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Percutaneous Microwave Ablation of Hepatocellular Carcinoma with a Gas-Cooled System: Initial Clinical Results with 107 Tumors

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Abstract

Purpose—To retrospectively review the results of hepatocellular carcinoma (HCC) treatment with a high-power, gas-cooled, multiantenna-capable microwave device.

Materials and Methods—A total of 107 HCCs in 75 patients (65 men) with a mean age of 61 years (range, 44–82 y) were treated via percutaneous approach. Combination microwave ablation and transarterial chemoembolization was performed for 22 tumors in 19 patients with tumors larger than 4 cm ($n = 10$), tumors larger than 3 cm with ill-defined margins ($n = 7$), or lesions not identified with ultrasonography ($n = 5$). Mean tumor size was 2.1 cm (range, 0.5–4.2 cm), with median follow-up of 14 months, for ablation alone; compared with 3.7 cm (range, 1.0–7.0 cm) and 12 months, respectively, for combination therapy. All procedures were performed with a single microwave system (Certus 140) with one to three 17-gauge antennas.

Results—Mean ablation time was 5.3 minutes (range, 1–11.5 min). All treatments were considered technically successful in a single session. Primary technique effectiveness rates were 91.6% (98 of 107) overall, 93.7% (89 of 95) for tumors 4 cm or smaller, and 75.0% (nine of 12) for tumors larger than 4 cm; and 91.8% (78 of 85) for ablation alone and 90.9% (20 of 22) for combination therapy. There was no major complication or procedure-related mortality. The overall survival rate was 76.0% at a median 14-month clinical follow-up, with most deaths related to end-stage liver disease ($n = 11$) or multifocal HCC ($n = 5$).

Conclusions—Treating HCC with a gas-cooled, multiantenna-capable microwave ablation device is safe, with promising treatment effectiveness.

Radiofrequency (RF) ablation is becoming increasingly accepted to treat unresectable tumors of the liver, kidney, lung, and bone (1). However, based on the results of multiple clinical trials (2,3), a broad consensus has now been reached about the limitations of treating

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tumors larger than 3.0 cm in diameter with RF alone. Microwave ablation has physical advantages that can potentially overcome many of the current limitations of RF ablation. These advantages include a wider zone of active heating resulting in shorter procedure times, insensitivity to charring, sustained tissue temperatures beyond the threshold of water vaporization, true multiple applicator capability that takes advantage of electromagnetic and thermal synergy, and less susceptibility to vascular heat sinks (4–6). However, until recently, clinical microwave systems available in the United States and Europe were limited by antenna shaft heating from reflected power, large antenna diameters, and low power output leading to small-diameter ablation zones (7–9). The introduction of water or gas antenna cooling has resulted in a proliferation of higher-power microwave systems in the United States, Europe, and Asia. Although a series of more than 1,000 patients with hepatocellular carcinoma (HCC) treated with a microwave system only available in Asia has been reported with promising results (10), data from the United States and Europe are limited and currently include only series performed with single-antenna, water-cooled systems (3,11). The purpose of the present study is to report our single-center results with the treatment of 107 HCCs with a high-powered, gas-cooled, multiple antenna-capable microwave system, with particular emphasis on the rate of local control and complications.

MATERIALS AND METHODS

Patient Selection

Institutional review board approval was obtained to deidentify a clinical database for research purposes, and a waiver of informed consent was granted. All patients who underwent percutaneous microwave ablation for HCC between December 2010 and March 2013 at a single tertiary-care hospital were included in the analysis. A total of 107 lesions were treated in 75 patients (10 women, 65 men) during 81 procedures. The mean patient age was 61.3 years (range, 44–82 y), and the mean Model for End-stage Liver Disease score was 10 (range, 6–18). Mean lesion diameter was $2.5 \text{ cm} \pm 1.2$ (range, 0.5–7.0 cm). All patients had cirrhosis with underlying causes that included hepatitis C (n = 37), combined hepatitis C and alcoholic liver disease (n = 16), alcoholic liver disease (n = 8), nonalcoholic steatohepatitis (n = 6), autoimmune hepatitis (n = 2), primary biliary cirrhosis (n = 2), hepatitis B, coexistent hepatitis B and C, hemochromatosis, and cryptogenic cirrhosis (n = 1 each). All patients had one to three foci of HCC at the time of the ablation (59 sessions treated one tumor each, 16 sessions treated two tumors, and six sessions treated tumors). All tumors were diagnosed as HCC per American Association for the Study of Liver Diseases guidelines except for the three tumors smaller than 1 cm treated in patients with coexistent larger tumors, all of which met the criteria of late arterial-phase hyper-enhancement and delayed washout (12). Percutaneous ablation was determined to be the best treatment option for each patient by a multidisciplinary team of radiologists, hepatologists, oncologists, and hepatic and transplant surgeons at a consensus conference. All patients referred for ablation of HCC during the study period underwent microwave ablation with the exception of two patients who underwent RF ablation within the first year based on operator preference.

Procedure

All ablations were performed under general anesthesia via a percutaneous approach by one of four radiologists experienced in tumor ablation (with 19, 10, 3, and 1 year of experience at the beginning of the study, respectively). Patients were administered cefazolin (or clindamycin if allergic) immediately before the procedure. All ablations were performed with a single high-powered, gas-cooled, multiple antenna-capable microwave system (Certus 140, 2.4 GHz; Neuwave Medical, Madison, Wisconsin) with one (33 sessions), two (33 sessions), or three (15 sessions) antennas (Fig 1). Duration of treatment and power application was determined by the performing physician based on manufacturer guidelines, with adjustment for tumor size, proximity to vulnerable structures, and real-time intraprocedural monitoring. Antenna placement was performed under real-time ultrasound (US; GE E9, GE Medical Systems, Waukesha, Wisconsin; 78 sessions) or computed tomographic (CT) fluoroscopy (Optima 580; GE Medical Systems; three sessions) guidance, with CT reserved for tumors not visualized by US. Procedures were monitored in real time by US and/or CT fluoroscopy to ensure that the visible zone of gas encompassed the tumor and an ablative margin of ~5 mm.

Combination therapy with transarterial chemoembolization within 2 weeks before microwave ablation was performed on 22 tumors in 19 patients (conventional chemoembolization, 21 tumors in 18 patients; chemoembolization with drug-eluting beads, one tumor in one patient). A total of five tumors in three patients underwent chemoembolization to localize tumors that could not be identified by US, and 17 tumors in 16 patients underwent chemoembolization because the largest tumor was greater than 4 cm ($n = 10$) or greater than 3 cm and ill-defined ($n = 7$; Fig 2). Two patients with tumors larger than 4 cm did not undergo chemoembolization before microwave ablation.

At the completion of 80 of 81 procedures, a contrast-enhanced biphasic (late arterial and portal venous) CT scan of the abdomen was performed to determine adequacy of ablation and evaluate for immediate complications. Noncontrast CT was performed in one patient because of a history of anaphylaxis with CT contrast agents. If there was residual enhancing tumor or the ablation zone did not cover the area of visible tumor on the preprocedure images on the postprocedural CT examination, repeat ablation was performed in the same session. Periprocedural complications were monitored and recorded during an overnight stay and via telephone contact 5–7 days after the procedure. Delayed complications were evaluated with follow-up imaging and at clinical visits. Complications were classified according to the Society of Interventional Radiology classification system for complications by outcome (13). The completion of each procedure was used to define technical success, and technique effectiveness was evaluated with serial imaging beginning 1 month after the procedure according to standard guidelines (2).

RESULTS

Technical Success and Primary and Secondary Effectiveness

The mean treatment time was 5.3 minutes $\pm$ 2.3 (range, 1–13 min), and the average total power used was 124.7 W $\pm$ 47.9 (range, 35–195 W). All treatments were considered

technically successful at the conclusion of the initial procedure. Median imaging follow-up was 13 months, and clinical follow-up was 15 months (maximum, 28 mo and 32 mo, respectively), with primary technique effectiveness based on imaging in 91.6% of tumors (98 of 107). Primary technique effectiveness for ablation alone was 91.8% (78 of 85), and that for combination microwave ablation and chemoembolization was 90.9% (20 of 22). Five of the nine primary treatment failures were treated with little or no margin as a result of compromised hepatic function (two patients with total bilirubin levels > 2.0 mg/dL) or proximity of vulnerable structures (three patients with tumor abutting colon or stomach that could not be displaced with adjunctive techniques). Results by tumor size stratified by pretreatment with chemoembolization are presented in the Table.

When excluding the 18 patients with 23 tumors who underwent transplantation and therefore were ineligible for repeat treatment, the secondary technique effectiveness rate was 94.0% (79 of 84) for ablation alone (two tumors) or combination therapy (one tumor). Of the five tumors in which treatment failed, all were controlled with transarterial chemoembolization (three tumors) or radioembolization (two tumors), with these treatments selected in view of distant progression elsewhere in the liver or proximity of local progression to vulnerable structures.

Treatment Success by Tumor Size

Tumors measuring as large as 4.0 cm in diameter had a local control rate of 93.7% (89 of 95) in a single session. Those tumors measuring between 3.1 and 4.0 cm had a local control rate of 100%, with 10 of these tumors treated with ablation alone and six treated with combination therapy. The secondary technique effectiveness rate for tumors measuring 4.0 cm or smaller was 96.0% (72 of 75). For tumors larger than 4 cm, primary and secondary effectiveness rates were lower, at 75.0% (nine of 12) and 77.8% (seven of nine).

New Disease/Survival

Remote disease progression, either within the liver or in the form of distant metastatic disease, occurred in 28.0% of patients (21 of 75) during the follow-up period, with 20 exhibiting new foci of intrahepatic tumor and one with a portocaval lymph node metastasis detected after transplantation. This progression was noted at a median of 6 months (range, 2–18 mo) after ablation. Patients with remote disease progression tended to have larger tumors than those in the general population (mean diameter, 2.8 cm; 12 of 21 tumors > 3.0 cm). Five of these patients underwent repeat ablation for new foci of HCC, among whom multifocal HCC developed in one. The other 16 patients with intrahepatic progression presented with multifocal disease on follow-up and were treated with an intraarterial therapy and/or sorafenib.

There were 18 deaths (24.0% of patients) during the follow-up period, one of which was periprocedural (5 d after the procedure) from an aspiration pneumonia that occurred 1 day after the procedure and for which the patient refused antibiotics or supportive treatment. Eleven deaths were attributed to end-stage liver disease, five to multifocal HCC, and one to multiorgan failure after liver transplantation.

Complications

There were no major procedure-related complications. There were no incidents of tumor seeding at median 13 months of imaging follow-up. The only minor complication was a nonocclusive asymptomatic main portal vein thrombus after treatment of a caudate-lobe HCC identified 1 month after the procedure, which resolved with a 1-month course of anticoagulation (complication classification B; Fig 3).

DISCUSSION

The results of the present study demonstrate that treating HCC with a single session of high-powered microwave ablation can result in excellent local control rates (94%) for HCCs as large as 4.0 cm in diameter, with minimal complications. Of the tumors not controlled locally, 55.6% were undertreated in view of baseline hepatic function or proximity to vulnerable structures. Tumors greater than 3 cm in size have historically been difficult to treat with percutaneous ablation, but, in the present series, the local control rate for tumors between 3 and 4 cm in diameter was 100% (16 of 16). The local control rate in tumors larger than 4 cm was lower when the tumors were treated with a single session of microwave ablation or with combination microwave ablation and transarterial chemoembolization (75.0%); however, when adding other locoregional therapies (ie, chemoembolization/radioembolization) to treat local tumor progression for tumors larger than 4 cm, the secondary local control rate increased substantially (100%). Therefore, in cases of local tumor progression after microwave ablation or combination microwave ablation and transarterial chemoembolization, serial treatments with intraarterial therapies appears to be highly effective.

Previous reports of local control of HCC with percutaneous microwave ablation are limited, particularly with devices available in the United States and Europe. A large series (10) that included 1,007 patients with 1,363 foci of HCC treated with a water-cooled system available only in China reported, in a research letter, a local tumor progression rate of 5.9%. Smaller series ranging from 31 to 144 patients and 89 to 270 tumors (7,9,11,14–16), most of which include metastatic lesions and operative ablations, show variable incomplete ablation and local tumor progression rates ranging from 2.0% to 22.0%. By way of comparison, RF ablation has shown excellent results for local control for tumors less than 2 cm, with a reported 2.8% local progression rate in one series (17). However, studies that include tumors larger than 2 cm have shown increased rates of local tumor progression of 10%–16.5% (18–20).

The reasons for the decreased effectiveness of RF for tumors larger than 3.0 cm are multifactorial, but physical limitations of tissue heating with RF are a substantial contributing factor (21). RF ablation creates only a narrow zone of active heating around the electrode that becomes self-limited by the charring and tissue desiccation seen with ablative temperatures. As a result, RF ablation has been associated with small ablation zones and a strong susceptibility to vascular heat sinks (22–24). Additional disadvantages include the need for ground pads (in monopolar RF), the lack of simultaneous electrode activation, and prolonged procedure times. These limitations of RF systems have led to the search for more effective ablation tools.

The adoption of microwave ablation for the treatment of HCC has historically been limited by concerns of safety and increased risk of complications (25,26). First-generation microwave systems were characterized by large-gauge uncooled antennas, which could cause skin and tract burns. However, newer high-power internally cooled systems first introduced in Asia are now being used to treat hepatic tumors in nonoperative candidates (16,25). An earlier 1,136-patient microwave ablation series (25) demonstrated a decrease in the major complication rate from 3.9% to 1.6% following the advent of water-cooled antennas. A survey of users of another single antenna water-cooled system (3) demonstrated a 3.0% rate of major complications when used to treat liver tumors percutaneously. This low rate of complications was attributed in part to operator experience, much of which was gained during the RF era (3). The results of the present study show a complication rate similar to or lower than published complication rates for RF ablation of 1.8–7.9% (17,27–29). Although these low rates of complications with microwave ablation may relate to collective operator experience, as suggested by Livraghi et al (3), it should be noted that the operators in the present study had a range of experience. Two of the four physicians had less than 3 years of tumor ablation experience, and two had more than 10 years of experience as of the beginning of the study period.

A notable finding in the present study was the ability of microwave ablation alone to effectively treat HCCs as large as 4.0 cm in diameter in a single treatment session. This is in contradistinction to RF ablation, with which a diameter of 3.0 cm is considered the practical upper limit for obtaining local control (2,3). The limited effectiveness of RF for larger tumors is likely a result of the increased biologic aggressiveness of larger tumors, an increase in peritumoral satellitosis, and the need to create much larger zones of ablation to encompass the tumor, satellites, and a margin (Fig 2) (30–32). For example, when tumor diameter increases from 3 cm to 4 cm, the increase in ablation zone volume necessary to cover a tumor and a 5-mm margin grows from 65.6 cm³ to 113.4 cm³ (a 73% volume increase). The excellent results with microwave ablation in tumors between 3 and 4 cm in diameter in the present study (100% local control in a single session) is likely a result of the large ablation volumes possible with the use of a high-powered, gas-cooled system, as well as the simultaneous use of multiple phased antennas in larger tumors to take advantage of electrical and thermal synergy (33).

The present study has certain limitations. The ablation procedures were performed at a single tertiary-care center with the use of a single microwave device. This may limit the applicability of the data in practices that use other microwave systems, which may use different power settings and/or a different frequency, be limited to single antenna use, and lack the ability to capitalize on electromagnetic and thermal synergy by using multiple in-phase antennas. The short imaging follow-up period (median, 13 mo) may underestimate the rate of local progression and limits conclusions about overall survival and progression-free survival, but is in line with other reports on local/regional therapy (11,14,15). The inclusion of combination microwave ablation/transarterial chemoembolization data may limit applicability of the general findings, but the authors have made every attempt to stratify these data when appropriate.

In conclusion, in the present study, microwave ablation of HCC was associated with promising local control and minimal complications at a median 13-month imaging follow-up for tumors less than 4 cm in diameter treated in a single session. Tumors larger than 4.0 cm were effectively treated with microwave ablation in combination with transarterial chemoembolization, even though multiple treatment sessions were often necessary. Further follow-up will be required to determine midterm and long-term efficacy of microwave ablation and the impact of this treatment on overall and progression-free survival.

ABBREVIATIONS

HCC hepatocellular carcinoma

RF radiofrequency

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Figure 1.

Images from a 62-year-old man with a 3.7-cm HCC treated with two antennas for 10 minutes at 80 W on each antenna. **(a)** Contrast-enhanced T1-weighted magnetic resonance (MR) image obtained 6 weeks before the procedure shows the tumor (arrow). **(b)** Image during the procedure shows antenna in place (white arrow) with instilled dextrose 5% in water for hydrodissection (black arrow). **(c)** Immediate postablation contrast-enhanced CT scan shows ablation zone (arrow) encompassing the tumor. **(d)** One-year follow-up contrast-enhanced T1-weighted MR image demonstrates the ablation zone (arrow) and no local tumor progression.

Figure 2.

Images from a 62-year-old man with a 3.4-cm HCC and satellite nodules treated with combination transarterial chemoembolization and microwave ablation. **(a)** CT image obtained during chemoembolization procedure demonstrates HCC (white arrow) and satellite nodule (black arrow). **(b)** Intraprocedure CT image shows two of the three microwave antenna within the tumor. **(c)** Immediate postablation contrast-enhanced CT shows ablation zone (arrows) encompassing the tumor and satellite nodules. **(d)** Three-month follow-up contrast-enhanced CT scan with no local tumor progression identified.

Figure 3.

Images from a 72-year-old man with a 3.1-cm HCC in the caudate lobe treated with two antennas for 11.5 minutes at 65 W on each antenna. **(a)** Preprocedure CT scan demonstrates the caudate-lobe HCC (white arrow) adjacent to the left portal vein (black arrow). **(b)** Intraprocedure CT scan shows one of the two antennas (white arrow) within the tumor adjacent to the left portal vein (black arrow). **(c)** One-month follow-up CT scan with thrombus noted in the portal vein (black arrow) adjacent to the ablation zone (white arrows). **(d)** CT scan obtained after 1 month of anticoagulation demonstrates resolution of the left portal venous thrombus (black arrow) and an involuting ablation zone (white arrows).

Table

Treatment Results by Tumor Size Stratified for Ablation Alone or Combination Chemoembolization and Ablation

Characteristic	Tumors 3 cm		Tumors 3.1–4.0 cm		Tumors > 4 cm	
	Ablation Alone (n = 73)	Combination (n = 6)	Ablation Alone (n = 10)	Combination (n = 6)	Ablation Alone (n = 2)	Combination (n = 10)
Diameter (cm)						
Mean	1.9	1.9	3.3	3.6	4.2	5.2
Range	0.5–2.9	1.0–2.9	3.1–3.9	3.4–4.0	4.2	4.4–7.0
Treatment time (min)						
Mean	4.9	4.1	5.8	6.0	8.8	7.2
Range	1–10	2–5	4–11.5	5–8	7.5–10	4–13
Maximum treatment power (W)						
Mean	104.6	122.5	156.5	170.8	175.0	182.3
Range	35–195	70–195	130–195	130–195	160–190	110–195
Primary effectiveness	67 (91.8)	6 (100)	10 (100)	6 (100)	1 (50)	8 (80.0)
Secondary effectiveness	70 (95.9)	6 (100)	10 (100)	6 (100)	1 (50)	9 (90.0)
Median imaging follow-up (mo)						
Mean	13.0	15.5	14.5	7.0	17.0	14.0
Range	1–28	3–25	7–19	6–20	15–19	8–27

Values in parentheses are percentages.