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Original Article

# Computed tomographic-guided percutaneous radiofrequency ablation with hydrodissection of hepatic malignancies in the subcapsular location: Evaluation of safety and technical efficacy

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# Abstract

*Background*: Image-guided percutaneous radiofrequency ablation (RFA) has been the most commonly used modality in the treatment of nonresectable hepatic malignancies. However, tumors in the subcapsular location are still technically challenging. This study was undertaken to evaluate the feasibility, safety, and efficacy of computed tomographic-guided percutaneous RFA with hydrodissection for hepatic malignancies in the subcapsular location.

*Methods*: A total of 103 patients with 253 hepatic lesions were treated with computed tomographic-guided percutaneous RFA. Computed tomographic-guided percutaneous RFA with hydrodissection was performed in 15 patients with 15 hepatic nodules. All tumors located in the hepatic subcapsular location were considered difficult to treat on planning sonography. Hydrodissection was performed with 5% dextrose in water or saline solution in displacing adjacent structures  $\geq$  10 mm away from the liver capsule. Two RFA systems with multitined expandable electrodes or straight internally cooled single electrodes were used for treatment of hepatic malignancies. The feasibility, safety, and efficacy of this technique were analyzed on follow-up contrast-enhanced computed tomography or magnetic resonance imaging.

*Results*: Hydrodissection was successfully achieved in 15 (100%) patients, displacing the adjacent structures  $\geq 10$  mm that were originally < 10 mm away from the liver capsule with administration of a mean of 376 mL of dextrose in water or saline solution. The average distance between an adjacent structure and the liver capsule after hydrodissection was  $1.50 \pm 0.40$  cm and  $0.11 \pm 0.15$  cm prior to hydrodissection, which was statistically significant (p < 0.001). No complication related to hydrodissection occurred during the follow-up period. The primary technical success rate of percutaneous RFA for tumor was 100% (15/15) at 1-month follow-up imaging. There were three minor complications (20%, 3/15) related to the RFA procedure.

*Conclusion*: Computed tomographic-guided percutaneous RFA with hydrodissection is a feasible, safe, and effective technique in the treatment of hepatic malignancies in the subcapsular location.

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Keywords: hepatic malignancy; hydrodissection; radiofrequency ablation

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# 1. Introduction

Among the methods used to treat hepatic malignancies, surgical resection is the proven curative treatment when hepatocellular carcinoma (HCC) or metastatic disease is limited to the liver. However, a majority of patients cannot undergo curative resection because of medical comorbidities and/or severely compromised liver function.<sup>1,2</sup>

Since the 1990s, radiofrequency ablation (RFA) has been most widely used for the treatment of hepatic malignancies, achieving good results in local tumor control and low morbidity and mortality.<sup>2–5</sup> Nonetheless, when the tumor is located in the subcapsular location, it is difficult to place the radiofrequency electrode into the tumor by sonographic guidance because of the partial visibility of the tumor or a poor electrode path. This situation also increases the risk of thermal injury to the adjacent structure resulting in major complications.<sup>6–8</sup>

Several technical methods have been developed to prevent complications and to increase the accuracy of electrode placement, including different approaches, e.g., percutaneous, laparoscopic, or open laparotomy,<sup>9</sup> artificial ascites or pleural effusion,<sup>10,11</sup> and different guiding techniques.<sup>2,10,12,13</sup> To our knowledge, limited data are available on the usefulness of computed tomographic-guided percutaneous RFA with hydrodissection in treating hepatic malignancies in the subcapsular location. Thus, we undertook this study to evaluate the feasibility, safety, and efficacy of computed tomographicguided percutaneous RFA with hydrodissection for hepatic malignancies in the subcapsular location.

# 2. Methods

# 2.1. Patient demographics and medical record review

The Institutional Review Board for Human Investigation of the Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan granted approval to conduct this study (TSGHIRB 098-05-260). Written informed consent was obtained from each patient prior to the percutaneous RFA of hepatic malignancies. Between January 2009 and August 2012 (3.5 years), a total of 103 patients with 253 hepatic tumors were treated with computed tomographic-guided percutaneous RFA at our institution. All patients met the following criteria for percutaneous RFA: up to five nodules with diameters of up to 8 cm, absence of refractory ascites and extrahepatic disease, a platelet count  $\geq$  50,000/mm<sup>3</sup>, and prothrombin activity  $\geq$ 50%. Among the study participants, 15 patients with 15 hepatic nodules underwent computed tomographic-guided percutaneous RFA with hydrodissection because all tumors were located in the subcapsular region (a portion of the tumor located within 5 mm of the liver capsule) and near vital structure (the distance between liver capsule and vital structure < 10 mm). All tumors were considered difficult to treat because of the poor tumor visibility or lack of safe radiofrequency electrode inserted pathway on planning sonography. The 15 patients (age range, 50-80 years; mean age, 63.7

years) had the following origin of hepatic malignancies: five HCCs, five colorectal carcinomas, two breast carcinomas, and one ovarian carcinoma. The tumor diameters prior to ablation ranged from 1.5 cm to 6.0 cm (mean,  $3.30 \pm 1.25$  cm). The follow-up period for all treated lesions ranged from 3 months to 36 months.

## 2.2. Hydrodissection technique

All patients were interviewed prior to the treatment, and all procedures for hydrodissection and percutaneous RFA were performed by one of the two interventional radiologists with 8 years and 12 years of experience in percutaneous RFA of hepatic tumors. Hydrodissection with 5% dextrose in water (D/W) or saline solution was performed with a 21-gauge needle (Chiba needle; Cook Incorporated, Bloomington, IN, USA) connected to a 50-mL syringe via connecting tubing. The choice of the puncture site for hydrodissection was based on the position of the patient and the discretion of the operator. After administering a local anesthetic to the skin at the puncture site, a 21-gauge needle was advanced into the perihepatic space with the goal of placing the needle tip near the interface between the hepatic tumor and the adjacent structure under computed tomographic or sonographic guidance. A 50mL bolus of D/W or saline solution at room temperature was then hand-injected into the perihepatic space. Repeat computed tomography (CT) imaging after the initial bolus of D/W or saline solution was performed to confirm the location of the needle tip and to evaluate the distribution of the solution. An additional 50 mL of D/W or saline solution was injected every 2 minutes until a separation of  $\geq$  10 mm between the liver capsule and the adjacent structure was achieved. At this point, we considered the hydrodissection technically successful.

#### 2.3. Radiofrequency ablation system

Two RFA systems were used. A 200-W generator with multitined expandable electrodes was used in 10 patients with 10 lesions (Boston Scientific, Waltham, MA, USA). A 200-W generator with straight internally cooled single electrode, which was composed of a 3-cm exposed electrode with a thermocouple on the tip and a pulsed current, was used in five patients with five lesions (Covidien Inc., Burlington, MA, USA). The choice of system used was at the discretion of the operator.

#### 2.4. Ablation procedure

In all cases, the treatment rationale was to achieve local control. Percutaneous RFA was performed under computed tomographic guidance. All RFA procedures were performed with either intravenous conscious sedation (n = 10) or general anesthesia (n = 5). Overlapping ablations, ranging from one to six ablations per tumor (mean 2.8), were performed using both generator systems. The RFA algorithm for the internally cooled electrodes consisted of a pulsed current, with each ablation lasting 12 minutes. With the 3-cm expandable electrode

(LeVeen electrode), an impedance-based algorithm was used, and the average time for each ablation was 7-12 minutes. During the RFA, the distance between the liver capsule and adjacent structure was monitored by CT in each ablation. If the distance was < 10 mm, an additional 50 mL of D/W or saline solution was injected until the separation was  $\geq 10$  mm.

## 2.5. Treatment course and follow-up

All patients underwent immediate follow-up without contrast-enhanced CT to evaluate immediate complications after percutaneous RFA. Follow-up contrast-enhanced CT or magnetic resonance imaging (MRI) of the abdomen was performed 1 month after the ablation to evaluate treatment efficacy. Triple-phase CT or MRI studies of the abdomen were obtained. The initial unenhanced scan of the abdomen was followed by enhanced scans obtained at 30 seconds, 70 seconds, and 180 seconds after intravenous contrast administration. Patient MRIs consisted of pre- and postgadolinium enhanced multiplanar T1- and T2-weighted images of the abdomen. A nonenhancing zone of ablation with a diameter greater than that of the hepatic tumor nodule in the axial, coronal, and sagittal planes was considered as a criterion for complete treatment. When nodular or irregular peripheral enhancement was identified within or along the margins of the ablation zone, additional radiofrequency treatments of a presumed residual viable tumor were performed, and follow-up imaging was obtained 1 month later. Thereafter, follow-up imaging was performed every 3 months for 1 year followed by semiannual follow-up imaging.

# 2.6. Definition of technical success of hydrodissection

Technical success was defined as the ability to separate the liver capsule and adjacent structure by a distance of  $\geq 10$  mm during RFA. To estimate the technical feasibility of hydrodissection, we recorded the number of needle punctures required to select the peritoneal space, the total amount of solution injected, the maximum distance between the liver capsule and adjacent structure, and the kind of image guidance used for hydrodissection.

To estimate the safety of hydrodissection, we evaluated whether the injected solution was shifted to the pleural space or retroperitoneal space. We then measured the Hounsfield units (H) of the injected solution between the RFA zone and the adjacent structure on CT, which was performed prior to and immediately after RFA to evaluate whether the injected solution may have a role in the development of hemoperitoneum after RFA. Follow-up contrast-enhanced CT or MRI study of the abdomen was performed 1 month after the ablation to evaluate delayed complications related to hydrodissection.

# 2.7. Definition of therapeutic effectiveness of percutaneous RFA

The results of each CT and MRI study were evaluated retrospectively by a consensus reading by two abdominal

radiologists with 7 years and 10 years of experience in abdominal imaging. The diameter of the tumors prior to the ablation was measured directly from the vascular phase images where the tumors were best visualized in an axial, coronal, or sagittal plane in CT or MRI studies. The data analyzed included tumor diameter, RFA electrode type (multitined expandable or internally cooled), and a diameter of the zone of ablation. The evolution of the diameter of the zone of ablation was based on the 1-month follow-up image study and was reported as the largest diameter of the nonenhancing zone in an axial, coronal, or sagittal plane where the zone of ablation was the largest. Nodular or irregular contrast enhancement within or at the margins of the zone of ablation during portal venous phase imaging after 1 month follow-up examination was considered to be the criterion of local tumor progression. Complications related to percutaneous RFA were also recorded. To assess the therapeutic efficacy of percutaneous RFA, we evaluated the primary technical effectiveness in terms of residual tumor with 1 month follow-up CT or MRI.

# 2.8. Statistical analysis

Continuous data were expressed as mean  $\pm$  standard deviation. The differences in qualitative variables were analyzed using Chi-square test, and differences between the means of the two groups were analyzed using Student *t* test. All *p* values were calculated using two-tailed tests. A *p* value < 0.05 indicated a statistically significant difference. The analyses were performed using the SPSS version 11.0 (SPSS Inc., Chicago, IL, USA).

# 3. Results

# 3.1. Technical feasibility, efficacy, and safety of hydrodissection

Fifteen structures were identified to be < 10 mm away from the liver capsule prior to hydrodissection. These included the ascending colon (n = 7), diaphragm (n = 7), and peritoneum (n = 1). Hydrodissection with D/W or saline solution was technically successful in all patients. The average distance between adjacent structure and liver capsule after hydrodissection was  $1.50 \pm 0.40$  cm (range, 1.0-2.1 cm) and  $0.11 \pm 0.15$  cm (range, 0–0.5 cm) prior to hydrodissection, which was statistically significant (p < 0.001). The technical details of hydrodissection for each patient are shown in Table 1. The average number of needle punctures for hydrodissection was  $1.2 \pm 0.41$  (range, 1–2). The average amount of solution for hydrodissection was 376.00 ± 340.50 mL (range, 100-1500 mL). Hydrodissection was performed on seven patients with lesions located over the medial margin of the liver surface under computed tomographic guidance (Fig. 1), and eight patients with lesions located over the lateral margin of the liver surface under sonographic guidance (Fig. 2).

No injected solution was observed in the right pleural space or retroperitoneal space in any patients during the immediate

Hydrodis	section for he	patic malignar	ncies in subcat	psular location in 15	patients.				
Patient	Segment	Guidance	No. of	Type of	Amount of	Distance between liver capsul	le and adjacent structure (cm)	Attenuation of ini	fused solution (H)
no.			punctures	infused solution	infused solution (mL)	Before	After	Before	After
1	Ν	CT	1	D/W	300	0.5	1.2	7	20
7	Ν	CT	1	D/W	350	0.2	1.9	4	14
3	>	CT	1	Saline	1500	0	2.1	12	23
4	Ν	CT	1	Saline	500	0.2	1.9	10	18
5	Ν	CT	1	D/W	300	0.3	1.6	13	24
9	Ν	CT	1	D/W	350	0	1.6	15	29
7	ΙΛ	CT	1	D/W	400	0.2	1.8	12	22
8	IIV	SU	1	D/W	120	0	1.1	8	23
6	IV	SU	2	D/W	200	0	1.0	6	18
10	IV	SU	1	D/W	200	0	1.2	15	25
11	IV	NS	2	D/W	120	0	1.0	4	22
12	IIV	SU	1	D/W	500	0	1.8	5	14
13	>	SU	1	Saline	500	0	2.0	13	32
14	NIII	SU	2	D/W	100	0.1	1.1	9	21
15	NIII	SU	1	D/W	200	0.2	1.2	5	29
CT = col	mputed tomog	graphy; D/W =	= 5% dextrose	in water; H = Houn	sfied units; $US = sonographics$	phy.			

follow-up CT. The average attenuation of the solution around the ablative zone after RFA was  $22.29 \pm 5.19$  H (range, 14-32 H) and  $9.20 \pm 3.95$  H (range, 4-15 H) prior to RFA, which was statistically significant (p < 0.001). No patients had abnormal vital signs until the day after the procedure. The injected solution was completely absorbed in all patients at the 1-month follow-up CT or MRI. No delayed complications related to hydrodissection such as hemoperitoneum or peritonitis developed during the 1-month follow-up.

## 3.2. Therapeutic effectiveness of percutaneous RFA

The primary technical effectiveness was 100% (15/15) for percutaneous RFA with hydrodissection and 90% (215/238) for percutaneous RFA at 1 month follow-up CT or MRI. The local tumor progression was identified in four lesions (26.7%, 4/15) of percutaneous RFA with hydrodissection and 71 lesions (29.8%, 71/238) of percutaneous RFA during the followup period. The patients' demographics and tumor characteristics are shown in Table 2. Three minor complications related to percutaneous RFA (20%, 3/15) included asymptomatic pneumothorax (n = 2; Fig. 1), and a small perihepatic biloma (n = 1; Fig. 2). All minor complications were managed conservatively.

# 4. Discussion

Many previous investigations have described imagingguided percutaneous RFA for hepatic malignancies in the subcapsular location as a technique with an elevated safety profile and minimally invasive in nature.<sup>11,14-17</sup> However, collateral thermal injury to the adjacent structures, such as the gastrointestinal tract, gallbladder, and diaphragm, is still a technical complication of percutaneous RFA because of poor localization of the tumor.<sup>6,18</sup> Recently, sonography-guided percutaneous RFA with hydrodissection has been recognized as a useful modality for the treatment of HCC in the hepatic dome.<sup>10,11,19</sup> Previous clinical studies using computed tomographic-guided percutaneous RFA with hydrodissection are relatively limited.<sup>20</sup> The results of our study showed that hydrodissection is technically feasible and effective in improving protection of the adjacent structures by separating them away from the liver capsule. The purpose of the present study was to evaluate the feasibility, safety, and efficacy of computed tomographic-guided percutaneous RFA with hydrodissection for hepatic malignancies in the subcapsular location.

Regarding the methods for hydrodissection, the use of a Chiba needle or angiosheath for insertion into the peritoneal space under sonographic guidance appears to be the most popular technique.<sup>3,4,14,17,21</sup> However, the tip of the needle or sheath is difficult to identify on sonography when the tumor is located in the medial margin of the right lobe of liver (segments V and VI). In this study, we used a 21-gauge Chiba needle for hydrodissection under sonographic guidance, when the tumors were located in the lateral margin of right lobe liver or hepatic dome (n = 8) and under computed tomographic

Table



Fig. 1. A 50-year-man with colorectal hepatic metastasis in the subcapsular location over the segment V after computed tomographic-guided percutaneous radiofrequency ablation (RFA) with hydrodissection. (A) Axial contrast-enhanced computed tomography shows a metastatic nodule about 4.3 cm in size in the subcapsular location over the segment V (arrow). (B) Hydrodissection was performed to displace the ascending colon under computed tomographic guidance. (C) Percutaneous RFA of the metastatic lesion with a multitined expandable electrode was performed. Asymptomatic pneumothorax occurred during the RFA procedure. (D) Local tumor progression is identified at the 10-month follow-up contrast-enhanced computed tomography (arrow).

guidance, when the tumors were located in the medial margin of right lobe liver (n = 7). To confirm that the distance between the liver capsule and adjacent structures was  $\geq 10$  mm, all the procedures of hydrodissection were monitored by CT during the ablation. Overall, the technical success rate of hydrodissection was 100% (15/15).

Song et al<sup>16</sup> reported that potential complications related to hydrodissection are bleeding, peritonitis, and tumor seeding. Our study showed that hydrodissection is a safe technique without complications. The H units of the injected solution between the ablative zone and adjacent structure after RFA were mildly higher than those of the injected solution prior to RFA ( $22.29 \pm 5.19$  vs.  $9.20 \pm 3.95$  H). No active bleeding or injected solution shifted to the pleural space or retroperitoneal space was identified in the immediate follow-up CT study after RFA. All patients showed complete absorption of the injected solution on the 1-month follow-up imaging study.

Rhim et al<sup>10</sup> reported that a mean of 348 mL of D/W was infused into the perihepatic space on sonography to improve the visibility in 93.4% (15/16) HCC nodules located in the hepatic dome. Song et al<sup>16</sup> also reported that a mean of 436 mL of D/W solution was injected into the perihepatic space on sonography to create a distance of  $\geq 10$  mm from the adjacent organ. In our study, hydrodissection induced with  $376.00 \pm 340.50$  mL of D/W or saline solution created a distance of  $\geq 10$  mm between the liver capsule and adjacent structure on CT. When classified by tumor location, the group of tumors located in the medial margin of right lobe liver had a larger amount of infused solution than the group of tumors located in the lateral margin (528.57  $\pm$  433.84 mL vs.  $242.50 \pm 164.03$  mL). One patient with a colorectal hepatic metastatic nodule in the medial margin of segment V of liver had 1500 mL saline solution for hydrodissection during the RFA procedure because of posture change, resulting in infused



Fig. 2. A 51-year-woman with breast carcinoma with hepatic metastasis in the subcapsular location over the segment V after computed tomographic-guided percutaneous radiofrequency ablation (RFA) with hydrodissection. (A) Axial contrast-enhanced computed tomography shows a metastatic nodule about 3.3 cm in size in the subcapsular location over the segment V (arrow). (B) Hydrodissection was performed to displace the peritoneum under sonographic guidance. (C) Percutaneous RFA of the metastatic lesion with a multitined expandable electrode was performed. One tine of the expandable electrode penetrated the liver capsule. (D) No local tumor progression but a small perihepatic biloma formation (arrow) is noted and other recurrent metastatic lesions over the right lobe liver are also identified at the 13-month follow-up contrast-enhanced computed tomography.

solution shifting away after the hydrodissection. The results of our study showed that a larger amount of infused solution for hydrodissection was needed for tumors located in the medial margin of the right lobe of liver.

D/W, saline solution, and sterile water have been used for hydrodissection during percutaneous RFA to protect structure adjacent to the ablation zone. Laeseke et al<sup>22</sup> reported that D/ W is particularly well suited to serve as a protective fluid. There are several advantages of D/W acting as insulator during RFA: it is nearly isoosmolar, is well tolerated in virtually every body space, and is rapidly absorbed. Most importantly, it is nonionic and thus does not conduct electricity or produce heating because of ionic agitation. In our study, D/W was used for hydrodissection in 12 patients and saline solution in three patients. No thermal injury of adjacent perihepatic structure or large shifts in systemic fluid was identified at the immediate follow-up CT.

Some authors have reported that tumors with a subcapsular location and abutting hollow viscera have a high rate of local tumor progression and increased risk of complications.<sup>23,24</sup> However, our results showed that the complete necrosis after RFA on the 1-month follow-up imaging was obtained in 15 (100%) of the 15 lesions. Additionally, local tumor progression was 26.7% (4/15) during the follow-up period. In the present study, all patients underwent percutaneous RFA under computed tomographic guidance to place the electrode into the lesion. When classified by the RFA system, the group of tumors treated using a multitined expandable electrode had a higher local tumor progression rate than the group of tumors treated using a straight internally cooled single electrode (40%, 4/10 vs. 0%, 0/5), but without statistical significance (p = 0.099, Chi-square test). The use of the straight internally cooled single electrode facilitated to place the electrode tip closer to the liver capsule than the use of the multitined

Table 2

Patients'	demographic	and tumor	characteristics	for 15	hepatic	malignancies.

Characteristic	Value
Age (y)	$63.67 \pm 9.80 (50 - 80)$
Sex (male/female)	9/6
Tumor origin <sup>a</sup>	7/5/2/1
Tumor size (cm)	$3.30 \pm 1.25 \ (1.5 - 6.0)$
RFA systems <sup>b</sup>	10/5
No. of ablations per tumor	$2.80 \pm 1.52 \ (1-6)$
Zone of ablation size (cm)	$4.59 \pm 1.02 \ (3.2-6.5)$
Primary technical effectiveness after RFA	100 (15/15)
Local tumor progression rate after RFA	26.7 (4/15)
Average local tumor progression time (mo)	5.75 ± 3.10 (3-10)
Average follow-up time (mo)	$11.73 \pm 8.65 (3-36)$

Data are presented as mean  $\pm$  standard deviation (range) or % (*n*/*N*), unless otherwise indicated.

RFA = radio frequency ablation.

<sup>a</sup> Hepatocellular carcinoma/colorectal carcinoma/breast carcinoma/ovarian carcinoma.

<sup>b</sup> Boston Scientific, Waltham, MA, USA/Covidien Inc., Burlington, MA, USA.

expandable electrode under computed tomographic guidance during percutaneous RFA.

It is easy to monitor the ablative zone on computed tomographic guidance using a multitined expandable electrode, but the shape of the ablation zone is not circular, and has the potential to puncture the adjacent structure.<sup>25</sup> In the present study, a small perihepatic biloma was observed in one patient after RFA. The patient with a metastatic nodule in the lateral margin of segment V was treated using a multitined expandable electrode. During the RFA procedure, one tine of the electrode penetrated the liver capsule resulting in thermal injury of the capsule after RFA. To prevent such complication, the use of computed tomographic guidance for monitoring the location of the deployed radiofrequency electrode is recommended.

This study has several limitations. First, the number of patients and tumors were small, limiting the power of the study. Second, we could not evaluate the true benefit of the hydrodissection to prevent thermal injury of the adjacent structures during RFA because we could not conduct a randomized controlled study. Third, the overall survival was not included in the outcome measures because the purpose of our study was to evaluate the benefit of computed tomographic-guided percutaneous RFA with hydrodissection for hepatic malignancies in the subcapsular location.

In conclusion, the present results indicated that computed tomographic-guided RFA with hydrodissection is a feasible, safe, and effective treatment for hepatic malignancies in the subcapsular location. This procedure is an alternative technique when percutaneous RFA under sonographic guidance is difficult to perform because of poor tumor visibility or lack of safe radiofrequency electrode inserted pathway.

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