Gadoxetic Acid-Enhanced MRI Versus Multiphase Multidetector Row Computed Tomography for Evaluating the Viable Tumor of Hepatocellular Carcinomas Treated With Image-Guided Tumor Therapy

Jiyoung Hwang, MD,1 Seong Hyun Kim, MD,1* Young-Sun Kim, MD,1 Min Woo Lee, MD,1 Ji Young Woo, MD,2 Won Jae Lee, MD,1 and Hyo K. Lim, MD1

Purpose: To compare the diagnostic performance of gadoxetic acid-enhanced MRI with that of multi-phase 40- or 64-multidetector row computed tomography (MDCT) to evaluate viable tumors of hepatocellular carcinomas (HCCs) treated with image-guided tumor therapy.

Materials and Methods: A total of 108 patients with 162 HCCs (56 lesions with viable tumor and 106 without viable tumor) treated by means of transcatheter arterial chemoembolization or radiofrequency ablation were retrospectively included in this study. All patients underwent multi-phase CT at 40- or 64-MDCT and gadoxetic acid-enhanced MRI using 3.0 Tesla (T). Two observers independently and randomly reviewed the CT and MR images of the treated lesions. The diagnostic performance of two techniques for the evaluation of the viable tumors in the treated lesions was assessed with a receiver operating characteristic (ROC) analysis.

Results: For each observer, the areas under the ROC curve were 0.953 and 0.969 for MRI, and 0.870 and 0.888 for MDCT (P < 0.05). The diagnostic accuracies (96.3% for each observer) and sensitivities (92.9% and 96.4%) of MRI in two observers were significantly higher than those (82.7% and 80.9%, 53.6% for each observer, respectively) of MDCT (P < 0.001). The negative predictive values (96.3% and 98.1%) of MRI in two observers were significantly higher than those (80.0% and 79.5%) of MDCT (P < 0.001). For each observer, specificities and positive predictive values did not differ significantly between the two techniques (P > 0.05).

Conclusion: Gadoxetic acid-enhanced MRI shows better diagnostic performance than that of MDCT for evaluating the viable tumors of HCCs treated with image-guided tumor therapy.

Key Words: hepatocellular carcinoma; image-guided tumor therapy; MDCT; gadoxetic acid-enhanced MRI

HEPATOCELLULAR CARCINOMA (HCC) is the most common primary liver cancer. Although surgery remains the treatment of choice for HCC, several minimally invasive techniques have been used as alternatives to surgery for the treatment of HCCs. These include transcatheter arterial chemoembolization (TACE) and image-guided tumor ablation therapies, including percutaneous ethanol injection therapy (PEIT), percutaneous microwave coagulation therapy, and radiofrequency ablation (RFA) (1). Although several therapeutic options have been proposed, the most widely used image-guided tumor therapies are TACE, RFA, or a combination of these two. After image-guided tumor therapy of HCCs, CT and MRI perform a crucial role in assessing the therapeutic efficacy and monitoring local tumor progression in the treated HCCs during follow-up and early detection of a viable tumor including residual tumor (i.e., incompletely treated tumor on immediate or 1-month follow-up CT after locoregional therapy) or local tumor progression (i.e., any growing or enhancing tumor in the treated lesion, where there had been no evidence of a residual tumor after locoregional therapy) can facilitate successful retreatment at an early stage (2–5).

MDCT, which has the advantages of greater speed, thinner slices, and multiphasic scanning, has improved the chances of detecting HCC (6,7). High-field-strength (3.0 Tesla [T]) MRI has been previously shown to have the advantages of better signal-to-noise ratio and image quality than 1.5T MRI, thereby...
improving lesion detection (8–10). Additionally, the use of liver-specific contrast agents such as gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (gadoteric acid disodium, Primovist, Bayer Schering Pharma) produces both dynamic and liver-specific hepatobiliary MR images, thus improving both detection and characterization of focal liver lesions (11–13). To the best of our knowledge, there have been no comparative studies of gadoteric acid-enhanced 3.0T MRI and multiphase 40- to 64-MDCT for the evaluation of viable tumor of HCCs after TACE or RFA of HCCs in patients with chronic liver disease. The purpose of our study, therefore, was to compare the diagnostic performance of gadoteric acid-enhanced MRI with that of multiphase 40- or 64-MDCT for the evaluation of viable tumors of HCCs treated with image-guided tumor therapies, such as TACE and RFA, in patients with chronic liver disease.

**MATERIALS AND METHODS**

**Patient Selection**

This study was conducted with the approval of the institutional review board of our institution. Informed consent was not required for this retrospective study. Between April 2008 and June 2009, among a total of 2680 consecutive patients with chronic liver disease suspected of having HCC on the basis of their imaging findings: the appearance of a new hypervascular tumor on CT or MRI during follow-up, the characteristic enhancement pattern on contrast-enhanced multiphase MDCT (hypervascular at arterial phase and wash-out at portal or equilibrium phase) and/or gadoteric acid-enhanced MRI (hypervascular at arterial phase, wash-out at portal or 3-min late phase, and hypointensity without uptake in hepatobiliary phase), and elevated serum a-fetoprotein level (a-fetoprotein level > 200 ng/mL), one study coordinator retrospectively collected 157 consecutive patients for whom the following criteria were fulfilled: chronic liver disease with HCCs that had been treated with TACE and/or RFA; had undergone both multiphase CT at 40- or 64-MDCT and gadoteric acid-enhanced MRI using 3.0T with less than a 3-month time interval (range, 5 – 90 days; mean, 52 days) between the two examinations were repeated usually every 3 months because of suspected complications or the clinician’s decision. Underlying liver cirrhosis was associated with viral hepatitis B in 86 patients, viral hepatitis C in 16 patients, and alcoholic cirrhosis in six patients. The initial diagnosis of the 162 HCCs (mean, 1.8 cm; range, 1.2–9.5 cm) before image-guided tumor therapy in patients with chronic liver disease were confirmed by means of ultrasonography-guided percutaneous needle biopsy for 24 tumors, and the remaining 138 tumors were identified as HCC by a combination of the characteristic imaging findings and laboratory findings.

Among 162 treated HCCs, 56 lesions were proved to have the viable tumors in treated HCC, as follows: compared with CT/MRI enrolled in the study, viable tumors that were diagnosed depending on the follow-up imaging findings of increase in size of enhancing area which is suspected of viable tumor in the treated lesion and/or sustained iodized-oil accumulations in the hypervascular area corresponding to suspected viable tumor of treated lesions seen on CT and MRI on the hepatic arteriography with repeated TACE. The size of viable tumors in 56 treated lesions ranged from 0.7 to 5.1 cm in diameter (mean diameter, 1.6 cm). For 56 treated lesions with viable tumors, the time interval between two techniques was less than 1-month (range, 5 –30 days; mean, 21 days). The remaining 106 lesions were proved to have no viable tumors in the treated HCCs, as follows: compared with CT/MRI enrolled in the study, stable lesion (no change or decrease in size of treated lesion with no hypervascular portion) or disappearance or decrease in size of hypervascular pseudolesions at the periphery of treated lesions on CT or MRI in 6-month or longer follow-up images, in addition to the negative findings on the follow-up iodized-oil CT after repeated TACE.

**Imaging Methods**

Multiphase (contrast-enhanced hepatic arterial, portal venous and equilibrium phases) CT was conducted with a 40-MDCT scanner (Brilliance 40, Philips Healthcare) in 15 patients, and with a 64-MDCT scanner (Aquilion 64, Toshiba Medical, and light speed VCT 64, GE healthcare) in 93 patients. Unenhanced CT scans were also obtained in all patients with HCCs treated with TACE. The scanning parameters were as follows: 120 kVp, 189–200 mAs, 5-mm slice thickness with an increment (overlap) of 2.5 mm, table speed of

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Role of Gadoxetic Acid-Enhanced MRI

26.5–39.37 mm/rotation (pitch, 0.828–1.07), and a single-breath-hold helical acquisition of 4–6 s depending on liver size. Images were obtained in the cranio-caudal direction. Hepatic arterial phase scanning began 30–40 s after the injection of 120 mL of a non-ionic iodinated contrast agent (iopamidol, iopamiro 300, Bracco) at a rate of 3–4 mL/s by means of a bolus-triggered technique (120 kVp; 40–60 mA; monitoring frequency from 12 s after the contrast injection, 1 s; trigger threshold, 100 HU in descending aorta; delay from trigger to initiation of scan, 18 s). The contrast agent was administered through the antecubital vein with a power injector. The portal and equilibrium phases of scanning began 70 s and 180 s after the injection of the contrast agent, respectively.

MRI was conducted using a 3.0T whole-body MRI system (Intera Achieva 3.0 T, Philips Healthcare) with a 16-channel phased-array coil as the receiver coil. The liver was imaged in the axial plane in all patients both before and after the administration of gadoxetic acid at a dose of 0.1 mL/kg (0.25 mmol/mL). The contrast agent was administered through the antecubital vein with a power injector at a rate of 2 mL/s, followed by a 20 mL saline flush.

The MRI protocol included a respiration-triggered T1-weighted turbo field-echo in-phase sequence (repetition time/echo time [TR/TE], 10/2.3; flip angle, 15°; matrix size, 288 × 230; bandwidth, 434.3 Hz/pixel) and an out-of-phase sequence (10/3.45; flip angle, 15°; matrix size, 288 × 230; bandwidth, 434.3 Hz/pixel), a respiration-triggered single-shot T2-weighted sequence with a reduction factor of 2 or 4 (1,342/80; flip angle, 90°; matrix size, 320 × 256; bandwidth, 506.4 Hz/pixel), a breath-hold multislab T2-weighted sequence with a reduction factor of 2 or 4 (2,161/70; flip angle, 90°; matrix size, 400 × 280; bandwidth, 235.2 Hz/pixel), a respiration-triggered single-shot heavily T2-weighted sequence with a reduction factor of 2 or 4 (1,573/160; flip angle, 90°; matrix size, 320 × 256; bandwidth, 317.9 Hz/pixel) with a 5–7-mm section thickness and a 1–2-mm intersection gap and a field of view of 32–38 cm. For gadoxetic acid-enhanced MRI, unenhanced, arterial phase (20–35 s; delay from trigger to initiation of scan, 18 s) and portal and equilibrium phases of scanning began 70 s and 180 s after the injection of the contrast agent, respectively. The diagnostic accuracy, sensitivity, and specificity of each technique for each observer was assessed by operating characteristic (ROC) curve was generated on a tumor-by-tumor basis. The diagnostic performance of each technique for each observer was assessed by calculating the number of lesions assigned a confidence level of 4 or 5. In clinical practice at our institution, viable tumors after RFA were considered as any enhancing lesions within or abutting the treated lesion at the arterial phase with washout pattern at the delayed phase of the CT examination based on previous reports (14,15). The definition for viable tumor on gadoxetic acid-enhanced dynamic MRI was similar to that on CT. In addition to the foregoing features, an area with moderate hyperintensity on T2-weighted MR images and hypointensity on gadoxetic acid-enhanced hepatobiliary phase MR image compared with surrounding liver parenchyma was considered a viable tumor based on previous reports (3,5,6,13). The criteria for viable tumors on CT and gadoxetic acid-enhanced MRI after TACE were similar to those for viable tumors after RFA, and these criteria were based on previous reports (2,4,6,16–18).

To avoid a mismatch between the findings on the scored lesions and the findings of treated lesions, each observer recorded the individual image number, the segmental location of all lesions, and the entire size of each treated lesion. For patients with two or more lesions in one segment, detailed descriptions of the location of the lesion in each segment were added to avoid confusion in the data analysis. The time interval between reviews of CT and MR images was established as at least 4 weeks to minimize any learning bias.

After the two observers had completed the review, the study coordinator with three years of experience in abdominal imaging with two observers compared the scoring results of each observer with the reference standard, and devised a possible explanation for the causes of the consensus false-positive and false-negative findings made by the observers.

Statistical Analysis

On the basis of the two observers’ reviews, a receiver operating characteristic (ROC) curve was generated on a tumor-by-tumor basis. The diagnostic performance of each technique for each observer was assessed by measuring the area under the ROC curve (A2), in accordance with the methods of Hanley and McNeil (19). The diagnostic accuracy, sensitivity, and specificity of each observer and technique in the detection of viable tumors were calculated. The true-positive lesions were identified as those that were assigned a confidence level of 4 or 5 by the observers, and were proved to have viable tumors. False-negative lesions were those assigned a confidence level of 1, 2, or 3, but which...
were actually determined to have viable tumors. False-positive lesions were those assigned a confidence level of 4 or 5, but which were actually determined to have no viable tumors. The differences in the diagnostic accuracy, sensitivity and specificity were statistically analyzed by means of McNemar’s test. Statistical analyses of differences in the calculated positive and negative predictive values for each observer and technique were based on a previous report (20). A value of \( P < 0.05 \) was considered statistically significant. An analysis of all false-positive and false-negative observations was also undertaken. To evaluate interobserver agreements in the evaluation of the viable tumor with each technique, kappa statistics were used. The degree of agreement was categorized as follows: kappa values of 0.00–0.20 were considered indicative of poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and 0.81–1.00, excellent agreement (21).

**RESULTS**

Table 1 shows the Az values for each observer and each technique for the evaluation of the viable tumors of HCCs treated with image-guided tumor therapy. Az values for gadoxetic acid-enhanced MRI were significantly higher than those for MDCT in two observers \(( P < 0.05)\). Table 2 shows diagnostic predictive values between the two techniques for each observer. Two observers achieved significantly higher diagnostic accuracy and sensitivity with gadoxetic acid-enhanced MRI than with MDCT \(( P < 0.001)\). The specificity of the two techniques for each observer was similar \(( P > 0.05)\). The negative predictive values of gadoxetic acid-enhanced MRI in two observers were higher than those of MDCT with significant difference \(( P < 0.001)\). The positive predictive values of gadoxetic acid-enhanced MRI in two observers tended to be higher than those of MDCT, although this difference was not significant \(( P > 0.05)\).

Two observers recorded 52 false-negative CT (22 HCCs treated with TACE and 28 HCCs treated with RFA, two HCC treated with both TACE and RFA) and six false-negative MRI (four HCCs treated with TACE and two HCCs treated with RFA) results. Forty-six of 52 false-negative CT findings were detected by MRI and none of six false-negative MRI findings were detected by CT. False-negative CT findings were attributed to viable tumors with hypervascular enhancement on arterial phase images with no washout pattern in 26 cases (mean size of viable tumors, Table 1)

| Technique                        | Observer 1     | Observer 2     |
|----------------------------------|----------------|----------------|
| MDCT                             | 0.870 ± 0.033  | 0.888 ± 0.031  |
| Gadoxetic acid-enhanced MRI      | 0.953 ± 0.020  | 0.969 ± 0.017  |
| Difference in Az                 | 0.083 ± 0.033  | 0.081 ± 0.032  |

Values are Az ± one standard error. The differences in Az of the two techniques for each observer are statistically significant \(( P < 0.05)\). Data in parentheses are 95% confidence intervals.

| Technique                        | Observer 1     | Observer 2     |
|----------------------------------|----------------|----------------|
| Diagnostic accuracy (%)          | 82.7 (134)     | 80.9 (131)     |
| Sensitivity per lesion (%)       | 53.6 (30)      | 53.6 (30)      |
| Specificity per lesion (%)       | 98.1 (104)     | 95.3 (101)     |
| Positive predictive value (%)    | 93.8 [30/32]   | 85.7 [30/35]   |
| Negative predictive value (%)    | 80.0 [104/130] | 79.5 [101/127] |

Numbers in parentheses in diagnostic accuracy, sensitivity, specificity, and positive and negative predictive values are the numbers of correctly interpreted lesions, true-positive, true-negative, false-positive, and false-negative lesions, respectively. For positive predictive value, numbers in brackets are the number of true-positive lesions divided by the total number of lesions assigned a confidence level of 4 or 5. For negative predictive value, numbers in brackets are the number of true-negative lesions divided by the total number of lesions assigned a confidence level of 1, 2, or 3. The diagnostic accuracies, sensitivities, and negative predictive values of two techniques for each observer were statistically significant \(( P < 0.05)\). The specificities and positive predictive values of two techniques for each observer were not statistically significant \(( P > 0.05)\).
1.1 cm; size range of viable tumors, 0.7–2.6 cm) (50%), small size of viable tumor (hypervascular at arterial phase and wash-out at equilibrium phase) in 15 cases (mean, 0.8 cm; range, 0.7–0.9 cm) (29%), heterogeneous uptake of iodized oil in the treated lesion in 10 cases (19%), and interpretation error due to adjacent vessels in one case (2%). False-negative MRI findings were attributed to small size of viable tumor (hypervascular at arterial phase, wash-out at 3-min late phase and hypointensity on hepatobiliary phase) in four cases (mean, 0.8 cm; range, 0.7–0.9 cm) (67%) and isointensity of the viable tumor compared with the surrounding liver on gadoxetic acid-enhanced hepatobiliary phase MR images in two cases (33%).

There were 14 viable tumors (four HCCs treated with TACE and 10 HCCs treated with RFA) in 13 patients that were not detected by any of two observers on MDCT but were detected on gadoxetic acid-enhanced MRI by all of two observers. In the retrospective review, eight viable tumors showed faint hypervascularity on arterial phase CT images and no washout pattern on equilibrium phase with poor conspicuity (Fig. 1). Two viable tumors (each 1.9 cm and 0.7 cm in diameter) in two treated lesions were masked due to heterogeneous uptake of iodized oil in the treated lesions, which interfered with contrast-enhanced assessment on arterial phase CT images. However, the viable tumors showed enhancement on gadoxetic acid-enhanced arterial phase MR images and hypointensity on the hepatobiliary phase without the influence of iodized oil (Fig. 2). The remaining four viable tumors were less than 1 cm in diameter.

All of two observers were unable to detect a viable tumor in only one lesion treated with TACE on both gadoxetic acid-enhanced MRI and MDCT (Fig. 3). Upon retrospective analysis, the viable tumor was

Figure 1. A 38-year-old man with a 1.2-cm-diameter viable HCC tumor treated with RFA in the right lobe of the liver. a: Contrast-enhanced CT scan obtained at arterial phase shows perilesional enhancement (arrow) around the treated lesion without washout pattern on equilibrium phase (not shown). All observers did not recognize a viable tumor in the treated lesion. b: On T2-weighted MR image, a hyperintense nodule (arrow) is seen at the margin of isointense ablated lesion (asterisk). c,d: On gadoxetic acid-enhanced arterial (c) and (d) hepatobiliary phase MR images, a viable tumor (arrow) shows hypervascular enhancement and hypointensity, respectively, at the margin of the treated lesion (asterisk). All observers recognized a viable tumor in the treated lesion. e: Unenhanced CT scan obtained after TACE reveals iodized-oil accumulation of the corresponding viable tumor (arrow) at the margin of treated lesion (asterisk).
small in size (1.2 cm) and located in the liver dome, which resulted in poor conspicuity with the isointense viable tumor on gadoxetic acid-enhanced hepatobiliary phase MR images and a faint hypervascularity with no washout on CT images.

For all observers, seven false-positive CT findings (two HCCs treated with TACE, four HCCs treated with RFA and one HCC treated with both TACE and RFA) and six false-positive MRI findings (three HCCs treated with TACE and three HCCs treated with RFA) were detected. False-positive CT findings were attributed to two heterogeneous uptake of iodized oil (29%), two arteriportal shunts (29%), and four interpretation errors (42%). False-positive MRI findings were attributed to four arteriportal shunts (Fig. 4) (67%) and heterogeneity of two treated lesions (33%).

The kappa values between the two observers showed excellent agreement with MRI and moderate agreement with CT (Table 3).

DISCUSSION

After image-guided tumor therapy in patients with HCCs, precise imaging evaluation for the viable tumor in treated HCCs is important because early detection of residual tumors or local tumor progression after image-guided tumor therapy is critical, and can facilitate successful retreatment at an early stage.

A variety of imaging techniques have been introduced for the evaluation of therapeutic efficacy after performing TACE and RFA for HCC (2–5). Several investigators suggested that dynamic MRI using 1.5T...
was the best modality for evaluating the therapeutic effect of TACE and RFA on HCC (4,5).

However, there have been no comparative studies of gadoxetic acid-enhanced 3.0T MRI and multiphase 40- to 64-MDCT for the evaluation of viable tumors of HCCs treated with TACE and RFA. In our study, two observers achieved significantly higher Az values, diagnostic accuracies, sensitivities and negative predictive values when using gadoxetic acid-enhanced 3.0T MRI as compared to MDCT. The previously reported sensitivity of CT and MRI for the detection of small foci of residual or recurrent tumors after RFA ranged from 36–89% in the published literature (22). Several investigators have reported a sensitivity of 45–49% for the detection of HCC recurrence after TACE with CT scans combined with serum α-fetoprotein level (18,23). Kubota et al (4) reported a sensitivity of 100% with dynamic MRI for the detection of viable tumors after TACE. Although the study design was different, our results (sensitivity 53.6% with MDCT and 92.9–96.4% with MRI) were comparable to those of previous reports.

In our study, several factors caused false-negative and false-positive results. The majority (50%) of false-negative CT findings were attributed to atypical enhancement pattern (hypervascular at arterial phase and no wash-out pattern at equilibrium phase), which may be confused with arterioportal shunt or reactive hyperemia around the treated lesion. Several investigators reported that, when HCCs are small, they

Figure 3. A 57-year-old man with a 1.2-cm-diameter viable HCC tumor treated with TACE in the dome of the right lobe of the liver. a: Unenhanced CT scan shows two foci of iodized-oil accumulation (arrows) in treated HCCs after TACE. b: Contrast-enhanced CT scan obtained at arterial phase at the same level as (a) shows a faint enhancement between two foci of iodized-oil accumulation (arrow) with no washout pattern at equilibrium phase (not shown). All observers did not recognize a viable tumor in the treated lesion. c: T2-weighted MR image shows a viable tumor (arrow) with moderate hyperintensity at the anterior margin of relatively hypointense treated lesion (arrowhead) with iodized-oil accumulation. d: Gadoxetic acid-enhanced arterial phase MR image shows a viable tumor (arrow) with enhancement at the anterior margin of the treated lesion (arrowhead). e: Gadoxetic acid-enhanced hepatobiliary phase MR image shows a viable tumor (arrow) with isointensity relative to surrounding liver parenchyma at the anterior margin of the treated lesion (arrowhead). All observers did not recognize a viable tumor in the treated lesion. f: Unenhanced CT scan obtained after TACE shows iodized-oil accumulation at the corresponding viable tumor (arrow) of the treated lesion.
have high chance of atypical enhancement pattern other than typical enhancement pattern of HCC (hypervascular at arterial phase and wash-out at portal and/or equilibrium phases) (24,25). In our study, the viable tumors in treated lesions that showed atypical enhancement pattern on MDCT were small (mean, 1.1 cm), which might be the main reason of false-negative CT results. We concluded that multiphase MDCT continues to be limited in terms of its ability to detect viable tumors with atypical enhancement in treated HCCs as in our cases, although this technique has high spatial and temporal resolution. On the other hand, we believe that additional information for differentiating the viable tumor with atypical enhancement from arteriportal shunt or reactive hyperemia can be acquired by means of gadoxetic acid-enhanced dynamic and hepatobiliary-phase MR images in addition to unenhanced MR images in some cases.

In our study, 29% of false-negative CT findings and 67% of false-negative MRI findings were attributed to small viable tumors in treated lesions, although they showed typical imaging findings of HCCs on retrospective review. We concluded that small viable tumors in treated lesions could be difficult to easily recognize from treated lesions, which may be obscured by inflammatory enhancement related to the procedure.

Our study showed that 19% of false-negative CT findings and 29% of false-positive CT findings were attributed to beam hardening artifacts of iodized oil. When evaluating the viable tumor on contrast-enhanced CT, it

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**Figure 4.** A 76-year-old man with no viable tumor in HCC treated with TACE in the right lobe of the liver. **a:** Contrast-enhanced CT scan obtained at arterial phase shows a treated lesion (arrow) with iodized-oil accumulation with no enhancement around the treated lesion as compared to unenhanced CT scan (not shown). All observers recognized no viable tumor in the treated lesion. **b:** T2-weighted MR image shows a treated lesion with a faint hyperintensity (arrows). **c:** Gadoxetic acid-enhanced arterial phase MR image shows a small nodular enhancement (arrow) in the periphery of the treated lesion. **d:** Gadoxetic acid-enhanced hepatobiliary phase MR image shows a treated lesion with hypointensity (arrow). The lesion was misinterpreted as the lesion with a viable tumor by two observers (false-positive result).

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**Table 3**
Interobserver Agreement for Presence of the Viable Tumor of Hepatocellular Carcinoma Treated With Image-Guided Tumor Therapya

| Technique                  | Observer 1 vs Observer 2 |
|----------------------------|--------------------------|
| MDCT                       | 0.567                    |
| Gadoxetic acid-enhanced MRI| 0.891                    |

aNumbers are kappa values.
has been thought that after TACE, assessment of contrast enhancement may prove difficult because of partial uptake of iodized oil within a tumor on contrast-enhanced CT, which results in beam-hardening artifacts due to the high attenuation of iodized oil. However, we believe that the contrast enhancement of MRI is not affected by the presence of iodized oil, which is one of the advantages of MRI improving diagnostic accuracy for detecting viable tumors, as previously reported (26) and our results.

In our study, 33% of false-negative MRI findings were attributed to isointensity of the viable tumor on gadoxetic acid-enhanced hepatobiliary phase images. We believe that correct interpretation may be limited for viable tumors with gadoxetic acid uptake on gadoxetic acid-enhanced hepatobiliary phase images as reported previously (6).

In our study, 29% of false-positive CT findings and 67% of false-negative MRI findings were attributed to arterioportal shunts. Hemodynamic alteration, such as microscopic arterioportal shunting around the treated HCC after RFA or TACE, or hypervascular enhancement around RFA representing inflammatory reactions to thermal injury, can occur (22,27). As described in several previous reports (2,3), we believe that this hemodynamic alteration owing to image-guided tumor therapy can resemble or mask HCCs. However, as in a previous report (6), and our retrospective review, none of this hemodynamic alteration showed hypointensity on gadoxetic acid-enhanced hepatobiliary phase images, which may prove helpful in the differentiation of those from viable tumor with典型 hyperintensity on hepatobiliary phase images.

In our study, 33% of false-positive MRI findings were attributed to the heterogeneity of the treated lesion. HCCs treated with TACE or RFA have been known to have variable signal intensity on unenhanced T1- and T2-weighted images due to coagulative necrosis and/or iodized oil (15,27,28). Generally, the hypointensity on T2-weighted images is representative of coagulation necrosis. Conversely, the hyperintensity corresponding to hemorrhage or residual tumor (4). Dromain et al (5) reported that moderate hyperintensity on T2-weighted images corresponded to the presence of viable tumors in all cases, and suggested that T2-weighted imaging is highly specific. However, we believe that the presence of areas of hyperintensity on T2-weighted images does not consistently correspond to the viable tumor, as in our cases and a previous report (3).

Our study has several limitations. First, not all of the included patients underwent surgical resection after TACE and RFA. Therefore, the lack of pathological correlation is one limitation of this study. However, it is not possible to obtain lesion-by-lesion histopathologic proof, because hepatic resection is not generally performed in patients who have been treated with image-guided tumor therapies such as TACE and RFA. Additionally, post-treatment biopsies cannot substitute for a resected specimen, as the material retrieved at biopsy does not represent the entire tumor, and small portion of the viable tumor can go undetected. Second, to exclude the possibility of false-negative results, all of the patients considered not to harbor viable tumors in treated HCCs were followed up for more than 6 months. Nevertheless, the follow-up period may have been insufficient to detect late tumor recurrences in the treated lesions. Third, we used state-of-the-art 3.0T MRI and standard CT technique with a relatively low iodine concentration (300 mg/mL) and a slow injection rate (3–4 mL/s). State-of-the-art CT technique with higher iodine concentration and a faster injection rate may yield results superior to those achieved using our study protocol.

In conclusion, gadoxetic acid-enhanced MRI shows better diagnostic performance than that of MDCT for the evaluation of viable tumors of HCCs treated with image-guided tumor therapies such as TACE and RFA. Therefore, when MDCT is inconclusive in detecting viable tumors of HCC treated with image-guided tumor therapy in patients with chronic liver disease, gadoxetic acid-enhanced MRI can provide more confident information regarding the viability of treated HCCs than can MDCT.
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