Radiology

Large (≥5.0-cm) HCCs: Multipolar RF Ablation with Three Internally Cooled Bipolar Electrodes—Initial Experience in 26 Patients[1]

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Purpose: To prospectively evaluate the safety and effectiveness of percutaneous multipolar radiofrequency (RF) ablation for the treatment of large (≥5.0 cm in diameter) hepatocellular carcinomas (HCCs).

Materials and Methods: Twenty-six patients (four women, 22 men; median age, 72 years) with cirrhosis (Child-Pugh class A disease, 22 patients; Child-Pugh class B disease, four patients) and at least one 5.0–9.0-cm-diameter HCC without invasion of the portal trunk or main portal branches were treated with multipolar RF ablation performed by a single operator. The procedure was performed with three separate bipolar linear internally cooled electrodes with ultrasonographic guidance. Twenty-seven of the 33 tumors treated had a diameter of 5.0 cm or greater (median diameter, 5.7 cm; range, 5.0–8.5 cm); 12 of these 27 tumors were infiltrative, and four invaded segmental portal vein branches. Ten patients had a serum α-fetoprotein level higher than 400 μg/L. Results were assessed by using computed tomography. Primary effectiveness, complications, tumor progression, and survival rates were recorded. Probabilities of survival were calculated by using the Kaplan-Meier method.

Results: One to two RF ablation procedures per patient (mean, 1.15 ± 0.43 [standard deviation]) led to the complete ablation of 22 (81%) of the 27 tumors (18 tumors after one and four tumors after two procedures), including three tumors that showed segmental portal vein invasion. All patients experienced postablation syndrome, and one experienced subcapsular hematoma and a segmental liver infarct, but no major complication occurred. After a mean follow-up of 14 months (range, 3–34 months), local and distant tumor progression and actual survival rates were 14% (three of 22), 24% (five of 21), and 65% (17 of 26), respectively. The probabilities of 1- and 2-year survival, respectively, were 68% (95% confidence interval: 49%, 86%) and 56% (95% confidence interval: 51%, 81%).

Conclusion: HCCs larger than 5.0 cm (but smaller than 9.0 cm)—even those that are infiltrative and those that involve a segmental portal vein—can be completely and safely ablated with multipolar RF ablation.

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In the case of monopolar radiofrequency (RF) ablation, complete ablation rates of up to 90% have been reported for hepatocellular carcinomas (HCCs) smaller than 3 cm in diameter (1,2). Unfortunately, with the same technique, complete ablation rates decrease dramatically (to less than 50%) for HCCs larger than 3 cm in diameter (3,4).

The poor performance of current monopolar techniques in large tumors is related to their limited tissue ablation capacity per application. Two studies in which the most widespread monopolar systems were compared in animal models revealed that one of these devices, which uses an expandable electrode, yields, at best, coagulation zones of approximately 3.5–4.5 cm on the short axis (5,6). Because the complete ablation of a tumor requires safety margins, these performances are clearly insufficient for the proper treatment of a tumor target larger than 3 cm in a single application. Therefore, to ensure entire coverage of the targeted zone with monopolar devices, multiple overlapping RF ablations with successive positionings of the electrode are required (7,8). However, in clinical practice, overlapping ablation is time consuming and might be technically difficult, especially with ultrasonographic (US) guidance, as the targeted area is progressively masked by a transient hyperechogenic pattern induced by tissue water vaporization.

It has been suggested that with simultaneous insertion of up to three coaxial bipolar electrodes, the multipolar RF ablation technique could lead to the complete ablation of liver tumors up to 7.4 cm in maximal size (9–12). However, these studies included both patients with HCC and patients with liver metastasis and included a large majority of tumors smaller than 5 cm.

Because HCC is still relatively frequently diagnosed at an advanced stage that is beyond the spectrum of efficacy of current monopolar RF devices, the aim of this pilot study was to prospectively evaluate the safety and effectiveness of percutaneous multipolar RF ablation for the treatment of large (≥5.0 cm in diameter) HCCs.

Advances in Knowledge

- The technical success of multipolar radiofrequency (RF) ablation for the treatment of large hepatocellular carcinomas (HCCs) is not limited by the need to position three electrodes.
- With the multipolar mode, the complete ablation of HCCs of up to 8 cm in diameter, even in the case of infiltration and/or segmental portal vein involvement, is a realistic goal for RF ablation alone.

Materials and Methods

Patient Selection and Tumors

This prospective pilot study was approved by the institutional review board of Jean Verdier Hospital. All patients were included after they signed an informed consent form. Between January 2004 and November 2006, 26 patients with cirrhosis and at least one 5.0-cm or larger HCC underwent percutaneous multipolar RF ablation with US guidance. The decision to treat patients with multipolar RF ablation was made by a multidisciplinary team (including hepatologists, a liver surgeon, an interventional radiologist, and an oncologist). The indications for treatment depended on the stage of the tumor, as assessed with computed tomographic (CT) or magnetic resonance imaging; the feasibility of the percutaneous approach, as assessed by an interventional radiologist; the patient's liver function; and the patient's general condition.

The selection criteria were as follows: *(a)* histologically proved cirrhosis, *(b)* a firm diagnosis of HCC according to either histologic findings or the noninvasive criteria proposed by the European Association for the Study of the Liver conference (13), *(c)* presence of at least one tumor 5.0 cm or larger but not exceeding 9.0 cm in diameter, *(d)* no more than three detectable tumors, *(e)* absence of tumoral invasion of the trunk or the main portal veins, *(f)* margin of the tumor(s) at a minimal distance of 1 cm from the colon wall and/or from the main right or left bile duct, *(g)* ineligibility for surgical resection or transplantation, *(h)* percutaneous accessibility of the tumor(s) with US guidance, *(i)* prothrombin activity of 50% or greater and platelet count of 40.10^3/mL or greater, *(j)* cirrhosis of Child-Pugh class A or B, and *(k)* no contraindication to general anesthesia. During the same period of study enrollment, 36 additional patients with cirrhosis and HCCs of 5.0 cm or larger were referred to our center. Among these patients, six underwent liver resection, and the remaining 30 were considered to be ineligible for surgery or multipolar RF ablation and were treated with transarterial chemoembolization (TACE).

The final study group of 26 patients included 22 men and four women (median age, 72 years; range, 41–88 years). Two of the 26 patients were treated for distant tumor progression of HCC—one after surgical resection and the other after (monopolar) RF ablation. All patients had histologically proved cirrho-

Implication for Patient Care

- Multipolar RF ablation is a curative therapeutic option for a patient with a large but not diffuse HCC who is considered ineligible for surgical treatment.

Published online before print
10.1148/radiol.2481071101

Radiology 2008; 248:288–296

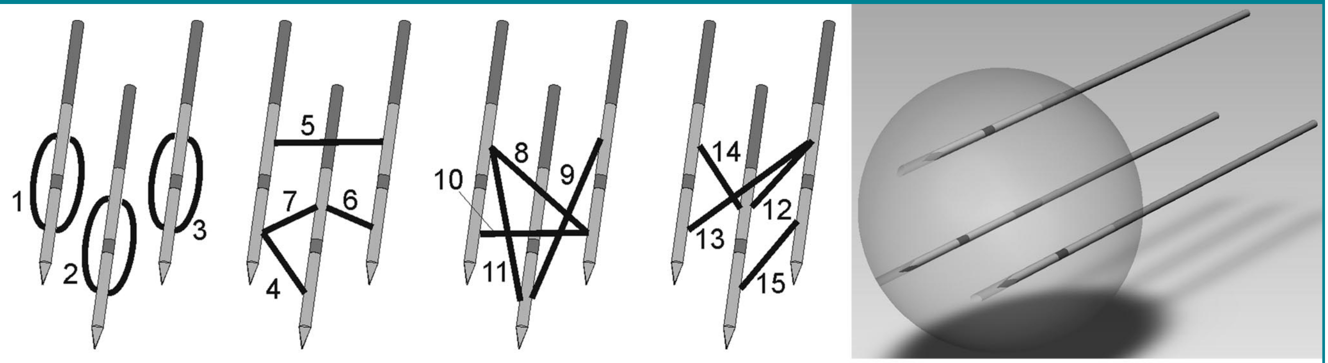
Abbreviations:
HCC = hepatocellular carcinoma
RF = radiofrequency
TACE = transarterial chemoembolization

Author contributions:
Guarantors of integrity of entire study, O.S., N.S.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, O.S., G.N., M.I.; clinical studies, O.S., G.N., Y.A., C.B., N.G., E.C., J.C.T., M.B., N.S.; statistical analysis, O.S., G.N.; and manuscript editing, O.S., G.N., M.B.

Authors stated no financial relationship to disclose.

sis related to alcohol (n = 14), viral hepatitis C (n = 7), viral hepatitis B (n = 3), or hemochromatosis (n = 2). Cirrhosis was classified as Child-Pugh class A in 22 patients and as Child-Pugh class B in four. The α-fetoprotein serum level ranged from 2 to 4321 μg/L and was higher than 400 μg/L in 10 patients. In addition to the main tumor (≥5.0 cm), four patients had one (n = 2) or two (n = 2) smaller tumors (≤4.9 cm). A fifth patient had two tumors that were larger than 5.0 cm. Thus, in this study, a total of 33 tumors, including 27 tumors that were

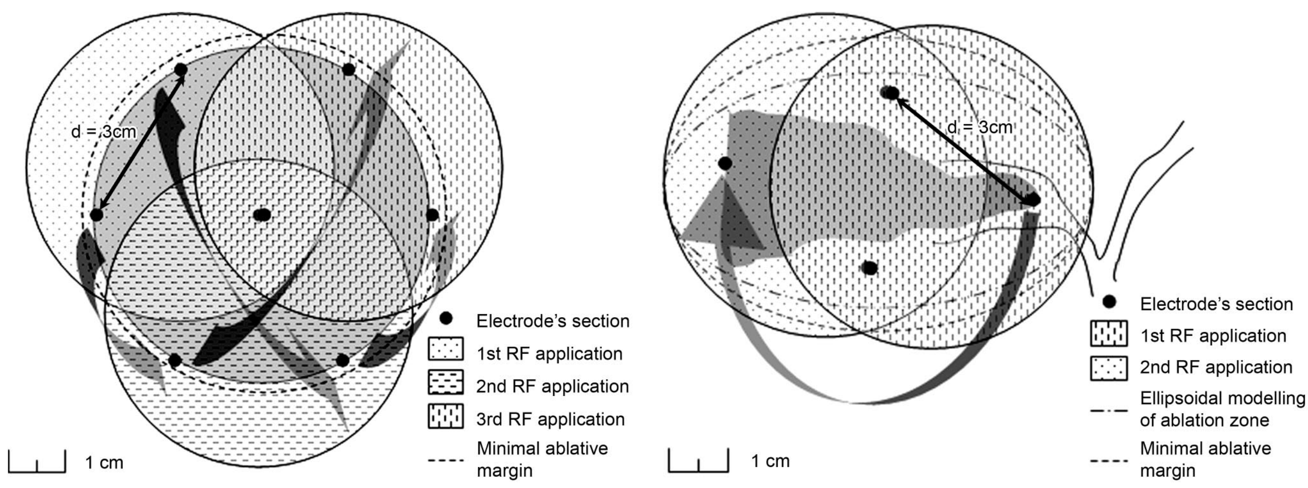
Figure 1



a. b.

Figure 1: Diagram of one multipolar RF application performed with three bipolar electrodes inserted according to equilateral triangular conformation with 3.0-cm sides. **(a)** The 15 possible bipolar combinations are sequentially activated for 2 seconds. Multiple overlapping electric fields are induced between active parts of electrodes. **(b)** After a cumulative energy deposition of about 120 kJ, a 6-cm spherical ablation zone can be achieved.

Figure 2



a. b.

Figure 2: Plan of multipolar RF ablation for large tumor (≥5.0 cm in diameter) requiring multiple overlapping applications. d = Distance from one electrode to another. **(a)** Diagram shows plan of multiple overlapping applications to ablate a 6-cm-diameter spherical tumor: The first application is performed with three electrodes inserted according to a equilateral triangular conformation (in which each side of the triangle is 3.0 cm) in the upper right tiers of the tumor; thereafter, the second application is performed by reinserting the peripheral two electrodes used in the first application to reformat the 3.0-cm–sided triangular configuration of electrodes in the lower tiers of the tumor, while the third electrode remains in the central location. Finally, to complete the ablation, a third, similar application is performed in the upper left tiers of the tumor. **(b)** Diagram shows plan for the ablation of an infiltrative 6-cm-diameter tumor that invades a segmental portal vein: First, the desired ablation zone is modeled to include an ellipsoid form around all areas involved by the tumor, which has invaded the parenchyma and portal tract. The first application is performed to ablate the medial part (vascular pole) of the tumor; the second is performed to ablate the lateral part of the tumor. This plan requires reinserting only one electrode: The medial electrode is simply transported to the lateral periphery of the tumor to re-form a symmetric opposite triangular electrode conformation, and the two electrodes left in place are used as external and internal landmarks.

5.0 cm or larger, were treated with multipolar RF ablation.

The diameter of the 27 larger tumors ranged from 5.0 to 8.5 cm, with a median value of 5.7 cm. Among these 27 tumors, 23 were subcapsular, 19 were in close contact with hepatic vessels that were larger than 3 mm (either the portal or the hepatic vein, or both), 12 were infiltrative, and four invaded subsegmental or segmental portal vein branches. Diagnosis of HCC was made on the basis of histologic findings at percutaneous biopsy for 14 tumors and on the basis of noninvasive criteria for the remaining 13 tumors. For all patients, liver resection was considered to be contraindicated because of an insufficient benefit-to-risk ratio related to the high risk of postoperative liver failure (n = 7), technical limitations related to the location or stage of the tumor (n = 8), the presence of severe comorbidities (n = 2), or a combination of several unfavorable conditions (n = 9). All patients had contraindications to transplantation because of tumor stage and/or their age.

Multipolar RF Ablation Procedure

All procedures were performed by the same operator (O.S., with 9 years of percutaneous treatment experience at the time the study began). General anesthesia with tracheal intubation was used for all patients. The drugs used were 0.1–2.0 μg of intravenous sufentanil (Sufenta; Janssen-Cilag, Issy-les-Moulineaux, France) per kilogram of body weight and 1.5–2.5 mg/kg intravenous propofol (Diprivan; AstraZeneca, Rueil-Malmaison, France). A US system with a convex 3.5-MHz probe (Aplio XV; Toshiba Medical Systems, Tokyo, Japan) was used for guidance in all procedures.

For tumors 5.0 cm or larger, the procedures were performed by using three separate internally cooled linear electrodes (CelonProSurge; Celon Medical Instruments, Telow, Germany) that were 1.8 mm in diameter and 15.0 cm in length (including a 4-cm collinear distal bipolar active part) (11). Sterile water at room temperature was pumped into the internal lumen of the electrodes by using a triple peristaltic pump (CelonAquaflow III; Celon Medical Instruments). The three electrodes were inserted inside the tumor at a 3.0-cm maximal distance from each other, ideally in parallel and with an equilateral triangular conformation (Fig 1). The electrodes were connected to a 250-W (maximal output power) and 470-kHz RF generator (CelonLabPower; Celon Medical Instruments), which provided sequential electric feeding of all 15 possible bipolar combinations between the three electrodes (Fig 1). Therefore, the volume of tissue located in and around 1 cm outside the triangular zone circumscribed by the three electrodes was automatically heated by switching overlapped electromagnetic fields in 15 different directions (Fig 1). The initial output power was set at 150 W but, from the beginning of the energy application, was dynamically adjusted according to automatic resistance tissue feedback (11).

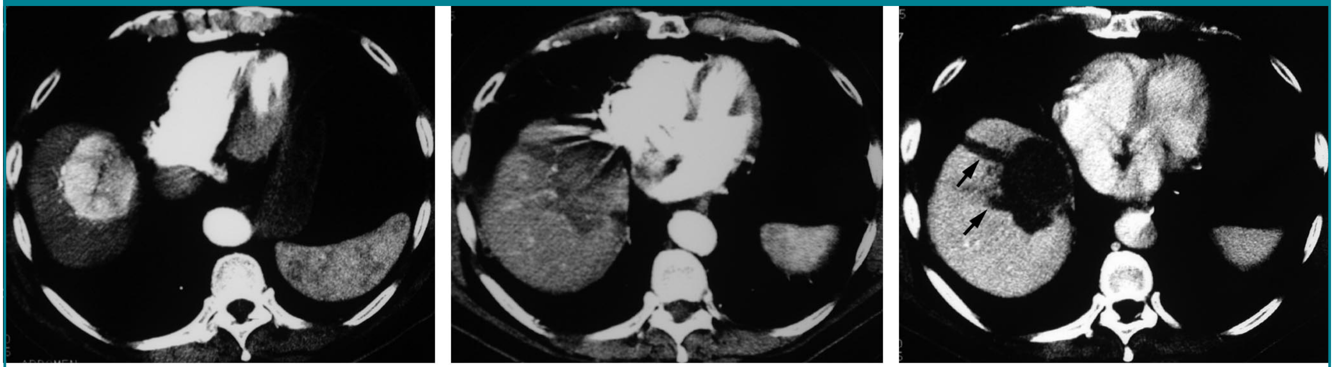
During the phase of energy deposition, the output power was automatically reduced to a level that depended on tissue properties. The end point of one application was the cumulative energy deposited in tissue, which was set to 120 kJ according to previous results (11,14) adapted from our own preliminary clinical experience in HCC ablation with the multipolar device. With this setting, a single application could theoretically result in complete ablation of a spherical 5.0-cm-diameter tumor with a 5.0-mm ablative margin. Thus, the number of applications depended mainly on the size and shape of the tumor. If more than one application was required because of the geometric characteristics of the tumor, one or two electrodes were removed and reinserted for each additional application according to a rotatory translation plan of electrode placement (Fig 2). The one or two electrodes remaining in situ were used as external and internal landmarks for reinserting electrodes in such a way that the new triangular 3.0-cm equilateral conformation was achieved. In practice, the theoretical plan of multiplying RF ablation applications could be adjusted according to the requirements of the patient's anatomy. In cases of infiltrative tumors or portal invasion, the procedure was planned to ablate spherical or ellipsoid tissue volumes, encompassing the whole

Figure 3

a. b.

Figure 3: Transverse CT scans in arterial phase show complete ablation of large infiltrative HCC invading the segmental portal vein in 82-year-old man with Child-Pugh class A cirrhosis related to alcohol abuse. **(a)** Scan obtained before treatment shows infiltrative 6.3-cm hypervascular mass (arrow) in segment VIII of the liver that invades the segmental portal vein. **(b)** On scan obtained one month after multipolar RF treatment consisting of two procedures, including three applications (total amount of RF energy delivered, 435 kJ), the mass, including the intravascular invasion, no longer enhances. The α-fetoprotein serum level decreased from 1330 to 4 μg/L, confirming the imaging results consistent with complete ablation. Note also the segmental infarct of liver (arrow) and the presence of a small posterior subcapsular fluid collection (arrowhead).

Figure 4



a. b. c.

Figure 4: Transverse CT scans show complete ablation of large HCC in 63-year-old man with Child-Pugh class A cirrhosis related to viral hepatitis C. **(a)** Before treatment, scan obtained in arterial phase shows 5.2-cm subdiaphragmatic hypervascular mass in segment VIII of the liver. **(b)** One month after multipolar RF ablation consisting of one procedure, including two applications (total amount of RF energy delivered, 240 kJ), scan obtained in arterial phase shows absence of tumor enhancement consistent with complete ablation. **(c)** On scan obtained during the portal phase of the same CT study at which **b** was obtained, the mass remains unenhanced. Note also the ablated electrode tracks (arrows).

zone thought to be part of the tumor with an ablative margin of at least 5.0 mm (Fig 2).

Treatment of the six multifocal tumors smaller than 5.0 cm in five patients was also performed with the multipolar RF ablation technique during the same procedure. Depending on the size of these smaller tumors, fewer than three electrodes were used to completely treat the tumor with a single application.

Thermal ablation of the needle track was performed separately for each electrode withdrawal.

Treatment Evaluation and Follow-up: Safety and Effectiveness

After each procedure, patients remained hospitalized for at least 24 hours. In all cases, early response was assessed 1 month after RF ablation with a three-phase CT examination performed by using a spiral CT unit (PQ 6000; Marconi-Philips, Cleveland, Ohio). Our standardized CT scan protocol included an initial unenhanced scanning pass of the entire liver with 8-mm collimation. This was followed by two contrast material–enhanced passes with 5-mm collimation 20 seconds after (for the arterial phase) and 60 seconds after (for the portal phase) the start of an intravenous power injection of 170 mL of iodinated contrast material (iohexol, Omnipaque [300 mg iodine per milliliter]; Amersham, Cork, Ireland) at 5 mL/sec. All images were obtained as continuous transverse scans in helical mode by using a pitch of 1.5, 220 mA, and 12 kVp. Hard copies of images were available for all patients. Assessment of early response included, in addition to CT examination, serum α-fetoprotein level determination in patients with initially elevated values.

CT scans were interpreted by one of four radiologists (Y.A., C.B., E.C., and N.S., who had 2–9 years of experience in interpreting postablation CT scans at the time this study began) and were systematically reviewed by the operator. A tumor was considered to be completely ablated if no nodular or irregular enhancement adjacent to the ablation zone was visible in the arterial phase. A thin (≤5.0-mm-thick) regular periablational ring of enhancement, visible in the arterial phase and persisting during the portal phase, was considered to be a benign physiologic response to thermal injury. In the case of visible residual tumor, an additional multipolar RF ablation procedure(s) was performed by using up to three electrodes (depending on the volume to be ablated) if the patient still satisfied the study inclusion criteria. If the additional procedure could not be attempted or did not achieve complete ablation, the patients were referred, if possible, for palliative treatment, especially TACE. Such situations were considered to represent primary failures of multipolar RF ablation treatment.

During follow-up, α-fetoprotein levels were obtained and US and three-phase spiral CT were performed every 3 months. Delayed complications and tumor progression were recorded. Local tumor progression was defined as the appearance of nodular or irregular enhancement adjacent to the ablation zone, and distant intrahepatic tumor progression was defined as the emergence of one or several tumor(s) not adjacent to the site of the initial ablation zone. If local or distant tumor progressions were detected, patients were referred for new multipolar RF ablation treatment if they still met the inclusion criteria. The number of applications and procedures, the amount of energy delivered per treatment, and the duration of procedures and applications were recorded. The following items were computed: primary technical success (defined as the achievement of the planned multipolar RF ablation procedure), primary treatment effectiveness (defined as the rate of complete tumor ablation as assessed at a CT examination performed 1 month after the last multipolar RF ablation procedure of the treatment course [which could involve one or several procedures, as long as local residual active tumor seen at a CT examination performed 1 month after each procedure was considered amenable to RF ablation]), and the rates of local and distant tumor progression. Survival and causes of death were recorded. Complications of multipolar RF ablation treatment were assessed according to the guidelines of the Society of Interventional Radiology (15).

Table 1

Characteristics of Tumors and Treatments in 27 HCCs 5.0 cm or Larger according to Early Response to Multipolar RF Ablation

Parameter	Complete Ablation (n = 22)	Incomplete Ablation (n = 5)
Tumor characteristic		
Diameter (cm)*	5.9 ± 0.9 (5.0–8.0)	6.2 ± 1.7 (5.0–8.5)
Multifocality†	4 (18)	2 (40)
Contact with vessels†‡	15 (68)	4 (80)
Subcapsular location†	18 (82)	5 (100)
Infiltrative form†	8 (36)	4 (80)
Portal invasion†§	3 (14)	1 (20)
Serum α-fetoprotein level greater than 400 µg/L†	6 (27)	5 (100)
Treatment characteristic		
No. of procedures*	1.2 ± 0.4 (1–2)	1.25 ± 0.5 (1–2)
No. of applications*	2.5 ± 2.1 (1–10)	3 ± 2.4 (1–7)
Amount of energy (kJ)*	205 ± 95 (90–435)	192 ± 103 (50–270)

Note.—Early response was assessed 1 month after the last RF procedure by using triphasic CT and α-fetoprotein serum levels.

* Data are mean values ± standard deviations, with ranges in parentheses.

† Data are numbers of tumors, with percentages in parentheses.

‡ Contiguous with normal hepatic vessels 3 mm or greater in diameter.

§ Involving segmental portal veins but not the trunk or main portal left or right branches.

Table 2

Characteristics of Tumors and Treatments in 22 of 27 HCCs 5.0 cm or Larger That Were Completely Ablated with Multipolar RF Ablation according to the Occurrence of Local Tumor Progression during Follow-up

Parameter	No Local Tumor Progression (n = 19)	Local Tumor Progression (n = 3)
Tumor characteristic		
Diameter (cm)*	5.8 ± 0.7 (5.0–7.5)	6.5 ± 1.5 (5.0–8.0)
Multifocality†	3 (16)	1 (33)
Contact with vessels†‡	13 (68)	1 (33)
Subcapsular location†	15 (79)	3 (100)
Infiltrative form†	7 (37)	1 (33)
Portal invasion†§	3 (16)	0
Serum α-fetoprotein level greater than 400 µg/L†	5 (26)	1 (33)
Treatment characteristic		
No. of procedures*	1.21 ± 0.42 (1–2)	1 ± 0
No. of applications*	2.16 ± 1.42 (1–6)	4.67 ± 4.73 (1–10)
Amount of energy (kJ)*	207 ± 97 (100–435)	193 ± 96 (90–280)

Note.— Mean follow-up was 14 months ± 8.

* Data are mean values ± standard deviations, with ranges in parentheses.

† Data are numbers of tumors, with percentages in parentheses.

‡ Contiguous with normal hepatic vessels 3 mm or greater in diameter.

§ Involving segmental portal veins but not the trunk or main portal left or right branches.

Statistical Analysis

One- and 2-year probabilities of survival were estimated with the Kaplan-Meier method by using software (MedCalc, version 8.2, 2007; MedCalc Software, Mariakerke, Belgium). Survival was computed from the date of the start of treatment to the date of the most recent information or the death of the patient. Patient data were censured at the date of the most recent information. The end date of the study was April 15, 2007.

Results

Technical Success

No technical failure occurred. The treatment of 27 tumors 5.0 cm or larger required a mean of 1.15 procedures ± 0.43 (standard deviation) that included a mean of 2.59 RF applications ± 2.15 (range, 1–10 applications). The mean ratio of RF applications per procedure was 2.25 ± 1.9 (range, 1–10). The mean amount of energy delivered was 202.5 kJ ± 94 per treatment of tumor. The mean time of a single procedure was 102 minutes ± 35 (range, 45–165 minutes), including a mean time of RF application of 81 minutes ± 21 (calculated as 36 minutes of mean time for a single RF application times the ratio of applications per procedure). Thus, the whole mean time allowed for electrode positioning per procedure (estimated from the difference between the mean time of a single procedure and the mean time of RF application per procedure) was 21 minutes and corresponded roughly to 20% (21 of 102 minutes) of the mean duration of a single procedure.

Safety

All patients experienced postablation syndrome, including fevers from 38°C to 39°C and general malaise that persisted for up to 2–3 weeks. No hepatic decompensation occurred. Within 72 hours after the ablation, four (15%) of 26 patients required a morphine injection to relieve postprocedural pain.

The mean hospital stay per procedure was 2.5 days ± 1.4 (range, 1–7 days).

No major or early complication, periprocedural death, or delayed complication (such as tumor seeding along the electrode tracks) was recorded. One month later, a second procedure was performed for the completion of the treatment of a 7.1-cm infiltrative HCC that involved the portal branches of segment VIII. CT revealed a segmental liver infarct and a small subcapsular fluid collection (Fig 3). Within a few weeks, this patient, who had been in mild pain, became asymptomatic. Follow-up CT showed progressive complete resolution of the fluid collection.

Primary Effectiveness

CT performed 1 month after a single procedure showed complete ablation of all five tumors that were smaller than 5.0 cm. Among the 27 tumors that were 5.0 cm or larger, 22 were completely ablated (18 after a single procedure and four after a second procedure). Thus, the primary effectiveness of multipolar RF ablation treatment for tumors 5.0 cm or larger was 81% (22 of 27) (Fig 4). Complete ablation was achieved for three of the four tumors that involved a segmental portal vein and for eight of the 12 infiltrative tumors (Fig 3, Table 1).

Tumor Progression and Survival

Mean patient follow-up was 14 months ± 8 (range, 3–34 months).

Local tumor progression.—Among the 22 tumors 5.0 cm or larger in which complete ablation was achieved, three (14%) had secondary local tumor progression at CT—8 months after initial treatment in one case and 9 months after initial treatment in two cases. One of these three instances of local tumor progression was successfully treated, again with multipolar RF ablation (Table 2).

Distant tumor progression.—Among the 21 patients for whom RF ablation led to the complete ablation of all tumors, five (24%) experienced distant tumor progression 1–7 months after initial treatment. One of these patients had synchronous local tumor progression. He was successfully re-treated for both types of tumor progression with a single multipolar RF ablation procedure. One other patient with secondary distant tumor progression was also successfully re-treated with multipolar RF ablation (Table 3).

Survival.—Nine patients died within a mean period of 8 months ± 6.5

Table 3

Characteristics of Tumors and Treatments in 21 Patients with HCCs 5.0 cm or Larger That Were Completely Ablated with Multipolar RF Ablation according to Occurrence of Distant Tumor Progression

Parameter	No Distant Tumor Progression (n = 16)	Distant Tumor Progression (n = 5)
Tumor characteristic		
Diameter*	5.9 ± 0.9 (5.0–8.0)	5.8 ± 0.9 (5.0–7.1)
Multifocality†	2 (12)	1 (20)
Contact with vessels†‡	10 (62)	3 (60)
Subcapsular location†	13 (81)	4 (80)
Infiltrative forms†	4 (25)	4 (80)
Portal invasion†§	1 (6)	2 (40)
Serum α-fetoprotein level greater than 400 μg/L†	3 (19)	2 (40)
Treatment characteristic		
No. of procedures*	1.12 ± 0.34 (1–2)	1.4 ± 0.55 (1–2)
No. of applications*	2.56 ± 2.22 (1–10)	2.6 ± 2.3 (1–6)
Amount of energy (kJ)*	215 ± 94 (100–435)	166 ± 113 (90–335)

Note.— Mean follow-up was 14 months ± 8.

* Data are mean values ± standard deviations, with ranges in parentheses.

† Data are numbers of tumors, with percentages in parentheses.

‡ Contiguous with normal hepatic vessels 3 mm or greater in diameter.

§ Involving segmental portal veins but not the trunk or main portal left or right branches.

Figure 5

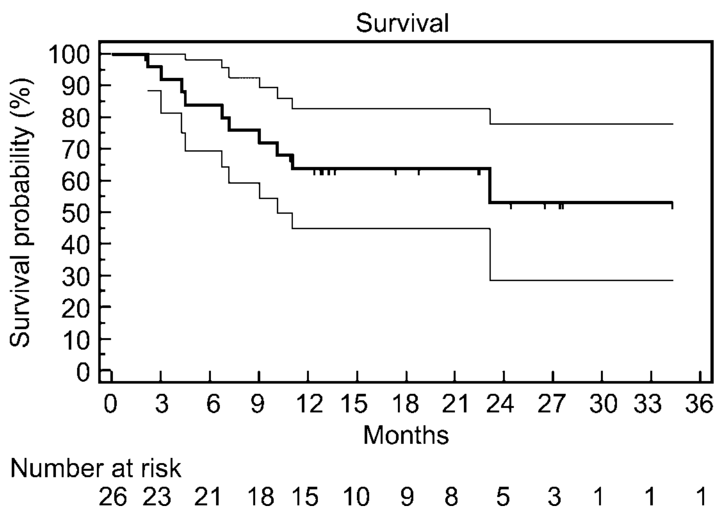


Figure 5: Graph shows probabilities of survival calculated with Kaplan-Meier method for 26 patients treated with multipolar RF ablation for large HCC (≥5.0 cm in diameter). Thin lines = boundaries of 95% confidence intervals. Marks on survival curve show the censored survivor patients at the time of the last available information.

(range, 3–11 months). Thus, the actual survival rate was 65% (17 of 26). Among the 17 surviving patients, 58% (15 of 26) were free of tumor progression according to the latest available information. The primary effectiveness rates of treatment in the survivor and no-survivor subgroups were 94% (16 of 17) and 67% (six of nine), respectively. Deaths were related to tumor progression in five patients, to intracranial hemorrhage in one patient with tumor progression, to stroke in one patient free of tumor progression, and to unknown causes in two patients (one of whom did not have tumor progression). Probabilities of 1- and 2-year survival were, respectively, 68% (95% confidence interval: 49%, 86%) and 56% (95% confidence interval, 51%, 81%) (Fig 5).

Discussion

Our study results show that the complete ablation of tumors up to 8 cm is feasible and safe in patients with HCC and cirrhosis and that multipolar RF ablation may overcome the main limitation of the percutaneous technique—namely, the size of the tumor. To overcome the limited effectiveness of monopolar RF ablation for medium and large HCCs, different techniques combined with therapeutic approaches have been suggested; in particular, a combination of monopolar ablation with TACE as a first step has been advocated (16,17). However, although the volume of tissue destruction per RF application is clearly increased after TACE, the benefit-to-risk ratio of such an approach remains to be demonstrated in terms of tumor progression and survival rates (18,19). Recently, further important technologic improvements to RF devices have been implemented. Preliminary results have suggested that a single RF application performed with a new multipolar RF device could induce a spherical ablation zone of 6 cm in diameter (14). Therefore, by using such a device, the complete treatment of tumors far larger than 3 cm with RF application becomes conceivable (11,12).

In our study, multipolar RF ablation alone led to the complete ablation of 81% (22 of 27) of HCCs larger than 4.9 cm (median diameter, 5.7 cm) without technical failure. Moreover, the high-volume tissue ablation capacity of the multipolar mode made it possible to achieve the complete ablation of infiltrative HCCs, which in three cases invaded segmental portal veins. Although in our study patients with these negative tumor characteristics had a tendency to more frequently experience distant tumor progression during follow-up, the results we obtained in this subgroup remain very encouraging. Thus far, infiltrative HCC involving portal branches has been regarded as beyond the spectrum of indications for RF ablation. Livraghi et al (3), using monopolar RF alone, treated medium and large HCCs and reported no case of complete ablation for these infiltrative forms. By contrast, in our study, complete ablation was achieved for eight of 12 patients with infiltrative forms. Moreover, four of these patients remained free of distant tumor progression and seven remained free of local tumor progression during the following months.

Despite requiring at least three tumor punctures, multipolar RF involved an acceptable procedure time (mean, 102 minutes ± 35). In practice, the technical success was greatly enhanced by the fact that only one or two of the three electrodes had to be repositioned for each additional RF application. Thus, the electrode(s) systematically left in place were used as external and internal landmarks for the accurate reinsertion of the other electrode(s). This point is essential, because up until now, using the monopolar RF mode, large-volume ablation required an overlapping multiple applications procedure planned according to a geometric modeling method that was particularly difficult to follow in clinical practice (8).

An increased rate of complications could have been expected because of the larger size of the ablation zone. Although all patients experienced postablation syndrome, no major complication occurred, despite the very large volumes of ablation induced with the multipolar RF mode. These results were achieved in a frail population; in particular, four patients had Child-Pugh class B cirrhosis, which is usually regarded as a contraindication to TACE because of the high risk of worsening liver function (20).

A limitation to the results of our pilot study was the relatively small number of patients, as well as the absence of a control group; this prevents definite conclusions about the real benefit of multipolar RF ablation in terms of survival. Nevertheless, the results are encouraging, as our patients all had a clearly advanced stage of HCC, often with multiple tumors and vascular involvement. In such difficult-to-treat patients, in selected cases, TACE could only have a palliative effect at a cost of nonnegligible morbidity.

In conclusion, the multipolar RF mode clearly extends the limits of tumor size for complete ablation of HCC. Thus, with the multipolar mode, complete tumor ablation can be achieved for large HCCs, even in the case of infiltrative and segmental portal invasion, with a low rate of complications and an acceptable rate of midterm secondary tumor progression. Assessment of the survival benefit of such treatment of HCC, however, still requires further investigation.

Acknowledgments: The authors thank A. Roggan, PhD, and T. Stein, PhD, from Celon/Olympus Company for their scientific support in describing the technical design of the multipolar RF device. The authors also thank J. Marty, MD, from the Department of Biostatistics of Jean Verdier Hospital, for her advice and support for survival calculation.

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