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Early assessment of coagulation necrosis after hepatic microwave ablation: a comparison of non-enhanced and enhanced T1-weighted images

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Abstract

Purpose: To compare the technical success and accuracy of hepatic microwave ablation (MWA) using non-enhanced and enhanced T1-weighted imaging early after ablation. Patients were evaluated with regard to the ablation zone and local tumor progression (LTP).
Methods: This retrospective study conducted between September 2014 and December 2015 which consisted of 56 patients with 56 hepatic malignant lesions who underwent percutaneous MWA. Non-enhanced and contrast-enhanced T1-weighted imagings were performed within 2 days after tumor ablation. The efficacy of ablation assessed according to the hyperintense middle zone on non-enhanced T1-weighted images and the non-enhanced area on contrast-enhanced T1-weighted images were compared. The development of LTP during ≥7 months of follow-up served as the end point.
Results: On the non-enhanced T1-weighted images, the ablated region had a characteristic two-zone structure featuring a hyperintense middle zone and a surrounding hypointense band. Among the 56 patients, LTP developed in ten including seven lesions, in which both the non-enhanced T1-weighted and portal-phase images showed incomplete tumor ablation. In two of the remaining three patients, incomplete tumor ablation was detected on the non-enhanced T1-weighted images, whereas the corresponding portal-phase images showed complete ablation. In the remaining patient, no residual tumor was detected on either the non-enhanced T1-weighted or the portal-phase images. In the 46 patients without LTP, there was no evidence of residual tumor on the non-enhanced T1-weighted or portal-phase images obtained early after ablation.
Conclusions: Non-enhanced T1-weighted images are useful in assessing the therapeutic efficacy of MWA of liver tumors early after the procedure.

Key words: Liver tumor—Microwave—Ablation—MRI

Percutaneous thermoablation is a well-accepted, minimally invasive treatment for hepatic malignancies, especially unresectable liver tumors. Microwave ablation (MWA) and radiofrequency ablation (RFA) are two of the most commonly used techniques for local tissue ablation [1, 2]. In the early stage after an ablation procedure, imaging studies are important to detect potential residual tumor, as in these cases retreatment should be performed as soon as possible.

Based on the results of an animal study, Onishi et al. reported that non-enhanced T1-weighted imaging can accurately determine the extent of the necrotic area soon after RFA [3]. Khankan et al. found that non-enhanced T1-weighted spoiled gradient-recalled acquisition (SPGR) was useful in early (2 days after the procedure) assessment of the therapeutic efficacy of RFA in hepatocellular carcinoma (HCC) [4]. However, compared with the low power output in RFA therapy, the temperature around the antenna rises rapidly at high output in MWA therapy, which may cause different signal changes around the inserted needle from that of RFA [5, 6]. Therefore, the diagnostic efficiency of T1-weighted images in evaluation of the therapeutic efficacy of RFA or MWA may be different.

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The purpose of this study was to compare the technical success and accuracy of hepatic MWA as evaluated by non-enhanced and enhanced T1-weighted imaging early after ablation. Both the ablation zone and local tumor progression (LTP) were assessed.

Methods

Patient population

This retrospective study was approved by our institutional review board (IRB). All patients provided informed consents for the MWA procedures and imaging examinations. The 56 patients (39 males and 17 females; age range, 42–80 years; mean age, 57.7 years) with 56 liver malignances (HCC 45; colon cancer 8; gastric cancer 3) underwent CT-guided percutaneous MWA at our institution, between September 2014 and December 2015. The lesions (mean diameter, 23.3 mm; range, 8.2–51.2 mm) were treated with curative intent. All patients underwent post-ablation imaging examinations, including MRI within 2 days after MWA therapy and follow-up MRI after up to 7 months.

MWA procedure

MWA was performed percutaneously under computed tomography (CT) guidance (Somatom Definition 16, Siemens) in patients administered with general anesthesia. The power output of the microwave delivery system (ECO-100A, 2450-MHz: Nanjing Yigao Microwave Electric Institute, Nanjing, China) ranged from 40 W to a maximum of 80 W; the time was set to 10 min.

Imaging methods and follow-up

All patients underwent contrast-enhanced CT (CECT) or contrast-enhanced MRI (CE-MRI) before the procedure as baseline examinations. CT was performed with a multidetector-row helical scanner (Somatom Sensation 64, Siemens). CE-MRI was performed with a 1.5-T MR scanner (Signa Horizon; GE Medical Systems, Milwaukee, Wisconsin, USA), with a body coil for transmission and an eight-channel, body-phased array coil for signal reception.

MRI was performed within two days and at 1 month after the therapy after the therapy, and every three months thereafter using the same protocol. Non-enhanced and contrast-enhanced T1-weighted SPGR images were repeatedly acquired using the liver acquisition with volume acceleration (LAVA) T1-weighted imaging sequence. Arterial-phase images were obtained in the axial plane at 30 s, portal-phase images at 1 min, and hepatic-phase images at 1.5 min after dynamic gadolinium injection (0.1 mL/kg) at a rate of 2 mL/s. The imaging protocol is described in detail in Table 1.

Image evaluation

Image evaluation was performed on a commercially available PACS workstation (JiveX Diagnostic; VISUS Technology Transfer, Germany).

Definition of completely necrotic area

Two radiologists experienced in the ablation procedure performed the quantitative measurements in consensus.

On non-enhanced LAVA T1-weighted images, the ablated region exhibited a two-zone structure, consisting of a hyperintense middle zone and a surrounding hypointense band. The hyperintense middle zone was considered to represent complete necrosis [5]. On the portal-phase images, the non-enhanced area was considered completely necrosis [7]. The long-axis and maximum short-axis diameters of the necrotic area were measured sequentially on the non-enhanced T1-weighted and portal-phase images. The diameter of the hypointense band was calculated by subtracting the long-axis diameter measured on the non-enhanced T1-weighted images from that measured on the portal-phase images.

Technical success and LTP

Two radiologists experienced in the ablation procedure carried out the qualitative analysis in consensus. Technical success was defined as complete coverage of the target tumor by the hyperintense middle zone as seen on the non-enhanced T1-weighted images or by the non-enhanced area on the portal-phase images. The position and extent of the necrotic area in relation to the tumor were assessed, as described by Koda et al. [8]: zone (+): continuous rim around tumor on multidirectional images visible; zone (0): discontinuous rim around tumor visible, but the tumor does not extend beyond the ablative zone; zone (−): tumor protrudes through the discontinuous rim. Zone (+) and zone (0) were classified as complete ablation, and zone (−) was classified as incomplete ablation.

LTP was suspected if the adjacent area of the ablation zone was enhanced in the arterial phase and hypoattenuated in the portal phase, or as the appearance of a bulge around the ablation zone not present on the earlier MR images.

Image subtraction of contrast-enhanced T1-weighted images

Subtracted datasets were created by subtracting the non-enhanced images from those obtained during each of the contrast-enhanced phases (arterial, portal, and hepatic) manipulated with imageJ (National Institutes of Health). The subtraction images were employed for detecting mild enhancement of the surrounding hypointense band.

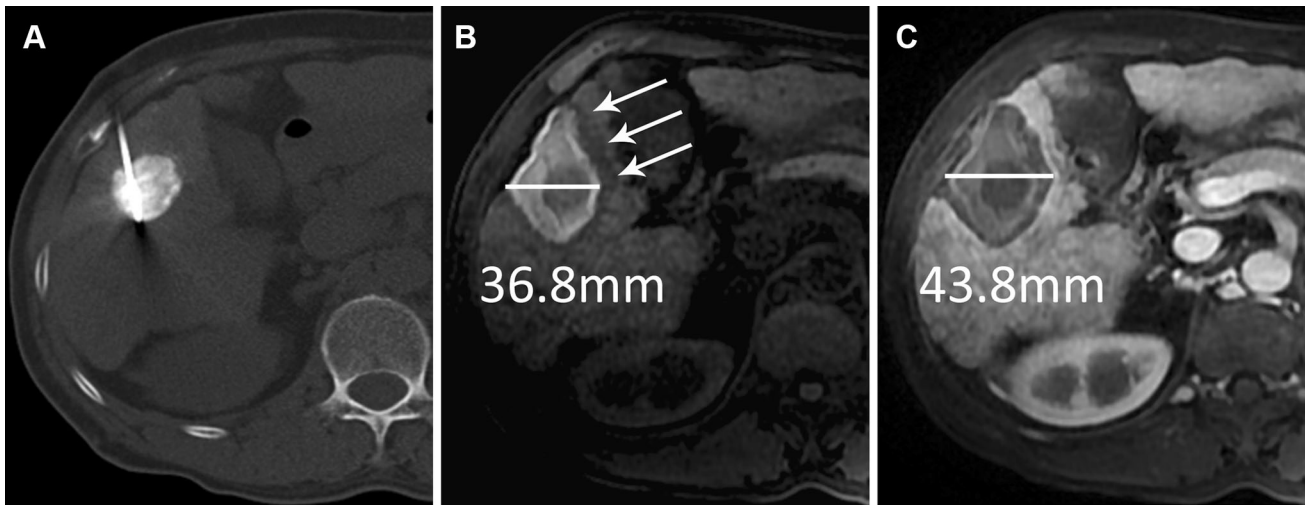

Fig. 1. Magnetic resonance imaging (MRI) shows the ablation zone 37 h after tumor ablation. **A** Axial unenhanced computed tomography (CT) image obtained during microwave ablation (MWA) shows the microwave antenna in situ and the clear deposition of Lipiodol. **B** On the non-enhanced T1-weighted images obtained early after MWA, the ablated region has a characteristic hyperintense middle zone and a surrounding hypointense band. The tumor is covered by the hyperintense middle zone. **C** The portal-phase T1-weighted image shows the absence of obvious enhancement of the ablated area, which is much larger than that of the hyperintense middle zone seen on the non-enhanced liver acquisition with volume acceleration (LAVA) T1-weighted image.

Statistical analysis

Statistical analysis was performed using SPSS (GraphPad Software, Inc., USA). Quantitative results were evaluated by means of a *t* test (paired, two-tailed). The sensitivity, specificity, and accuracy of an incomplete ablation were evaluated using the McNemar test of the non-enhanced T1-weighted and CE-MRI images. A P value <0.05 was considered to indicate a statistically significant difference.

Results

All MWA procedures were performed without major procedure-related complications. The mean follow-up was 328.7 days ($n = 56$; range, 220–640 days). Of the 56 tumors, 55 with a long diameter of 8.2–42.8 mm were treated by ablation with one antenna. The other tumor had a long diameter of 51.2 mm and was treated by ablation with two antennas used simultaneously.

Quantitative image analysis

The surrounding hypointense band detected on the non-enhanced T1-weighted images was not enhanced on the portal-phase images. Thus, the necrotic area measured on portal-phase images was usually larger than that measured on the non-enhanced T1-weighted images. The mean long-axis diameter of the necrotic areas was 51.2 ± 10.0 mm (range, 23.7–72.4 mm) on the non-enhanced T1-weighted images and 54.3 ± 10.0 mm (range, 28.4–72.0 mm) on the portal-phase images ($P = 0.00$). The mean short-axis diameter was 31.1 ± 7.3 mm (range, 15.0–46.0 mm) and 34.4 ± 7.4 mm (range, 15.8–46.9 mm; $P = 0.00$). The mean diameter of the hypointense band was 2.8 ± 2.4 mm (range, 0–8.4 mm) (Fig. 1).

Efficacy and LTP

Data on the technical success and efficacy of treatment for the 56 tumors are shown in Table 2. LTP was detected in 10 lesions (17.8%), resulting in a local effectiveness of 82.2% (mean time to LTP was 67 days; range, 2–78 days).

The positional relationship between the necrotic area and the lesion was classified as zone (0) on the portal-phase images of two of ten lesions, but zone (−) on the respective non-enhanced T1-weighted images (Fig. 2). In seven of the remaining eight lesions, local residual tumor was detected both on the non-enhanced T1-weighted and portal-phase images. In the last lesion, no residual tumor was detected on either the non-enhanced T1-weighted or the portal-phase images. One patient with LTP detected during early MRI underwent additional MWA 5 days after the first therapy. In the other nine patients, recurrent disease was detected at follow-up MRI. Four of these patients again underwent MWA and five of them were treated with transcatheter arterial chemoembolization.

In the 46 lesions without subsequent LTP, no residual tumor was suspected based on the non-enhanced T1-weighted or portal-phase images early after ablation. In

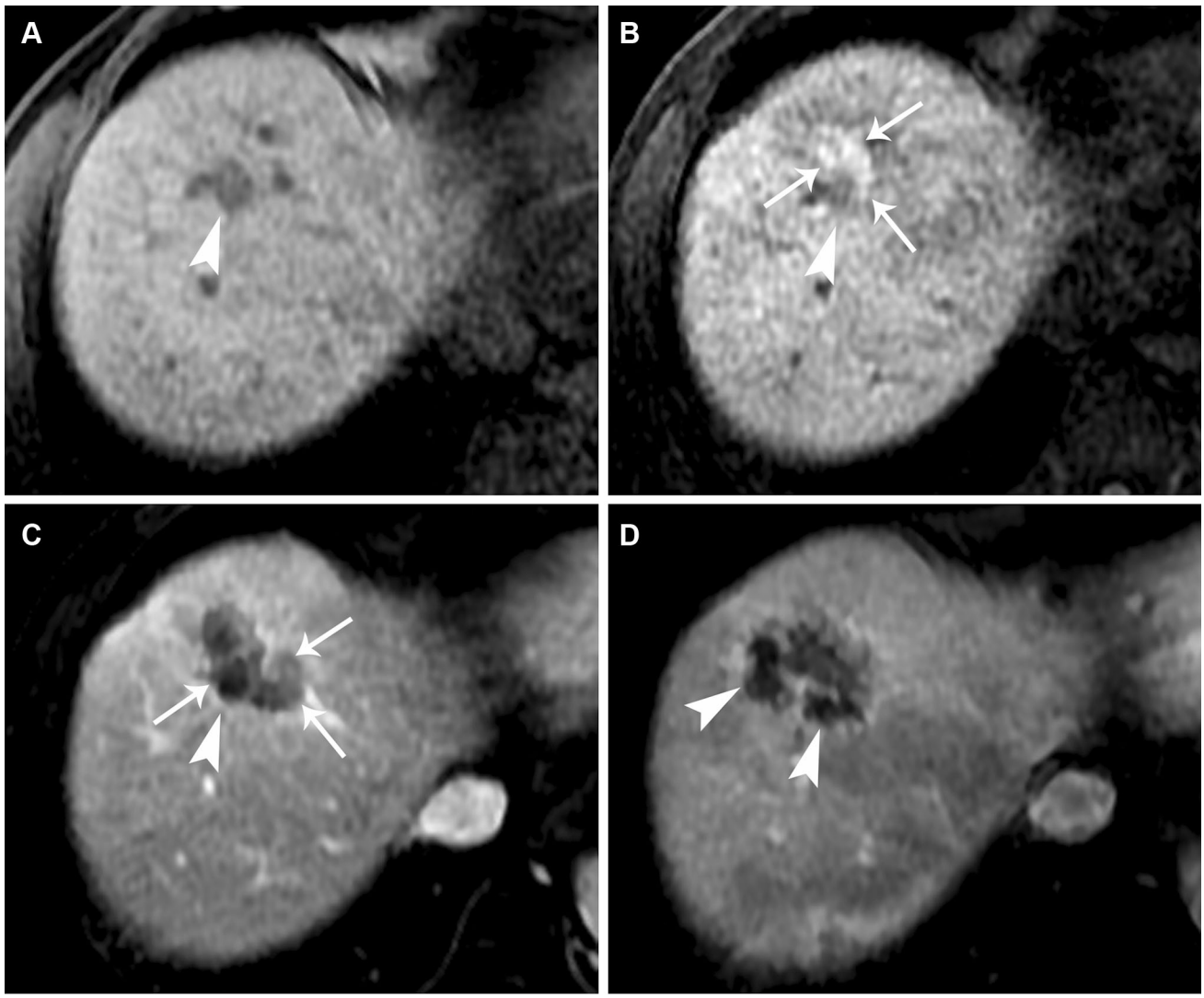

Fig. 2. Residual tumor detected by non-enhanced T1-weighted imaging. **A** A metastatic lesion from colon cancer was detected in segment eight of the liver before ablation. **B** On the non-enhanced T1-weighted image, obtained 2 days after MWA, the hyperintense central zone (*arrows*) does not cover the lesion (*arrowhead*) completely [zone (−)], whereas **C** on the portal-phase images, the non-enhanced area (*arrows*) coverage of the lesion (*arrowhead*) is complete [zone (0)]. **D** Local tumor progression observed as new lesions (*arrow heads*) besides the ablative zone shows mild enhancement on the 5-month follow-up MRI scan after the ablation procedure.

five of these 46 cases, the positional relationship between the necrotic area and the lesion as determined from the portal-phase images was classified as zone (+), whereas on the non-enhanced T1-weighted images it was classified as zone (0). In the other 41 cases, the positional relationship between the necrotic area and the lesion was classified as zone (+), both on the portal-phase and the non-enhanced T1-weighted images.

In lesions with incomplete ablation, non-enhanced T1-weighted and portal-phase imaging had a sensitivity of 90.0% and 70.0%, respectively ($P = 0.50$), whereas the specificity was 100% for both imaging techniques. The accuracies were 98.2% and 94.6%, respectively ($P = 0.19$).

Subtraction image analysis

On the subtraction images, a typical ring-like hyperperfusion was identified in the periphery of the ablated region on arterial-phase images ($n = 48$). Mild enhancement was detected in the surrounding hypointense band on the portal-phase images ($n = 8$) and on the hepatic-phase images ($n = 49$) (Fig. 3).

Discussion

A zonal pattern of ablated region was found on non-enhanced T1-weighted images within 2 days after MWA of liver tumors, including a broad hyperintense middle zone and a surrounding hypointense band [3, 5]. The size

Table 1. Magnetic resonance imaging protocol for post-ablation and follow-up imaging

Sequence	Plane	Fat saturation	TR (ms)	TE (ms)	FA	ST	Gap
T2W FRFSE	Axial	Yes	6000	85	90	6	6
DWI	Axial	Yes	6666	67.5	90	6	6
T1WI LAVA (non-enhanced)	Axial	Yes	3.81	1.81	15	4.8	2.4
T1WI LAVA dynamic (arterial, and portal phase)	Axial	Yes	3.81	1.81	15	4.8	2.4
T1WI LAVA (hepatic phase)	Axial	Yes	3.81	1.81	15	4.8	2.4

Injection of Gd-BPTA (0.1 mL/kg; 2 mL/s)
DWI diffusion-weighted imaging (*b*-values, 50, 600 s/mm^2), *FA* flip angle, *FRFSE* fast relaxation fast spin echo, *LAVA* liver acquisition with volume acceleration, *ST* slice thickness, *TE* echo time, *TR* repetition time

Table 2. Technical success and efficacy assessed by magnetic resonance imaging within 2 days of the ablation procedure

Non-enhanced T1-weighted images		Portal-phase images		Follow-up(LTP)	
Category	*n*	Category	*n*	Yes	No
zone (+)	25	zone (+)	25		25
		zone (0)	/		
		zone (−)	/		
zone(0)	22	zone (+)	5		5
		zone (0)	17	1	16
		zone (−)	/		
zone (−)	9	zone (+)	/		
		zone (0)	2	2	0
		zone (−)	7	7	0

zone (+): continuous rim around tumor visible
zone (0): discontinuous rim around tumor visible, but the tumor does not extend beyond the ablative zone
zone (−): tumor protrudes through the discontinuous rim
zone (+) and zone (0) were classified as complete ablation, and zone (−) was classified as incomplete ablation
LTP local tumor progression

of the necrotic area measured on portal-phase images was larger than that measured on the non-enhanced T1-weighted images. Both non-enhanced MRI as well as CE-MRI are well suited for the immediate assessment of the technical success of MWA of liver tumors.

In a previous study, time-related signal changes on MRI after RFA were described. The coagulated region showed heterogeneous intensity on T1-weighted images obtained 3 days after RFA, and a time-related elevation in the signal intensity in the coagulated region was observed by 12 weeks [5]. Khankan et al. reported that the utility of non-enhanced T1-weighted images in early assessments of the therapeutic efficacy of RFA of HCC was evident 2 days after treatment [4]. In our study, in contrast to the signal change pattern caused by RFA, the coagulated region was of homogeneous hyperintensity with a sharp margin on the T1-weighted images 2 days after MWA of the liver tumors. Similar time-related signal changes after MWA were reported previously [9, 10]. The difference in the signal intensity change in the areas of coagulated necrosis on the T1-weighted images of MWA- and RFA-treated lesions may depend on the temperature distribution around the inserted needle [6]. In microwave coagulation therapy, the temperature rises rapidly such that at a high output (60–80 W) the tissues carbonize, while in RFA therapy, the temperature rises gradually in response to the low output (30–50 W) [5]. Similarly, unlike low-power output microwave systems (such as the uncooled Medwaves system with a maximum power of 36 W), ablation zones created with a high-power microwave system, such as used in this study, may have an altered imaging appearance. Hoffmann et al. performed MRI-guided MWA of liver tumors. While the ablation zones of those tumors presented as hyperintense areas on T1-weighted images, they could still be verified by contrast-enhanced T1-weighted imaging [11]. Our results demonstrate the importance of confirming the ablation zone without the use of contrast agent, such as might also be possible under MRI-guidance during the procedure.

The larger ablation zone on the portal-phase than on the non-enhanced T1-weighted images might be attributed to the lack of enhancement or only mild enhancement of the surrounding hypointense band. The surrounding hypointense bands were slightly enhanced on the portal-phase images of eight lesions, but on the hepatic-phase images of 49 lesions. On pathological analysis, the surrounding hypointense band corresponded to the presence of necrotic and granulation tissue in the acute phase, perhaps including viable cells [3, 5]. Accordingly, the hyperintense middle zone on the non-enhanced T1-weighted images accurately reflected coagulation necrosis after tumor ablation, with presumably complete ablation of the nodule located within the

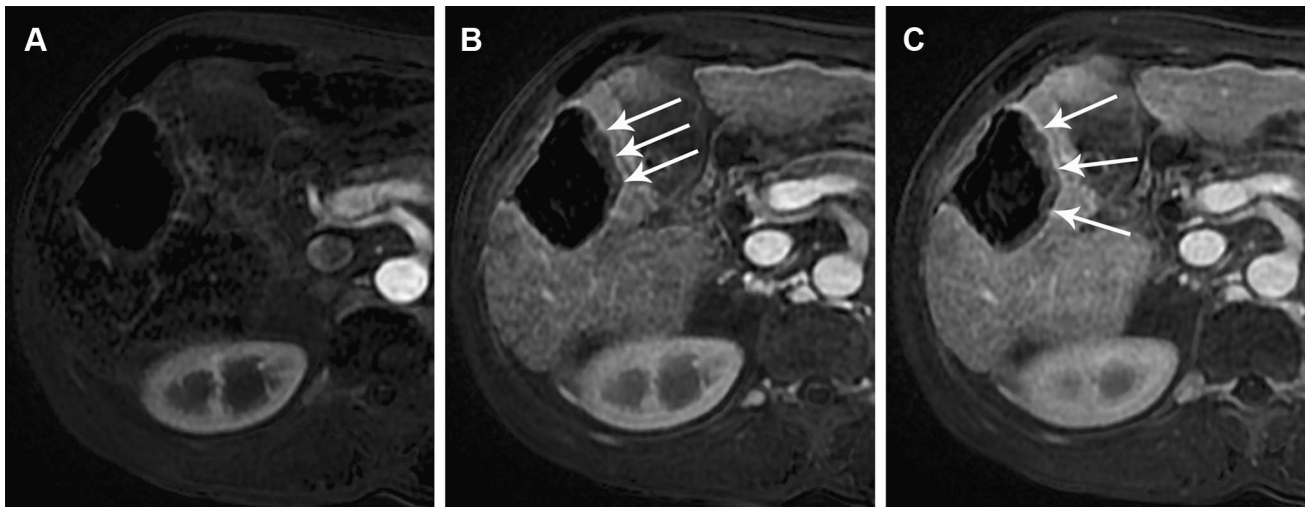

Fig. 3. Subtraction images of the tumor shown in Fig. 1. **A** Arterial-phase subtraction image reveals hyperperfusion in the periphery of the ablated region, but no enhancement in the ablated region. **B** Mild enhancement of the surrounding hypointense band is detected on the portal-phase subtraction image (*arrows*), with better visualization than on the original image (Fig. 1C). **C** Mild enhancement in the surrounding hypointense band is detected on the hepatic-phase subtraction image (*arrows*).

middle hyperintensity zone on the T1-weighted images [3, 4]. However, in routine clinical practice, the original LAVA T1-weighted images (instead of subtracted images) are used to detect enhancement, such that mild enhancement in the marginal zone may be largely ignored, especially for metastases with reduced contrast enhancement on the portal venous phase. Thus, if part of the tumor is located in the surrounding hypointense band, on CE-MRI it may be classified as complete ablation and on non-enhanced T1-weighted MRI as incomplete ablation. In Ringe's opinion, CE-MRI performed 24 h after ablation is of limited value in qualitative assessments of the ablative margin and in the determination of prognosis regarding LTP [12]. If the surrounding hypointense band is taken into consideration, then a more accurate determination of prognosis concerning LTP may be achieved with post-ablation MRI. In this study, one patient without any sign of residual tumor on both the non-enhanced T1-weighted and the portal-phase images obtained early after MWA had LTP, perhaps attributable to the existence of a tiny satellite nodule.

The interpretation of CE-MRI or CECT finding within 24 h after ablation is difficult for reasons that include capillary leakage, vessel injury, and the resultant perfusion changes of the lesions. Typical ring-like hyperperfusion located in the periphery of the ablated region was detected on the arterial-phase images of 48 of the 56 patients, and was interpreted as periablation hyperemia due to the inflammation induced by thermal injury. These foci may be mistaken as local residual tumor [13, 14]. Thus, necrotic areas may be more readily identified as hyperintensities on non-enhanced T1-weighted images, and then therapeutic efficacy may be evaluated based on the positional relationship with the tumor seen on the images obtained before therapy.

This study had several limitations. First, because only MWA was performed, the MRI signal changes could not be compared directly with those seen on the T1-weighted images of RFA-treated lesions. However, the MRI signal changes pattern subsequent to MWA vs. RFA differs, as reported in previous studies [4, 5, 15]. Second, some tumors were identifiable on the pre-procedural images, but on the post-procedural images could not be distinguished from the ablated area, especially when the borderline of the ablation zone was close to the borderline of the tumor. In these cases, therapeutic efficacy had to be evaluated by comparing the positional relationship of the tumor and its surrounding structures on the post- vs. pre-procedural images. Third, within 2 days after MWA, the ablation zone usually showed a blurred margin with hypointensity or heterogeneous intensity on T2-weighted images, and heterogeneous intensity on diffusion-weighted images. However, the diagnostic value of these two sequences in the detection of residual tumor was not evaluated in this study.

In conclusion, in patients with liver tumors, non-enhanced T1-weighted images are useful for assessing therapeutic efficacy early after MWA. The potential for the early detection of LTP after an ablation procedure may allow for timely retreatment.

Compliance with ethical standards

Funding No funding was received for this study.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Statement of informed consent was not applicable since the manuscript does not contain any patient data.

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