Original Article Intra-procedural real-time ultrasound fusion imaging improves the therapeutic effect and safety of liver tumor ablation in difficult cases

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Abstract: In certain difficult cases involving tumors unclear in B-mode ultrasound or tumors in a high-risk location, image-guided liver tumor thermal ablation was previously contraindicated. The aim of this retrospective study was to investigate the value of intra-procedural ultrasound fusion imaging in improving the therapeutic effect and safety of liver tumor ablation in difficult cases. A total of 502 patients (441 males and 61 females, aged 52 \pm 11 years) with 805 liver tumors (16 \pm 6 mm; range, 4-29 mm) who underwent thermal ablation with intra-procedural fusion imaging from October 2010 to June 2018 in our hospital were enrolled. Fusion imaging was employed for targeting, puncture guidance and immediate evaluation of the therapeutic response. Contrast-enhanced computed tomography (CT)/magnetic resonance imaging (MRI) was performed one month after ablation and every 3~6 months in the follow-up period. 511 and 294 liver tumors were in classified in the difficult case group and the non-difficult case group, respectively. The technical efficacy rate was 99.4% (800/805), and no difference was found between the difficult case group (1 year: 3.2%; 3 years: 7.6%; 5 years: 7.6%) and non-difficult case group (1 year: 2.1%; 3 years: 5.5%; 5 years: 11.6%) (P=0.874). The major complication rate was 1.8% (11/608). Injury to adjacent organs occurred in only 1 patient who sustained a bile duct injury. We conclude that intra-procedural fusion imaging can improve the therapeutic efficacy and safety of thermal ablation in difficult cases and may expand the indications for thermal ablation.

Keywords: Fusion imaging, liver tumor, difficult cases, thermal ablation

Introduction

Percutaneous ablation has been recognized as one of the three curative therapies for liver tumors and has the advantages of micro-invasiveness, an exact therapeutic effect and relatively low cost [1, 2]. According to the updated guidelines, percutaneous ablation is mainly indicated for very early-stage or early-stage liver cancers in a relatively safe location [2], yielding a technical efficacy rate of 92.2-99.6% [3-9] and a major complication rate of 1.3-9.5% [3-9]. However, in some difficult cases [10], such as those involving tumors that are unclear on B-mode ultrasound (US), tumors located in a high-risk location [11], image-guided thermal ablation was previously considered contraindicated due to a low technical efficacy rate or a high complication rate.

In general, the key problems in difficult cases are a lack of efficient imaging guidance and an inability to accurately assess the treatment response intraoperatively. Regarding the lack of efficient imaging guidance, for approximately one-third of liver tumors that are unclear on B-mode US or plain computed tomography (CT) [12], image-guided electrode or antenna puncture is somewhat difficult and inaccurate. For some tumors located in high-risk locations, a lack of a three-dimensional imaging guidance may lead to injury to adjacent critical organs [13-16] or incomplete ablation to avoid complications. Another problem is the lack of an accurate method to assess the treatment response immediately during the ablation procedure. As the widely used methods to evaluate the immediate treatment response. US. contrast-enhanced US (CEUS) and even contrast-enhanced CT cannot distinguish residual tumor tissue from the hyperemia zone surrounding the index tumor [17] and cannot assess tumors with a poor blood supply. Since the index tumor may become inconspicuous after ablation, whether an adequate ablative margin (AM) has been achieved cannot be evaluated. All of these factors may be important contributors to residual tumor tissue in difficult cases. Therefore, the ideal imaging modality should display not only good delineation of the target tumor and critical structures at risk of injury [18] but also the spatial relationship between the target tumor and the ablative zone.

Real-time US fusion imaging is a novel technique to generate fused real-time US and reconstructed CT/magnetic resonance imaging (MRI) images based on electromagnetic tracking system [19-23]. With this technique, the index tumor can be outlined on pre-ablation multiplanar CT/MRI and displayed simultaneously with real-time US images, which are useful for targeting and puncture guidance in tumors that are inconspicuous on ultrasound or even plain CT scans [24-26]. Additionally, with the overlapping of pre-ablation images and intra-procedural US images, the operator can accurately evaluate whether the tumor has been completely ablated and determine whether supplemental ablation is needed [27, 28]. Previous reports [18] have shown that intra-procedural real-time fusion imaging can increase the confidence of operators and improve the accuracy of the ablation procedure. However, evidence supporting whether intra-procedural fusion imaging can improve the outcome and safety of thermal ablation in difficult cases remains limited.

Therefore, the purpose of this retrospective study was to explore the value of intra-procedural fusion imaging in improving the therapeutic effect and safety of thermal ablation for such difficult cases.

Methods

Study population and lesions

This study retrospectively enrolled patients diagnosed with hepatocellular carcinoma or other malignancies that underwent US-guided thermal ablation with an intention to achieve complete necrosis of the tumor at our center from October 2010 to June 2018. The study was approved by the institutional ethics review board, and the present study complied with the Declaration of Helsinki. Informed consent was obtained from every participant.

Inclusion criteria were as follows: (1) The patients was diagnosed as liver malignant tumors; (2) Single or multiple tumors, with the maximum size of 30 mm; (3) Indicated for thermal ablation; (4) Fusion imaging was performed in the procedure.

The diagnosis of hepatocellular carcinoma was mainly based on typical imaging features or pathological results [2], while other liver malignancies was diagnosed generally according to the pathological results.

The indications for liver tumor thermal ablation were as follows: (1) liver function status was assessed to be Child-Pugh A or B; (2) no intractable ascites nor uncorrectable coagulopathy; (3) a prothrombin activity above 40%, a platelet count greater than $50*10^{9}/L$ and no uncorrectable coagulopathy; and (4) patients unsuitable for or refusing hepatectomy.

The exclusion criterion was as follows: (1) No contrast-enhanced CT/MRI acquired one month after ablation procedure. (2) Cases that were treated combined with ethanol injection.

Definition of difficult cases

The enrolled lesions were classified as difficult cases or non-difficult cases by two independent senior sonographers based on pre-ablation US, CEUS and CT/MRI images. If their opinions differed, a consensus was reached after discussion. A difficult case was defined according to previous literature [10]. Difficult cases mainly refer to previously contraindicated lesions that are difficult to completely ablate under US guidance or are associated with ablation-related complications due to their location and conspicuity. Two types of lesions were considered difficult: (1) lesions located in a highrisk location adjacent to critical structures at a distance of less than 10 mm [11]; and (2) lesions that are unclear on B-mode US.

Equipments and contrast-enhanced agent

Radiofrequency ablation (RFA) and microwave ablation (MWA) were employed in the present study. A cooled-tip RFA system (Covidien, Mansfield, MA, USA) was employed for RFA. A 17-gauge, internally cooled-tip electrode with a 3-cm tip was used. An internally cooled microwave (MW) antenna (Kangyou Cor., Nanjing, China) was employed for MWA with an generator of 2450 MHz (Kangyou Cor., Nanjing, China).

MyLab 90, MyLab Twice and MyLab Class US machines (Esoate, Genoa, Italy) with Virtual Navigator (VN) software were used for US and fusion imaging guidance. Convex probe CA541 (frequency: 1-8 MHz) or CA431 (frequency: 4-10 MHz) was used. A magnetic field generator was positioned adjacent to the patient's right shoulder to emit a magnetic field. A sensor was attached on the convex probe for navigation.

SonoVue (Bracco, Milan, Italy) was employed as the contrast-enhanced agent. It was injected intra-venously as a rapid bolus of 1.5-2.0 ml with 5 ml of saline followed.

Thermal ablation procedure

The ablation procedure was performed under endotracheal general anesthesia by three interventional doctors (ZRQ, LK, and XEJ) with at least 5 years of experience in ablation procedures at the beginning of the study. The protocol for thermal ablation, including the ablation method and necessary auxiliary procedures, were discussed before the procedure. The patients were in a supine position. Single or overlapping multiple punctures were performed to cover the index tumor and a 5-mm AM if possible.

Steps for fusion imaging

The detailed steps for CT/MRI-US/CEUS fusion imaging were as follows. (1) Acquisition of CT/ MRI volume images. CT/MRI images acquired within two weeks before the ablation procedure were imported into the US equipment in Digital Imaging and Communications in Medicine (DICOM) format and multiplanar volume images were generated automatically. The index tumor and its AM were depicted in a certain color on the volume images. (2) Registration. Primary registration was carried out based on the plane of the left portal vain, which was parallel to the transverse section of the CT/ MRI. (3) Fine tuning. Precise fine tuning was performed using the small vascular structures proximal to the target tumor as an anatomical landmark. (4) Navigation. By moving the probe, the real-time US images were spontaneously fused with the CT/MRI images in different angle and plane [28-30].

Intra-procedural real-time US fusion imaging

Real-time US fusion imaging was employed for targeting, puncture guidance, monitoring and immediate treatment response assessment intra-procedurally.

For tumors unclear on B-mode US, the tumors were depicted on the pre-ablation CT/MRI images and displayed synchronously with realtime US. US-CT/MRI fusion imaging enabled the index tumor to target and puncture guidance.

For tumors in high-risk locations, multiplanar CT/MRI images were reconstructed, and the relationship between the lesion and adjacent critical structures could be clearly visualized in different planes by the operator. Puncture was performed under US-CT/MRI fusion imaging guidance to cover the whole tumor while avoiding the injury to the critical structures.

CEUS was performed 15 minutes after the ablation procedure to observe the avascular ablation zone. With fusion imaging, the index tumor depicted on the pre-ablation images was synchronously displayed with the CEUS images. By moving the probe, the relationship between the index tumor and the avascular zone on CEUS could be clearly observed in different planes, helping to evaluate whether there was residual tumor. Supplemental ablation would be performed until the avascular zone covered the whole tumor and its 5-mm margin if an AM was needed.

Follow-up

The patients were closely monitored during the peri-operative and follow-up period. US examination was performed on the first day after thermal ablation to exclude early complications. Contrast-enhanced CT/MRI was performed one month after thermal ablation as a reference standard for the technical efficacy. After that, CT/MRI as well as the serum tests were performed every 3~6 months.

Technical efficacy was defined as complete necrosis of the index tumor confirmed by con-

trast CT/MRI. Local tumor progression (LTP) was defined as the appearance of tumor recurrence at the edge of the ablation zone after at least one contrast-enhanced imaging follow-up study confirmed complete necrosis of the index tumor. A major complication was defined as an event that leads to substantial morbidity and disability, increases the level of care, lengthens the hospital stay or results in hospital admission. Other events such as pain were classified as side effect.

Statistical analysis

SPSS 22.0 (SPSS, Chicago, IL, USA) and Graphpad Prism 8.3.1 (Graphpad Software Inc., San Diego, CA, USA) were used for statistical analysis. Continuous measurement data are presented as the mean \pm standard deviation if they were normally distributed or as the median (range) if the data were not normally distributed. Enumeration data are presented as percentages. The technical efficacy rate and complication rate were compared between the difficult case group (DC group) and the non-difficult case group (NDC group) with the χ^2 test and Fisher's exact test. The cumulative curves of local tumor progression (LTP) were analyzed with the Kaplan-Meier method. P values less than 0.05 were considered to indicate dramatic differences.

Results

Patients and lesions

In total, 1414 liver tumors in 866 patients were subjected to thermal ablation in our center from October 2010 to June 2018. Five hundred and sixty three patients (878 lesions) satisfied the inclusion criteria. Among them, 46 patients (54 lesions) were excluded due to combined treatment with ethanol injection (18 lesions in 17 patients) or loss to follow-up (36 lesions in 29 patients). Finally, a total of 824 liver tumors in 517 patients (623 ablation sessions) were enrolled in the present study. During ablation, successful registration was achieved in 502 patients with 805 liver tumors in 608 ablation sessions.

The baseline features of the patients and lesions are listed in **Table 1**. The lesions were divided into the DC group (511 liver tumors, 401 sessions) and the NDC group (294 liver tumors, 207 sessions), and the baseline features of these two groups are presented in **Table 2**.

Intra-procedural application of US fusion imaging

Among the 824 liver cancer lesions in 517 patients, successful registration was achieved in 805 liver cancer lesions in 502 patients, yielding a registration success rate of 97.7% (805/824). The reasons for unsuccessful registration included liver deformation after injection of artificial ascites (9 liver cancer lesions in 7 patients), a lack of anatomical structures for registration due to a subcapsular location (6 liver cancer lesions in 5 patients), and liver deformation after ablation (4 liver cancer lesions in 3 patients).

Among the 805 enrolled tumors with successful registration, real-time fusion imaging combined with CEUS was used for targeting and guidance, monitoring and assessment of the treatment response and supplemental ablation guidance (**Figures 1**, **2**).

Detailed information on thermal ablation

Detailed information regarding thermal ablation is provided in **Table 3**. The ablation type, utilization of auxiliary procedures, number of ablation, supplemental ablation and assessment results were significantly different between the DC and NDC groups.

Technical efficacy

Overall, 800 liver tumors exhibited complete necrosis after one session as confirmed by contrast-enhanced CT/MRI, yielding a technical efficacy rate of 99.4% (800/805). No significant difference in the technical efficacy rate was noted between the DC group and the NDC group (**Table 4**).

Five lesions confirmed to be incompletely ablated by contrast-enhanced CT/MRI. These 5 lesions were all inconspicuous and located in the high-risk location.

Local tumor progression

The medium follow-up period was 30 months (1-96 months). LTP was observed in 5.9% (30/511) of the tumors in the DC group and in

Table 1. Baseline features	of the patients and lesions
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Characteristic	Total
Patients	N=502
Sex (Male/Female)	441 (87.8%)/61 (12.2%)
Age	52 ± 11; 27-87
Hepatitis virus infection (Yes/No)	473 (94.2%)/29 (5.8%)
Cirrhosis (Yes/No)	416 (82.9%)/86 (17.1%)
Cause of cirrhosis (HBV/HCV/HBV+HCV/alcohol)	484 (96.4%)/15 (3.0%)/1 (0.2%)/1 (0.2%)/1 (0.2%)
AFP (<200/≥200)	420 (83.7%)/82 (16.3%)
Child Pugh (A/B)	477 (95.0%)/25 (5.0%)
Lesions	N=805
Diagnosis (primary liver cancer/liver metastasis)	793 (98.5)/12 (1.5%)
Primary/Recurrence	327 (40.6%)/478 (59.4%)
Clinical diagnosis/Pathological diagnosis	773 (96.0%)/32 (4.0%)
Tumor number (single/multiple)	387 (48.1%)/418 (51.9%)
Maximum diameter (mm)	16 ± 6; 4-29
Segment (1/2/3/4/5/6/7/8)	10 (1.2%)/43 (5.3%)/39 (4.8%)/93 (11.6%)/146 (18.1%)/132 (16.4%)/167 (20.7%)/175 (21.7%)
Difficult cases#/Non-difficult cases	511 (63.5%)/294 (36.5%)
High-risk location/Non-high-risk location	482 (59.9%)/323 (40.1%)
Unclear on B-mode US	68 (8.4%)/737 (91.6%%)

Note: AFP: α-fetoprotein; HBV: hepatitis B virus; HCV: hepatitis C virus. #The two types of difficult lesions included the following: 1. lesions in high-risk locations; and 2. lesions that were unclear on B-mode US.

Table 2	Raseline	features	of the	lacione	in the	DC and	NDC groups
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Characteristic	DC group	NDC group	Р
Lesions	N=511	N=294	
Diagnosis (primary liver cancer/liver metastasis)	506 (99.0%)/5 (1.0%)	287 (97.6%)/7 (2.4%)	0.114
Primary/Recurrence	188 (36.8%)/323 (63.2%)	139 (47.3%)/155 (52.7%)	0.004
Clinical diagnosis/Pathological diagnosis	493 (96.5%)/18 (3.5%)	280 (95.2%)/14 (4.8%)	0.472
Tumor number (single/multiple)	239 (46.8%)/272 (53.2%)	150 (51.0%)/144 (49.0%)	0.245
Maximum diameter (mm)	15, 4-29	16, 5-29	0.166
Segment (1/2/3/4/5/6/7/8)	10 (2.0%)/35 (6.8%)/24 (4.7%)/63 (12.3%)/85 (16.6%)/74 (14.5%)/110 (21.5%)/110 (21.5%)	0 (0.0%)/8 (2.7%)/15 (5.1%)/30 (10.2%)/61 (20.7%)/58 (19.7%)/57 (19.4%)/65 (22.1%)	0.013
High-risk location/Non-high-risk location	482 (94.3%)/29 (5.7%)	/	/
Clear/Unclear on B-mode US	443 (86.7%)/68 (13.3%)	/	/

Note: DC group: difficult cases group; NDC group: non-difficult cases group; AFP: α -fetoprotein.



Figure 1. A patient with Segment 7 hepatocellular carcinoma underwent radiofrequency ablation. A. Contrast-enhanced ultrasound revealed a nodule with hypo-enhancement in Segment 7, which was inconspicuous on conventional US. B. Ultrasound-MRI fusion imaging was applied to locate the tumor. C. Puncture was performed under US-MRI fusion imaging guidance. D. The ablation procedure was monitored by ultrasound-MR fusion imaging. E. After the ablation procedure, contrast-enhanced ultrasound-MRI fusion imaging was used to assess the technical success again. The avascular zone on contrast-enhanced ultrasound images covered the whole nodule (blue cycle) and its 5-mm ablative margin (red cycle). F. One month later, contrast-enhanced MRI confirmed the technical efficacy.



Figure 2. A patient with Segment 4/8 hepatocellular carcinoma underwent WMA. A. Contrast-enhanced US revealed a nodule with hyper-enhancement in S4/8 adjacent to the right hepatic bile duct. B. Contrast-enhanced CT also demonstrated a hypo-density nodule. C. Ultrasound-CT fusion imaging was employed to visualize the three-dimensional relationship between the tumor and the right hepatic bile duct. D. The ablation procedure was monitored by ultrasound-CT fusion imaging. E. A small residual tumor abutting the right hepatic bile duct was detected by contrast-enhanced ultrasound-CT fusion imaging. F. Supplemental ablation to cover the residual tumor while avoid-

ing the right hepatic bile duct was performed under ultrasound-CT fusion imaging guidance. G. The avascular zone on contrast-enhanced ultrasound images covered the whole nodule (blue cycle) and its 5-mm ablative margin (red cycle). H. One months later, contrast-enhanced MRI confirmed the technique efficacy.

6.1% (18/294) of the tumors in the NDC group (P=0.885). The cumulative occurrence rates of LTP at 1, 3, and 5 years were 3.2%, 7.6%, and 7.6% for the DC group and 2.1%, 5.5%, and 11.6% for NDC group, respectively. The LTP cumulative occurrence curves are shown in **Figure 3**. The difference in the cumulative LTP occurrence rate between the DC and NDC groups was not significant (P=0.874).

Complications

A total of 608 treatment sessions to cure 805 lesions were performed for the 502 enrolled patients. Among the 608 treatment sessions, 401 treatment sessions involved at least one difficult lesion and 207 sessions involved no difficult lesions.

The major complication rate was 1.8% (11/ 608), including bleeding (n=1, 0.16%), hemothorax and pyothorax (n=3, 0.49%), liver abscess (n=5, 0.82%), encapsulated peritoneal effusion (n=1, 0.16%) and bile duct injury (n= 1, 0.16%). These complications resolved after administration of hemostatic agents or drainage. No procedure-related mortalities were noted. The major complication rate of the 207 treatment sessions with no difficult lesions (n=2, 1.0%) was not significantly different from that of the 401 treatment sessions with at least one difficult lesion (n=9, 2.2%) (*P*=0.532).

In addition, post-procedural pain occurred after 17.9% (109/608) of the sessions, postablation syndrome occurred in 21.2% (129/608) of the sessions, asymptomatic biloma occurred in 1.2% (7/608) of the sessions, and asymptomatic pleural effusion occurred in 10.2% (62/608) of the sessions. These minor complications resolved spontaneously or after symptomatic treatment.

Discussion

The present study demonstrated that real-time US fusion imaging can be applied for targeting, guidance, monitoring and treatment response assessment during the ablation procedure for difficult cases. The technical efficacy rate for difficult cases in the present study was higher than that of previous reports [11, 31-33], while the LTP rate was not higher than previously reported rates [31]. No significant difference in either technical efficacy or LTP was observed between difficult and non-difficult cases. The major complication rate was lower than that reported in most of previous studies [11, 31-33]. These results indicated that real-time fusion imaging played an important role in improving the therapeutic effect and safety of thermal ablation for difficult cases.

The main reasons for this outcome are as follows. First, real-time fusion imaging serve as an ideal guidance tool for difficult cases. Real-time fusion imaging allowed side-by-side and synchronous visualization of pre-ablation CT/MRI images and real-time US images and generated three-dimensional images. For liver tumors that are unclear on B-mode US, the tumors can be accurately targeted with fusion imaging, and puncture can be performed under fusion imaging guidance. In addition, even when gas produced during ablation renders the index tumor inconspicuous on US, the subsequent puncture can be performed under the guidance of fusion imaging, ensuring accurate needle placement and reducing experience dependence. For tumors located in high-risk locations, the application of fusion imaging helps the operator to better visualize the spatial relationship between the index tumor and the surrounding structures, increasing the operator's confidence in achieving complete ablation while reducing injury to extrahepatic organs. This finding is confirmed by our data, which show a low incidence of critical organ injury and a high technical efficacy. Second, US fusion imaging was performed to directly display the spatial relationship between the ablative zone and the index tumor in different planes and angles. Therefore, the operators were able to assess the treatment effect and determine whether supplemental ablation was needed. Approximately 25% of the enrolled patients and lesions underwent supplemental ablation and achieved technical success in one session. According to our data, the percentage of supplemental ablation for difficult cases was higher than that for non-difficult cases, possibly be-

Table 3. Detailed information o	on thermal	ablation
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Characteristic	DC group	NDC group	Р
Lesions	N=511	N=294	
Combined therapy (TACE/Surgery/none)	50 (9.8%)/5 (1.0%)/456 (89.2%)	29 (9.9%)/5 (1.7%)/260 (88.4%)	0.671
Ablation type (RFA/WMA)	410 (80.2%)/101 (19.8%)	189 (64.3%)/105 (35.7%)	<0.001
No. of electrodes/antennas (one/two)	508 (99.4%)/3 (0.6%)	287 (97.6%)/7 (2.4%)	0.043
Puncture path (Percutaneous/Transhepatic)	509 (99.6%)/2 (0.4%)	294 (100.0%)/0 (0.0%)	0.536
Auxiliary procedures* (1/2/3/4/1+2/1+4/none)	57 (11.2%)/50 (9.8%)/1 (0.2%)/1 (0.2%)/12 (2.3%)/2 (0.4%)/388 (75.9%)	25 (8.5%)/7 (2.4%)/1 (0.3%)/2 (0.7%)/0 (0.0%)/1 (0.3%)/258 (87.8%)	<0.001
No. of punctures	1 (1-6)	2 (1-7)	0.002
No. of ablation sessions	3 (1-8)	3 (1-11)	0.858
Supplemental ablation (Yes/No)	132 (25.8%)/379 (74.2%)	49 (16.7%)/245 (83.3%)	0.003
Assessment results (AM achieved/AM not achieved)	458 (89.6%)/53 (10.4%)	282 (95.9%)/12 (4.1%)	0.002

Note: DC: difficult cases; NDC: non-difficult cases; TACE: transarterial chemoembolization; US: ultrasound; RFA: radiofrequency ablation; WMA: microwave ablation; AM: ablative margin. *Auxiliary procedures: 1. artificial ascites, 2. artificial hydrothorax, 3. open surgery, 4. laparoscopic surgery.

 Table 4. The technical efficacy rates of difficult and nondifficult cases

	Technical efficacy rate
DC group#	99.2% (507/511)
High-risk location (Yes/No)	99.2% (478/482)/100% (29/29)
Unclear on B-mode US (Yes/No)	99.1% (439/443)/100% (68/68)
NDC group	99.7% (293/294)
Р	0.658

#The two types of difficult lesions included the following: 1. lesions in highrisk locations; and 2. lesions that were unclear on B-mode US.



Figure 3. The cumulative incidence curves of local tumor progression (LTP) for the difficult case group (DC group) and the non-difficult case group (NDC group).

cause incomplete ablation occurred more often in difficult cases. The immediate assessment by fusion imaging greatly reduced the incidence of secondary procedures. By the end of the ablation procedure, approximately 89.6% of difficult cases achieved complete ablation with an adequate AM. In summary, real-time fusion imaging was useful for targeting, guidance and assessment during the ablation procedure in difficult cases and significantly improved the technical efficacy and safety.

However, residual tumors remained in 5 cases. These 5 cases were classified as difficult cases due to the inconspicuousness as well as highrisk locations of the tumors. The inconspicuousness of tumors may result in mistargeting, while a high-risk location may lead to difficulties in supplemental ablation. A recent report [34] concerning mistargeting under fusion imaging guidance indicated that the most frequent cause of mistargeting was a small tumor size, followed by confusion with pseudolesions, subcapsular and subphrenic locations, and poor conspicuity. Therefore, for some rare cases, the registration accuracy of fusion imaging was affected, resulting in mistargeting and the occurrence of residual tumors. Additionally, if a tumor location is directly adjacent to critical organs, it may also contribute to the presence of residual tumors due to the difficulty of supplemental ablation. The application of an auxiliary procedure may be one solution to solve this

problem. According to our data, the percentage of auxiliary procedure use was also significantly higher for difficult cases than that for non-difficult cases.

The major complication rate was 1.8% in the enrolled patients, and 2.2% in the DC group, which is lower than or comparable to those reported in most previous studies [3, 4, 8, 11, 14-16, 35]. Specifically, injury to adjacent organs occurred in only 1 patient who sustained a bile duct injury, which resolved after drainage. This complication rate is obviously lower than the reported incidence of critical structure injuries [11, 15, 31]. The application of fusion imaging is expected to provide better visualization of the relationship between tumors and critical organs as well as reduce major complications related to adjacent structure injuries. The remaining complications, such as bleeding, liver abscess, hemothorax, pneumothorax and peritoneal effusion, were probably caused by poor liver function and infection, which were somewhat difficult to avoid even with the application of fusion imaging.

Some limitations existed in this study. First, the present study was a retrospective single-arm study performed in one center without a control group. Thus, a randomized controlled trial (RCT) may be needed to further verify the results. Second, this study did not evaluate long-term survival data in difficult cases, which could be included in a future study.

In conclusion, intra-procedural application of real-time US fusion imaging can improve the therapeutic effect and safety of thermal ablation in difficult cases, reduce experience dependence, and expand the indications for ablation.

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Disclosure of conflict of interest

None.

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