumors pre- and post-contrast administration and the T1 reduction rate among all tumors.

Results: The T1 values measured before and after contrast enhancement were 1056 ± 292 ms and 724 ± 199 ms for hepatocellular carcinoma, 1757 ± 723 ms and 1033 ± 406 ms for metastatic liver tumor, 2524 ± 908 ms and 1071 ± 390 ms for hepatic hemangioma, and 3793 ± 207 ms and 3671 ± 241 ms for liver cysts, respectively. The T1 values obtained before and after contrast administration showed significant differences for all tumors except liver cysts (P < 0.0001). T1 reduction rate was not significantly different between hepatocellular carcinoma and metastatic liver tumor, but was significantly different among other tumors (P < 0.05).

Conclusions: T1 mapping using the PSIR sequence is useful to differentiate focal liver lesions.

1. Introduction

Gadoxetic acid is widely used as a liver-specific contrast agent for differentiating focal liver tumors [1–7]. Gadoxetic acid not only enables vascularity assessment during dynamic studies but also increases the T1 contrast between normal liver parenchyma and tumor in the hepatobiliary phase (HBP). However, uptake of gadoxetic acid into liver parenchyma is reduced by impaired liver function, which may cause focal liver lesions to be missed [8,9]. Although most malignant liver lesions present with hypointensity in the HBP, benign liver lesions such as hemangiomas also show hypointensity in the HBP, making it difficult to distinguish these lesions [10–12]. For this reason, various methods for differentiating focal liver lesions have been investigated and reported [13–16].

T1 mapping enables quantification of T1 values for comparisons across images, and the usefulness of focal liver lesion differentiation using T1 values has been reported [17–19]. However, the conventional T1 mapping method still has problems related to versatility and T1 measurement accuracy [20,21]. In contrast, T1 mapping using phase-sensitive inversion recovery (PSIR) has been validated in studies of phantoms and healthy subjects, and has been reported to have high T1 value measurement accuracy [22]. Furthermore, the use of PSIR for T1 mapping has been frequently employed for cardiac magnetic resonance imaging (MRI) recently, and this approach may be applied to various...
regions due to its high versatility [23,24].

In this study, we measured the T1 values of focal liver lesions using PSIR before and after gadoxetic acid injection, examining the usefulness of T1 mapping using PSIR in the differential diagnosis of focal liver lesions.

2. Materials and methods

2.1. Subjects

This study was approved by our Institutional Review Board, and written informed consent was obtained from all participants before the MR examinations. We enrolled 183 patients who underwent gadoxetic acid-enhanced MRI at our hospital from May 2018 to October 2019. We excluded patients with liver lesions that had not been confirmed by computed tomography (CT) and/or MRI. After applying this criteria, a total of 87 patients (50 men, 37 women; age range, 35–91 years; mean age, 69 ± 13 years) were enrolled in this study, including 28 patients (16 men, 12 women) diagnosed with 38 hepatocellular carcinomas (HCCs), 27 patients (19 men, 8 women) diagnosed with 33 hepatic hemangiomas, 21 patients (10 men, 11 women) diagnosed with 30 metastatic liver tumors, and 11 patients (4 men, 7 women) diagnosed with 14 liver cysts (Fig. 1). No magnetic resonance (MR) examinations were performed for other tumors in this study. The primary metastatic liver tumors were colorectal cancers in all patients. All of the liver lesions were diagnosed on the basis of typical CT and/or MRI features.

2.2. MRI protocol

All studies were performed on a 3.0-T clinical MRI system (Ingenia, Philips Healthcare, Best, the Netherlands) with a 32-channel phased-array body receiver coil. First, all patients underwent two-dimensional T1-weighted fast gradient-echo (GRE) in phase and opposed phase, T2-weighted turbo spin-echo, diffusion-weighted imaging, and T1-weighted three-dimensional (3D) fast GRE sequences based on the standard liver MR examination protocol at our institution. Details of the MR parameters of the respective sequences are shown in Table 1. Second, for T1 mapping, PSIR was performed before and 15 min after injection of gadoxetic acid consistently in each patient. The T1 mapping method using the PSIR sequence has been described in a previous report [22]. The major characteristic of the PSIR is the 3D turbo field echo (TFE) readouts at the two inversion times (TIs) after applying a non-selective adiabatic inversion recovery pulse. The T1 values were estimated using two T1 images acquired from the inversion recovery-prepared data and reference data with the same flip angle (FA). The imaging parameters were as follows: repetition time, 20 ms; echo time (TE), 1.82, 5.82, 9.82, 13.82, and 17.82 ms; TFE factor, 35; FA, 10°; shot interval, 1500 ms; TIs, 500 and 2500 ms; field of view, 360 × 300 mm²; matrix, 180 × 120; slice thickness, 6 mm; number of slices, 1; number of slices, 5; acceleration factor, 2; k-space profile ordering, low–high; fat-suppression, spectral pre-saturation with inversion recovery; and scan time, 13.5 s (a single breath-hold). Although PSIR can be used to measure not only the T1 value but also the T2* value acquired with multi TEs, we did not measure T2* values in this study. All patients were administered body weight-adjusted (0.025 mmol/kg) doses of gadoxetic acid as bolus injections in 4 s.

2.3. Image analysis

We measured the T1 values of the focal liver lesions of each patient. The region of interest (ROI) was set on the lesions as precisely as possible, and the T1 value was obtained on a T1 map (Fig. 2). The T1 reduction ratios were calculated using pre-contrast and post-contrast T1 values as follows:

\[ \text{T1 reduction ratio} = \frac{\text{pre-T1 value} - \text{post-T1 value}}{\text{pre-T1 value}} \times 100 \]

The ROIs were defined by one of the authors (M. M. with more than 10 years of experience with MRI). T1 maps were generated using image-processing software (MATLAB2015a, MathWorks, Natick, MA, USA). The specific calculation method of the T1 value was the same as that reported previously, and the T1 value was calculated based on the relationship between the two IR magnetization evolutions [22].

2.4. Statistical analyses

Statistical analyses were performed using Prism 6.0 (GraphPad software, La Jolla, CA, USA). We compared pre-contrast and post-contrast T1 values in each focal liver lesion using the Wilcoxon matched-pairs signed-rank test. The Kruskal-Wallis test with Dunn’s post-hoc test for multiple comparisons was used to analyze the differences in pre-contrast T1 values, post-contrast T1 values, and T1 reduction rates among focal liver lesions. Additionally, receiver operating characteristic (ROC) curves were used to determine T1 cut-off values for optimal differentiation among focal liver lesions. The diagnostic performance for differentiating focal liver lesions were evaluated by calculating the area under the ROC curve (AUC), and the optimal T1 cut-off values were calculated with Youden index. A P value less than 0.05 was considered to indicate a significant difference for each tests.

3. Results

The pre- and post-contrast T1 values and T1 reduction rates are shown in Table 2. Liver cysts showed the longest pre- and post-contrast T1 values, and the shortest pre- and post-contrast T1 values were observed for HCC. The T1 reduction rate was the highest for hepatic hemangiomas and lowest for liver cysts. HCCs, hepatic hemangiomas, and metastatic liver tumors showed shortened T1 values after injection of gadoxetic acid, with significant differences between pre- and post-contrast T1 values (Fig. 3). The Kruskal-Wallis test with Dunn’s multiple comparisons test showed no significant difference in the pre-contrast T1 value between hepatic hemangioma and liver cyst (P = 0.076) or the post-contrast T1 value between hepatic hemangioma and metastatic liver tumor (P > 0.99). The T1 reduction rate was not significantly different between HCC and metastatic liver tumors (P = 0.66). The comparisons of other combinations of focal liver lesions showed statistically significant differences (Fig. 4). Table 3 shows the T1 cut-off values between each pair of focal liver lesions determined by the ROC analysis.

4. Discussion

In this study, we applied T1 mapping using PSIR to measure T1 values of focal liver lesions. Although MR signal intensity (SI) does not
correlate linearly with the concentration of contrast agent, a change in the longitudinal relaxation rate (1/T1) is directly proportional to the concentration of the contrast agent in the tissue [25]. As such, it is important to measure T1 values of focal liver lesions. Additionally, T1 mapping may serve as a quantitative assessment method that is less affected by MR parameters and MR systems than SI measurements [26–28]. However, there are some problems in the conventional T1 mapping method. The dual FA method requires two optimal FAs, and it is necessary to know the T1 value to be measured in advance [20]. The Lock-Locker method shows high T1 value dependence, because of which the measurement error increases as the T1 value becomes longer [21]. By contrast, PSIR applied in this study is less dependent on the T1 value, offering the advantage of more accurate T1 measurements than the conventional T1 mapping method [22].

Furthermore, because PSIR uses a non-selective adiabatic inversion recovery pulse, measured T1 values may be less susceptible to B1 inhomogeneity than those of the dual FA method. In addition, another advantage of PSIR is its feasibility in clinical practice because it is a sequence commonly used in the cardiac area [23, 24]. These findings suggest that T1 mapping using PSIR can be applied in various body regions due to its high measurement accuracy and versatility.

According to Table 1, the pre-contrast T1 values for HCC and metastatic liver tumors were 1056 ± 292 ms and 1757 ± 723 ms, respectively. These values were close to those of a previous study, suggesting that T1 mapping using PSIR yields reproducible results that are similar to those of previously reported methods [19]. On the contrary, the T1 values for liver cysts and hepatic hemangiomas were longer than those for HCCs and metastatic liver tumors. The results could be explained by the abundance of liquid components inside these tumors [29]. A previous study reported that the pre-contrast T1 value for hepatic hemangioma was 1432 ± 600 ms [19]. The pre-contrast T1 value of hepatic hemangiomas measured using PSIR was 2524 ± 908 ms, which was longer than the previously reported value. The conventional T1 mapping
Fig. 3. Representative T1 mapping images obtained using phase-sensitive inversion recovery before (left side) and after contrast agent administration (right side) in patients with (a) hepatocellular carcinomas, (b) metastatic tumor, (c) hemangioma, and (d) cyst.

Fig. 4. Results of multiple comparisons among focal liver lesions. (a) Pre-contrast T1 value, (b) post-contrast T1 value, and (c) T1 reduction rate.
### Table 3

|                  | Pre-contrast T1 value (ms) | T1 reduction rate (%) | 95% CI       |
|------------------|---------------------------|-----------------------|--------------|
|                  | T1                        |                       |              |
| HCC vs. metastatic tumor | 0.817                      | 0.633                 | <0.001       |
| HCC vs. cyst      | 1.000                      | 1.000                 |              |
| Hemangioma vs. cyst | 0.903                      | 1.000                 |              |
| Metastatic tumor vs. cyst | 0.988                  | 1.000                 |              |

*CI: confidence interval.*
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Declaration of Competing Interest
The authors report no declarations of interest.

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