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ORIGINAL ARTICLE

Overcoming the heat-sink phenomenon: successful radiofrequency thermal ablation of liver tumors in contact with blood vessels

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PURPOSE
To evaluate the efficacy and safety of computed tomography (CT)-guided radiofrequency thermal ablation (RFA) of liver tumors (hepatocellular carcinoma and liver metastases) >3 mm in diameter that were in contact with blood vessels.

MATERIALS AND METHODS
During a 3-year period RFA was performed in 28 patients (age range, 36–83 years; male/female ratio, 17:11) with liver tumors (primary and metastatic) that were in contact with blood vessels >3 mm in diameter. Tumor diameter ranged from 1.7 to 5.1 cm. To evaluate the immediate response, dual-phase dynamic CT images were obtained after intravenous contrast material administration. Imaging follow-up was at 1, 3, 6, and 12 months post-RFA, and every year thereafter.

RESULTS
All of 28 patients were treated with a total of 36 sessions. In 22 (79%) of the patients, complete ablation of the tumor was achieved. The remaining 6 (21%) patients showed irregular peripheral enhancement and underwent a second session. At 1-year follow-up 2 of the tumors showed a recurrent lesion and a new ablation was performed. The local tumor progression rate at 1-year follow-up was 8.7% and disease-free survival was achieved in 82.1% of the patients. Complications occurred in 4 patients (14.3%); 2 patients presented with a small sub-capsular hematoma, and 2 patients had a partial liver infarction.

CONCLUSION
RFA is a safe and effective method, even with high-risk tumors adjacent to large blood vessels, which can lead to good results with minimal complications and a low rate of tumor progression.

Key words: • *liver tumors* • *radiofrequency thermal ablation* • *percutaneous catheter ablation*

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Hepatocellular carcinoma (HCC) is one of the most common types of cancer worldwide, with an estimated incidence of at least one million new patients per year (1). The liver is second only to the lymph nodes as the most frequent site of metastasis from other solid cancers (2), especially from colorectal adenocarcinoma (3).

Surgical resection remains the gold standard treatment of primary and metastatic liver cancer (4). Surgical resection of HCCs and metastases from colorectal cancer isolated in the liver can result in a long-term survival benefit in 20%–40% of patients (5–8). Unfortunately, hepatectomy is not ideal for treating all tumors, as some patients are unable (due to comorbidities) or unwilling to undergo surgery, or tumor size and location are exclusionary (9). In fact, only 5%–20% of patients with HCC or colorectal cancer liver metastases undergo potentially curative resection (10–11). In recent years an alternative method has been used therapeutically with promising results, radiofrequency thermal ablation (RFA). It's a low cost and minimally invasive technique that can be completed during a single treatment session during a short hospitalization, or even on an outpatient basis. Furthermore, complications associated with the procedure are minimal when performed by an experienced radiologist (12–20). It works by converting radiofrequency waves into heat. The temperature inside the ablated tissue must be greater than 60 °C to achieve coagulation necrosis.

It has been demonstrated that liver tumors adjacent to large blood vessels are inadequately ablated because of heat loss that is the result of convection by tissue from the blood flow, which acts as a heat-sink (21–23). The presence of vessels ≥3 mm in diameter near the tumor that must be ablated is a strong independent predictor of incomplete thermal tissue destruction (24). At the same time, ablating such tumors is dangerous, as vessels may be damaged directly by the electrode needle and indirectly by the heat induced inside the tumor.

Herein we present a retrospective review on our experience with a number of cases involving such tumors treated with RFA under CT guidance. We identify the efficacy of the method based on follow-up and report the complications that occurred.

Materials and methods

Between January 2001 and December 2003 RFA was performed in 28 patients with liver tumors in contact with blood vessels >3 mm in diameter. All patients were evaluated by a liver surgeon and were considered not to be surgical candidates. The 17 male and 11 female patients had a mean age of 60 years (range, 36–83 years). All patients had undergone dual-phase spiral CT and percutaneous CT-guided core needle biopsy with an 18 gauge × 10-cm automated core biopsy needle (Somatex® Medical Technologies GmbH, Germany) for histological tumor evalu-

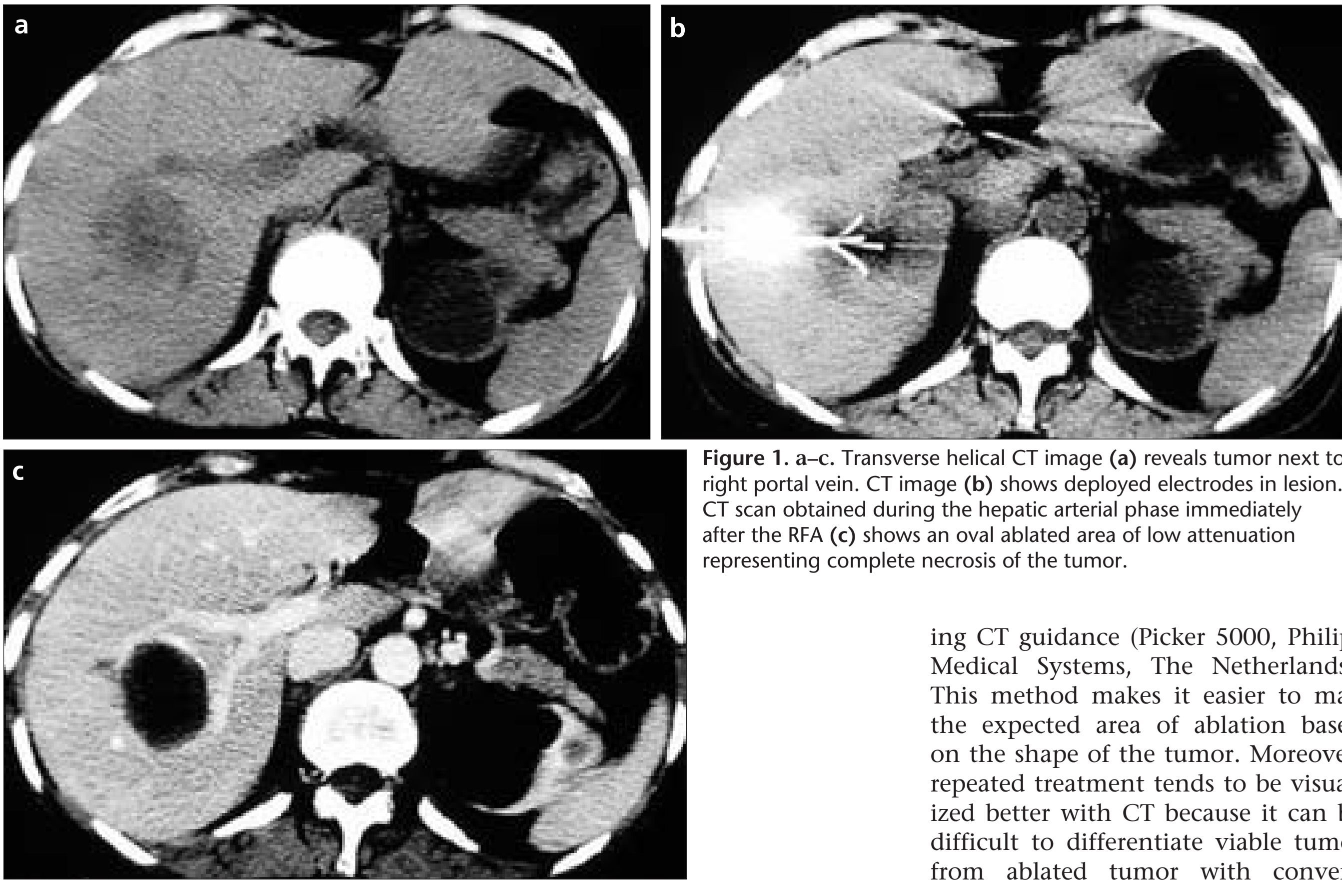

Figure 1. a–c. Transverse helical CT image **(a)** reveals tumor next to right portal vein. CT image **(b)** shows deployed electrodes in lesion. CT scan obtained during the hepatic arterial phase immediately after the RFA **(c)** shows an oval ablated area of low attenuation representing complete necrosis of the tumor.

ation. The histopathologic result was HCC in 9 of the 28 patients and was metastatic cancer in the other 19. The primary site of malignancy was known in all 19 cases; 14 had colon adenocarcinoma, 3 had stomach cancer, 1 had breast cancer, and 1 had lung cancer. After careful examination of patients' demographics, tumor histology, size, and location, their physician, in agreement with the radiologist, proposed percutaneous RFA.

All RFAs were performed in the CT suite by a consulting radiologist specializing in RFA interventions since 1996. Initially, the entire procedure and the expected result were explained to the patients to enhance their participation in the process, and informed consent was obtained from each one. Before RFA, medical history was obtained and a physical examination was performed. In all patients with primary carcinoma a metastatic tumor evaluation was performed, which included CT of the abdomen and chest. All patients were also subjected to blood screening, including hemoglobin, hematocrit, WBC, platelet count, internationalized normalized ratio (INR), thromboplastin time (PTT), and serum tumor markers (AFP, CEA, etc.). All were trained in regular breathing and breath-holding (suspended respiration) before the procedure, which was performed in the CT suite after the patient was administered antidepressant and analgesic [3 mg of bromazepam (Lexotanil®, Roche) per os 45 min before the procedure and 75 mg D-propoxyphen hydrochloride (Zideron®, Norma Hellas S.A., Greece). All procedures were performed under local anesthesia (lidocaine hydrochloride [Xylocaine® 2%, AstraZeneca, Monts, France]).

In all patients the size, exact location, and with which vessel the tumor was in contact were recorded. HCCs ranged in size from 2 to 4.7 cm, while that of the metastases ranged from 1.7 to 5.1 cm. All lesions were located adjacent to large blood vessels. The term adjacent was defined as the absence of normal liver parenchyma between the tumor and the wall of a vessel > mm in diameter, as confirmed with CT images.

All ablations were accomplished percutaneously by a consulting radiologist specializing in biopsies and RFA, using CT guidance (Picker 5000, Philips Medical Systems, The Netherlands). This method makes it easier to map the expected area of ablation based on the shape of the tumor. Moreover, repeated treatment tends to be visualized better with CT because it can be difficult to differentiate viable tumor from ablated tumor with conventional ultrasonography. All patients were placed in the supine position and surgical skin cleaning was performed (10% povidone-iodine). Two different types of electrosurgical generators were used: A RITA® 1500 (Rita Medical Systems, Inc., Mountain View, California USA) with a 7- or 9-array multi-tined expandable electrode and a Miras (Invatec, S.r.l., Roncadelle, Italy) with a spiral expandable electrode. The choice of the electrode type was based on lesion size and location.

Afterwards, the insertion of the electrode began in a stepwise manner, while the tip of the trocar was controlled with 3 contiguous 5-mm CT slices. When it was confirmed that the tip was placed approximately 1 cm from the center of the lesion, the electrodes were deployed slowly (Figs. 1a, b). We attempted to position the electrode tip near vessel's lumen for better tissue ablation. After a final check the device and the dispersive electrodes were connected to the generator.

The generator was set to the desired setting and changes were made during the ablation according to the manufacturer's instructions. A pulsed RF energy was applied for 15–20 min (depending on the size of the lesion and the vessel

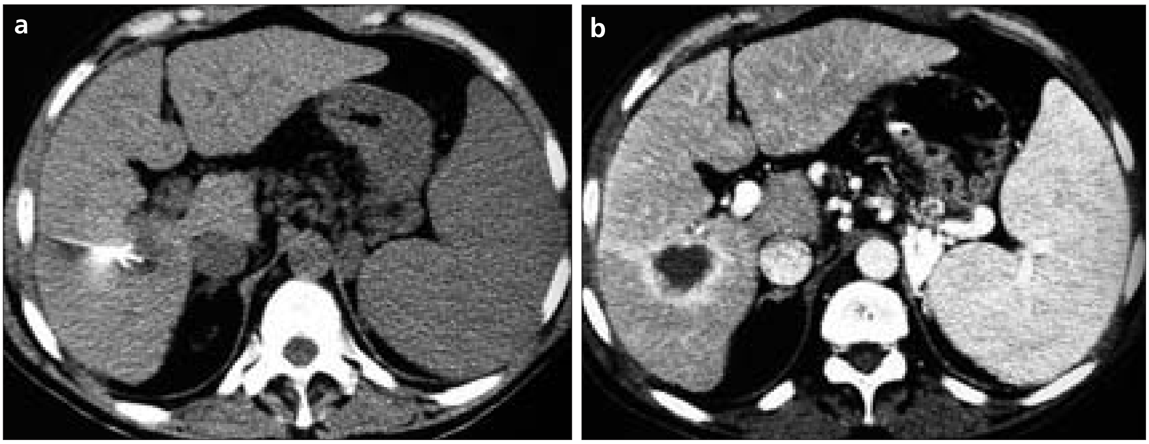

Figure 2. a, b. Transverse helical CT image **(a)** reveals tumor next to porta hepatis. CT image obtained immediately after the RFA **(b)** shows an oval ablated area of low attenuation representing complete necrosis of the tumor and enhancement of the surrounding liver tissue, due to hyperemia.

next to it). If patients complained of mild to moderate pain during the procedure, 1–2 ml of local anesthetic was infused at the puncture site or via the RF electrode in RITA-type cases. Tissue temperature and impedance were recorded during the ablation. The tissue temperature needs be over 70 °C and the impedance might have a reduction indicative of effectual tissue burning. When the tissue was completely burned the impedance was suddenly hiked and ablation, with MIRAS device, was terminated. After the ablation was completed the electrodes were retracted and low-pulse RF energy was applied for track ablation in all cases to prevent tumor seeding.

To evaluate the lesion's immediate response to ablation and to identify any potential complications, dual-phase dynamic contrast-enhanced CT was performed (Fig. 1c). After ablation patients were hospitalized for 24-h monitoring. Immediate and long-term complications were recorded as well.

Follow-up was performed with serum tumor markers and dual-phase dynamic contrast-enhanced CT at 1, 3, and 6, 12 months post-RFA, and every 6 months afterwards.

Results

All of 28 patients were treated for a solitary liver tumor (9 HCC and 19 metastatic) with a total of 36 sessions. All tumors were next to vessels >3 mm; 5 lesions were in contact with the inferior vena cava, 2 with the left portal vein, 4 with the right portal vein, 16 with the hepatic vein, and 1 with the porta hepatis (Table 1).

All procedures were performed percutaneously under CT guidance. Mean RF energy application time was longer in tumors that were not near large vessels (in an attempt to overcome the heat-sink phenomenon) than in tumors of equal size that were near large vessels. RFA was the sole treatment modality for these hepatic tumors. In 2 HCCs and 9 metastatic lesions a MIRAS device with a spiral expandable electrode (this type of electrode is for lesions ≤ cm, the 19G trocar is less traumatic) was used. In 3 HCCs and 4 metastases a RITA device with a 9-array multi-tined expandable electrode (for lesions ≤5 cm) was used. In 4 HCCs and 6 metastases a RITA device with a 7-array multi-tined expandable electrode (for lesions ≤3 cm) was utilized. In 3 HCCs and 5 metastases 2 overlapping ablations were performed during 1 session; in 1 metastatic lesion 3 overlapping ablations were performed.

Contrast-enhanced CT images obtained immediately following RFA revealed partial or total cystic transformation of the ablated tumor and enhancement of the surrounding liver tissue due to hyperemia (Fig. 2). The final result of tumor necrosis was estimated at the 1-month follow-up. The first month's follow-up image revealed cystic-type attenuation values and no enhancement in 22/28 (79%) of the tumors. Among those 22 lesions, 7 (31.8%) were reduced in size and 15 (68.2%) remained stable. In 6/28 (21%) of the tumors (3 HCCs and 3 metastases) a residual viable part was seen. The viable tumor had the same imaging with its pre-ablation CT or magnetic resonance imaging control (irregular enhancement during the arterial phase in HCCs and a hypodense, non-cystic part in the metastases). All these lesions underwent a second RFA session with complete technical success. Imaging with dual-phase spiral CT and serum tumor markers were also used for monitoring the response to RFA therapy. In all patients that had elevated serum tumor marker values

Table 1. Types of blood vessels in contact with radiofrequency thermal ablation-treated tumors

Blood vessel near the tumor	Mean size (cm)	Number
Inferior vena cava	3.5	5
Left portal vein	2.6	2
Right portal vein	2.4	4
Hepatic vein	3.3	16
Porta hepatis	4.8	1

before RFA, a reduction was observed post-RFA. This attenuation was considered to be indicative of successful ablation of the lesions. Serum AFP levels rose again in 6 patients who presented with local tumor progression, but the levels remained normal after the second RFA session.

The 3- and 6-month follow-ups revealed no tumor progression or new lesions. Five patients with metastatic disease died before the 1-year follow-up (1 from brain hemorrhage, 1 from heart fibrillation, and 3 from dissemination of their disease). Their last follow-up revealed no signs of residual tumor in the ablation site. At the 1-year imaging follow-up 10/23 (43.5%) lesions (4 HCCs and 6 metastases) were the same size and 13/23 (56.5%) lesions (5 HCCs and 8 metastases) were smaller. Of the tumors that did not change size, 2, the biggest HCC and the biggest metastasis, had a recurrent lesion in contact with the ablated tissue, away from the bordering vessel. A second ablation was performed with complete technical success in each case.

Among the 9 patients with HCCs, 1 underwent liver transplantation 18 months after RFA, and 1 died due to a heart attack and 1 died from pulmonary edema 18 and 21 months, respectively, after RFA; 1 patient at his 3-year follow-up had new foci. The remaining 4 patients were alive with normal imaging findings and normal serum AFP 39, 42, 49 and 51 months after RFA. The ablated HCCs remained silent.

As for the 14 patients with metastases, 1 died in a car accident 24 months after RFA (there was no evidence of recurrence in the ablated lesion or of dissemination), 9 died from generalized disease, and the remaining 4 patients had no signs of active disease 37, 43, 48, and 49 months after RFA. All patient data (lesion size, location relative to a large vessel, the type of electrode used), 1-month and 1-year imaging follow-up, and survival are shown in Table 2.

Immediate complications occurred in 4 patients (14.3%) (36 RFA sessions): 2 patients developed a small sub-capsular hematoma (not requiring transfusion or surgical management), and 2 patients developed a partial liver infarction without clinical sequel. The patients that felt pain at the puncture site after the procedure received analgesic treatment. There were no periprocedural or delayed complications in the vessels that were in contact with the ablated lesions (damage, laceration, or thrombosis). There were no deaths as the direct result of the RFA procedure. There were no complications in all repeated RFA sessions.

Discussion

Although surgical resection remains the gold standard treatment for hepatic tumors (particularly primary tumors), it is possible in only 20% patients at the time of tumor diagnosis (4). Several interventional techniques that aim to provide local destruction of the tumor have been developed and clinically tested over the past few years. Since the 1980s, RFA, a minimally invasive technique, has gained a great deal of attention as an alternative to surgical resection of liver tumors. With RFA the complication rate is lower, the cost is reduced (25), and finally, repeated treatment is possible. RFA can effectively treat deep lesions while preserving hepatic parenchyma. The aim of RFA is to create an area of thermocoagulation with a diameter larger than or at least equivalent to that of the tumor.

In many patients with hepatic tumors, resection is not feasible because the lesion is adjacent to critical vascular structures. For those patients RFA seems to be a viable alternative. The presence of local tumor progression after RFA of lesions adjacent to large blood vessels due to the heat-sink phenomenon (tissue cooling by blood flow that causes thermal loss) has also been described. Wood et al. (4) mentioned that the tissue under ablation nearby the vessel wall is inadequately ablated due to heat loss and is a high-risk site for persistent or progressive disease. Also, Lu et al. (24) report that the presence of vessels ≥ 3 mm, contiguous to hepatic tumors, is a strong independent predictor of incomplete tumor destruction by RF energy.

In our study we retrospectively reviewed all liver tumors treated with RFA that were adjacent to large blood vessels. The therapeutic efficacy of RFA for treating these tumors was evaluated and the complications were recorded in order to measure the safety of the procedure for lesions that were in a dangerous location.

All of 28 patients with liver tumors (primary and metastatic) in contact with blood vessels >3 mm were treated. The type of tumors, the exact locations, and mean size of the lesions are presented in Tables 1 and 2.

The area of ablation usually appeared round or oval, and had low attenuation in contrast-enhanced CT images at follow-up, which represents tumor necrosis. The 1-month follow-up with contrast-enhanced dual-phase spiral CT of 22 tumors revealed the appearance that was mentioned before; however, at this first follow-up, 6 patients had a residual tumor located next to the bordering vessel. This residual tumor enhanced with contrast material administration. Identifying these results we observed that 5 index tumors were initially 3.1–5.1 cm and 1 was smaller, about 2.8 cm. Among them, 4 of the partially-ablated tumors were nearby the IVC wall and 2 were nearby the HV. Three of the local progressive tumors were HCCs. We think that the effectiveness of ablation depends on high-energy deposition and good tissue heating. This seems to correlate well with the size of the tumor (heat loss in the periphery), vascularity of the tumor itself (in HCC and in hypervascular metastases the attained temperature was lower due to cooling from inside the blood vessels), and finally, with the contiguity of the tumor to large vessels (heat sink phenomenon). When these 3 parameters co-exist the tissue has a greater possibility of inadequate ablation. Following these observations we decided to increase the total time of ablation up to 3 min during the second RFA session we performed for tumors located adjacent to large blood vessels and even longer if the lesions were hypervascular. When lesion size was quite large we repositioned the electrode at a different site inside the lesion. No local tumor progression was observed after those adjustments. So, we observed that by increasing the duration of RFA the percentage of residual tumor decreased. For the lesions <2 cm in diameter (n = 3, 10.7%) RFA lasted 10 min. The emission of radiofrequency to 19 (67.9%) tumors that were between 2 and 4 cm was 15 min. The remaining 6 (21.4%) lesions, which were between 4.1 and 5.1 cm, were ablated for 20 min.

Two patients, 1 with HCC and 1 with metastasis, that already had 2 ablation sessions for the same tumor showed irregular peripheral enhancement at the 1-year imaging follow-up. These findings were not near the bordering vessel and were considered recurrence of the tumor.

The local tumor progression rate in the present study was 8.7%. Previous studies have reported highly variable local tumor progression rates associated with RFA, ranging from 0% to 100% (4, 18, 26–28). Curley et al. (18) reported a local tumor progression rate of 1.8% in one of the largest series published to date.

It is remarkable that 26 from the 28 patients we treated with RFA had no signs of recurrence in the ablated lesions, even though they revealed new lesions or dissemination of their disease. The ablated lesion remained silent.

The complications of the 36 procedures were 2 small sub-capsular liver hematomas, which did not require treatment, and 2 partial infarcts

Table 2. Clinical, radiologic, and histopathological data for 28 patients with primary and metastatic liver carcinoma treated with percutaneous radiofrequency thermal ablation under CT-guidance

				1-month follow-up			1-year follow-up			
A/A	Histologic cancer type	Baseline tumor size	Type of vessel	Tumor size	Tumor necrosis	RFA	Tumor size	Tumor necrosis	RFA	Survival (months)
1	HCC	7R3.1 cm	IVC	U	Residual tumor	+	U	Complete ablation	–	39
2	HCC	M2.2 cm	LPV	↓	Complete ablation	–	↓	Complete ablation	–	51
3	HCC	9R4.7 cm	HV	U	Residual tumor	+	U	Recurrence	+	19, dissemination
4	HCC	M2.8 cm	HV	U	Complete ablation	–	↓	Complete ablation	–	18, transplantation
5	HCC	7R 3.4 cm	HV	U	Complete ablation	–	U	Complete ablation	–	42
6	HCC	9R 4.9 cm	IVC	U	Residual tumor	+	↓	Complete ablation	–	18, heart attack
7	HCC	7R 3.1 cm	HV	U	Complete ablation	–	U	Complete ablation	–	21, pulmonary edema
8	HCC	7R 2.9 cm	HV	U	Complete ablation	–	↓	Complete ablation	–	49
9	HCC	9R 3.6 cm	HV	↓	Complete ablation	–	↓	Complete ablation	–	36, new foci
10	Colorectal ca	7R 2.8 cm	IVC	U	Residual tumor	+	U	Complete ablation	–	19, dissemination
11	Colorectal ca	M 1.7 cm	HV	U	Complete ablation	–	↓	Complete ablation	–	43
12	Colorectal ca	M 1.9 cm	RPV	U	Complete ablation	–	↓	Complete ablation	–	48
13	Colorectal ca	9R 5.1 cm	HV	U	Residual tumor	+	U	Recurrence	+	22, dissemination
14	Colorectal ca	9R 4.6 cm	HV	U	Complete ablation	–	↓	Complete ablation	–	24, car accident
15	Colorectal ca	7R 3.2 cm	RPV	U	Complete ablation	–				11, brain hemorrage
16	Colorectal ca	7R 2.9 cm	HV	U	Complete ablation	–	U	Complete ablation	–	24, dissemination
17	Colorectal ca	9R 4 cm	HV	↓	Complete ablation	–	↓	Complete ablation	–	23, dissemination
18	Colorectal ca	M 2.7 cm	HV	U	Complete ablation	–				10, ventricle fibrillation
19	Colorectal ca	9R 4.1 cm	IVC	U	Residual tumor	+	U	Complete ablation	–	25, dissemination
20	Colorectal ca	7R 3 cm	LPV	U	Complete ablation	–	↓	Complete ablation		26, dissemination
21	Colorectal ca	M 2.1 cm	HV	↓	Complete ablation	–	↓	Complete ablation	–	49
22	Colorectal ca	M 4.8 cm	PH	U	Complete ablation	–				11, dissemination
23	Colorectal ca	M 1.8 cm	RPV	U	Complete ablation	–	↓	Complete ablation	–	37
24	Stomach ca	M 2.2 cm	HV	U	Complete ablation	–	U	Complete ablation	–	24, dissemination
25	Stomach ca	M 2.4 cm	IVC	↓	Complete ablation	–				10, dissemination
26	Stomach ca	7R 3.1 cm	HV	↓	Complete ablation	–				11, dissemination
27	Lung ca	M 2.8 cm	RPV	U	Complete ablation	–	U	Complete ablation	–	13, dissemination
28	Breast ca	7R 3.3 cm	HV	↓	Complete ablation	–	↓	Complete ablation	–	25, dissemination

HCC: hepatocellular carcinoma; 7R: RITA with 7 electrodes; 9R: RITA with 9 electrodes; M: MIRAS; IVC: inferior vena cava; LPV: left portal vein; RPV: right portal vein; HV: hepatic vein; U: stable size; ↓: decreased size.

without clinical sequel. There were no complications (thrombosis or occlusion) in the adjacent large blood vessels. Although the complication rate was 11%, all of the complications were minor and conservatively treated. There were no major bleeding complications and no deaths related to the RFA procedure.

Several studies refer to the effectiveness of RFA after temporary occlusion of the hepatic artery or portal vein, or both with balloon occlusion or with gelatin sponge particles, in order to reduce heat-sink effect (21, 22, 29, 30). Reducing blood flow during the RF procedure is known to increase the coagulation area. Some studies have reported differences in the size of the area of radiofrequency-induced coagulation obtained with arterial occlusion alone or in combination with venous occlusion (21, 22, 29, 30). Temporary vascular occlusion is an invasive procedure and the addition of an RF procedure, during or soon after vascular occlusion, adds to the complexity, cost, and patient discomfort of the procedure. Our aim was to find an alternative method of increasing the area of RF-induced coagulation in tumors that are adjacent to large vessels.

In conclusion, initial results have shown that RFA is a safe and effective procedure, even for high-risk tumors adjacent to large blood vessels. The complication rate and the progressiveness rate appear to be acceptable (18, 26, 27, 31). It is superior to other treatment methods for liver tumors, such as chemotherapy and radiotherapy. We think that by increasing total ablation time by 3–4 min (depending on vessels type and size, and tumor volume and vascularity) we can overcome the possibility of local tumor progression due to the heat-sink effect, without such side effects as vessel thrombosis. Careful selection of patients and optimum technique can lead to good results with minimal complications and a low rate of progressiveness. The method can lead to debulking and provide non-operable patients with a better quality of life.

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