Surg Endosc
DOI 10.1007/s00464-015-4261-3

Laparoscopic microwave thermosphere ablation of malignant liver tumors: an initial clinical evaluation

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Received: 17 February 2015 / Accepted: 19 May 2015

Abstract

Background Microwave ablation (MWA) has been recently recognized as a technology to overcome the limitations of radiofrequency ablation. The aim of the current study was to evaluate the safety and efficacy of a new 2.45-GHz thermosphere MWA system in the treatment of malignant liver tumors.

Methods This was a prospective IRB-approved study of 18 patients with malignant liver tumors treated with MWA within a 3-month time period. Tumor sizes and response to MWA were obtained from triphasic liver CT scans done before and after MWA. The ablation zones were assessed for complete tumor response and spherical geometry.

Results There were a total of 18 patients with an average of three tumors measuring 1.4 cm (range 0.2–4). Ablations were performed laparoscopically in all, but three patients who underwent combined liver resection. A single ablation was created in 72 % and overlapping ablations in 28 % of lesions. Total ablation time per patient was 15.6 ± 1.9 min. There was no morbidity or mortality. At 2-week CT scans, there was 100 % tumor destruction, with no residual lesions. Roundness indices A, B and transverse were 1.1, 0.9 and 0.9, respectively, confirming the spherical nature of ablation zones.

Conclusions To the best of our knowledge, this is the first report of a new thermosphere MWA technology in the laparoscopic treatment of malignant liver tumors. The results demonstrate the safety of the technology, with satisfactory spherical ablation zones seen on post-procedural CT scans.

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Keywords Malignant liver tumors · Liver tumor ablation · Microwave · Laparoscopic

Since its introduction in late 1990s, radiofrequency thermal ablation (RFA) has been the preferred modality for ablation of malignant liver tumors [1, 2]. Its low morbidity and the reproducibility of ablation zones have been critical in the adoption of this technology. Nevertheless, local treatment failure rates up to 30 %, and long treatment sessions have led to the investigation of other technologies for tumor destruction. Among these thermal ablation modalities, microwave ablation (MWA) offers significant theoretical advantages over RFA due to its physical properties. MWA uses a wider area of active heating, producing higher intratumoral temperatures, and is less affected by the "heat-sink" phenomenon. Since charring and desiccation do not occur, larger ablation zones in a shorter time compared to RFA are possible [3–8]. Nevertheless, the early microwave systems have suffered from large antenna diameters, antenna shaft heating, small ablation zones created due to low power outputs and concerns for thermal injuries [9, 10]. A significant criticism for MWA was that spherical ablation zones were not possible with a single antenna. Nevertheless, there have been advances in microwave antenna and generator design, with a recent development of a 2.45-GHz system using a cooled tip antenna that is capable of producing spherical ablation zones. This system was approved by FDA in 2014. This study reports the initial surgical experience with this new tumor ablation system.

Methods

This was a prospective study, performed under the Cleveland Clinic Institutional Review Board approval to evaluate the safety and efficacy of thermal ablation therapies for

Published online: 20 June 2015

malignant liver tumors. Between September 2014 and January 2015, 18 patients underwent MWA of liver tumors by one surgeon (EB). In three patients, MWA was performed open in combination with liver resection. The remaining 15 patients underwent laparoscopic MWA. The indications for MWA in these 15 patients were unresectable disease in eight (inadequate liver remnant in four and underlying cirrhosis with portal hypertension in four) and patient decision in seven patients after the pros and cons of resection versus ablation were discussed.

Informed consent was obtained.

Surgical technique

The procedures were performed under general anesthesia. Antibiotic prophylaxis was maintained with intravenous cefazolin. Patients with neuroendocrine tumors received 100 µg of sandostatin intravenously to prevent a carcinoid crisis. Abdominal access was obtained using a 12-mm optical trocar in the right upper quadrant (RUQ). Subsequently, another 12-mm trocar was placed in the RUQ. Diagnostic laparoscopy was performed, followed by laparoscopic ultrasound using a rigid linear side-viewing 10 MHz transducer (Hitachi Aloka. Medical America, Inc. Wallingford, CT). When deemed necessary, a tru-cut biopsy was performed using an automatic biopsy gun. The 2.45-GHz MWA antenna (Emprint, Covidien, Boulder, CO) was introduced through the skin through a 2-mm puncture in the first case (Fig. 1). Nevertheless, since the MWA antenna is not as stiff as an RFA needle, it was introduced through 3- to 5-mm trocars in the subsequent cases (Fig. 2). The lesions were ablated under laparoscopic ultrasound guidance using algorithms derived from FDA-approved data. There are no grounding pads, and the antenna is attached to the generator using a pin connection. The generator is controlled using a foot pedal, operated by the surgeon. The system uses a saline infusion to cool the antenna. The generator was run at 100 W for 2.5 min for a 3-cm ablation, 10 min for a 4-cm ablation and 15 min for a 5-cm ablation. Based on real-time ultrasound feedback, repeat ablations were performed if necessary. For capsular lesions, an initial ablation at 45 W for 30 s was performed to prevent rupture of the liver parenchyma, followed by the subsequent cycle at 100 W using the same algorithm. The antenna was then pulled out, by applying track ablation at 50–100 W of power and staying at each centimeter of depth for 2–3 s. If bleeding was seen to persist from the liver puncture site, the duration of track ablation was extended until hemostasis was observed. Additional ablation cycles were performed, if on ultrasound there was incomplete coverage of the lesion at the end of the first treatment. Additional 5-mm trocars were used in patients requiring adhesiolysis. No drains were used. For open MWA, a subcostal incision was used. A Thompson retractor was used. The same equipment and parameters were used to perform the ablations.

Patients who underwent laparoscopic MWA were discharged home the next day. The hospital stay for the patients who underwent combined MWA and resection depended on the recovery from the hepatectomy procedure. Laboratories including complete blood count, liver function tests, metabolic panels, prothrombin time, INR, aPTT were obtained on postoperative day 1 and day 14, when

Fig. 1 MWA needle (**A**) and generator (**B**) used in the study. The needle is 30 cm, 13.5 G and the generator is 2.45 GHz. The system uses saline circulation to cool off the antenna

Fig. 2 Intraoperative photo showing the trocar placement for laparoscopic MWA. Two 12-mm trocars are used for the laparoscope and ultrasound probe. The microwave antenna is placed through a 3- to 5-mm trocar. The procedure is monitored in real time with laparoscopic ultrasound

they were also seen in the outpatient clinic. Imaging studies included triphasic liver CT scans obtained within a month before and 2 weeks after the MWA procedure. Ninety-day morbidity was recorded. Tumor and ablation zone sizes were measured by radiologists. Roundness index was calculated as reported by Park et al. [11], where transverse diameter A was measured as the longest transverse diameter and transverse diameter B as the transverse diameter perpendicular to transverse diameter A. To assess the spherical zone formation, roundness index A was calculated as transverse diameter A divided by longitudinal diameter and roundness index B as transverse diameter B divided by longitudinal diameter. Roundness index transverse was calculated by dividing transverse diameter B by transverse diameter A. A spherical geometry is represented by a value near 1 and an oval geometry by a value distant from 1.

Data were analyzed with descriptive statistics using JMP software version 10.0.0 (SAS, Cary, NC). Continuous data are presented as mean ± standard error of the mean.

Table 1 Patient and tumor characteristics

Parameter	Value
Age (years)	62.4 ± 2.6
Sex (female/male)	8/10
Tumor type, *n* (%)	
Colorectal	7 (38.9)
Primary	3 (16.7)
Neuroendocrine	3 (16.7)
Ovarian cancer	2 (11.1)
Esophageal cancer	1 (5.5)
Leiomyosarcoma	1 (5.5)
Uveal melanoma	1 (5.5)
Number of lesions per patient, *n* (range)	3 (1–12)
Lesion size (cm) (range)	1.4 ± 0.1 (0.2–4.4)
Total tumor volume (ml) (range)	7.4 ± 1.9 (0.5–31)
Liver segmental location, *n* (%)	
Segment I	1 (1.9)
Segment II	10 (18.5)
Segment III	6 (11.1)
Segment IV a	7 (13.0)
Segment IV b	5 (9.2)
Segment V	8 (14.8)
Segment VI	4 (7.4)
Segment VII	9 (16.7)
Segment VIII	4 (7.4)
Blood vessel proximity, *n* (%)	
Near	26 (48.1)
Away	28 (51.9)
Location of lesions, *n* (%)	
Peripheral	26 (48.1)
Central	28 (51.9)
Number of ablations per lesion, *n* (%)	
Single	39 (72.2)
Multiple	15 (27.8)
Total ablation time per patient, (range) (minutes)	15.6 ± 1.9 (3–30)

Continuous variables are presented as mean ± SEM

Results

Table 1 shows the demographic and clinical data. There were 18 patients with 54 tumors. The most common tumor type was colorectal cancer (seven patients), followed by hepatocellular cancer (three patients), neuroendocrine (three patients) and other metastatic cancers (five patients). The patients had an average of three tumors (range 1–12) measuring 1.4 cm (range 0.2–4.4 cm). Total liver tumor volume averaged 7.4 ± 1.9 ml. The lesions were evenly divided between peripheral and central location and

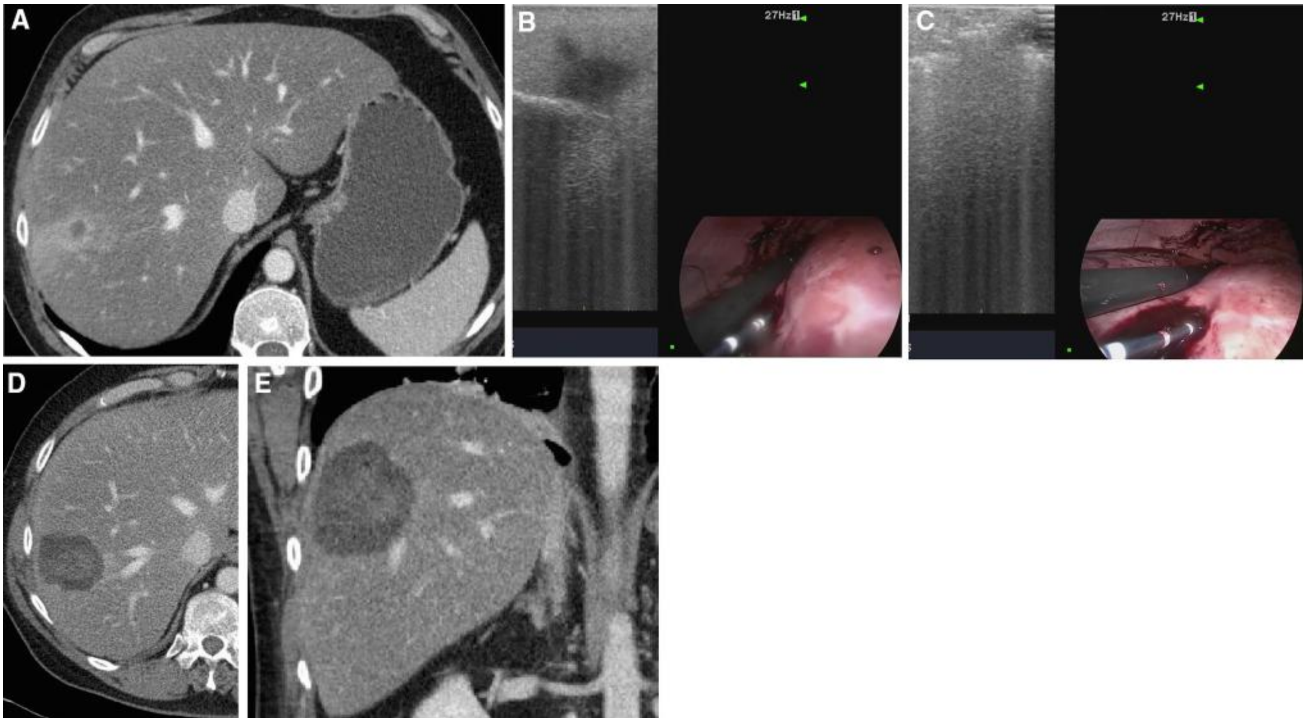

Fig. 3 Preoperative CT scan (**A**) shows a 1.6 × 1.7 × 1.3 cm neuroendocrine metastasis in segment 7, associated with satellite lesions in a 51-year-old patient with a total of seven bilobar lesions. This lesion was targeted with the Emprint microwave antenna (**B**) and treated at 100 W for 15 min (**C**). Two-week CT scans (**D**, **E**) showed a 5.5 × 4.9 × 5.4 cm ablation zone encompassing the tumor and surrounding satellite lesions

distributed across all liver segments. A single ablation cycle was performed for 3/4 of the tumors, whereas 1/4 required overlapping ablations for complete coverage with the ablation zone. A single probe was used in all patients. Total ablation time was 15.6 min per patient. Hospital stay was 1 day for the laparoscopic procedures. There was no 90-day morbidity or mortality. There were no untreated lesions at 2-week CT scans. In all patients, the planned ablation zone was achieved (Fig. 3). Figure 4 shows the size of the ablation zones created for each lesion. Roundness indices A, B and transverse were 1.1, 0.9 and 0.9, respectively (Table 2).

Serum transaminase and bilirubin levels increased after the procedures, returning back to baseline at 2 weeks. There was no evidence of tumor lysis syndrome or coagulopathy on postoperative laboratories (Fig. 5).

Discussion

This study is the first to report on the safety and efficacy of a new thermosphere MWA system in the destruction of malignant liver tumors. The results demonstrate the safety of this technology in the first 18 patients treated. An algorithm is also provided as a reference to create ablation

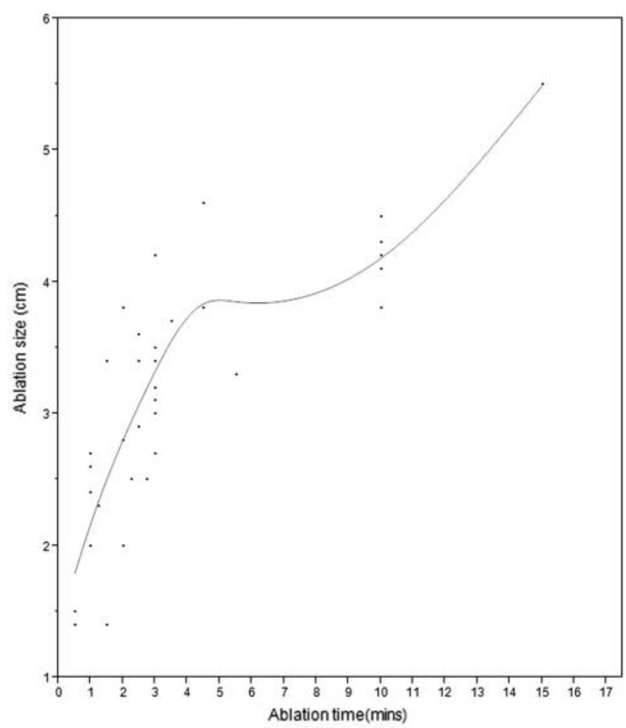

Fig. 4 Scatter plot showing the largest CT diameter of ablation zones obtained over time at 100 W of power in the study

Table 2 Mean ± SEM values for three perpendicular dimensions and roundness indices of the ablation zones

Ablation zone	Single ablations (n = 39)	Multiple ablations (n = 15)
Longitudinal diameter (mm)	2.9 ± 0.2	3.9 ± 0.1
Transverse diameter A (mm)	3.1 ± 0.2	4.1 ± 0.3
Transverse diameter B (mm)	2.7 ± 0.2	3.4 ± 0.2
Roundness index A	1.1 ± 0.03	1.1 ± 0.1
Roundness index B	0.9 ± 0.03	0.8 ± 0.1
Roundness index transverse	0.9 ± 0.02	0.8 ± 0.03

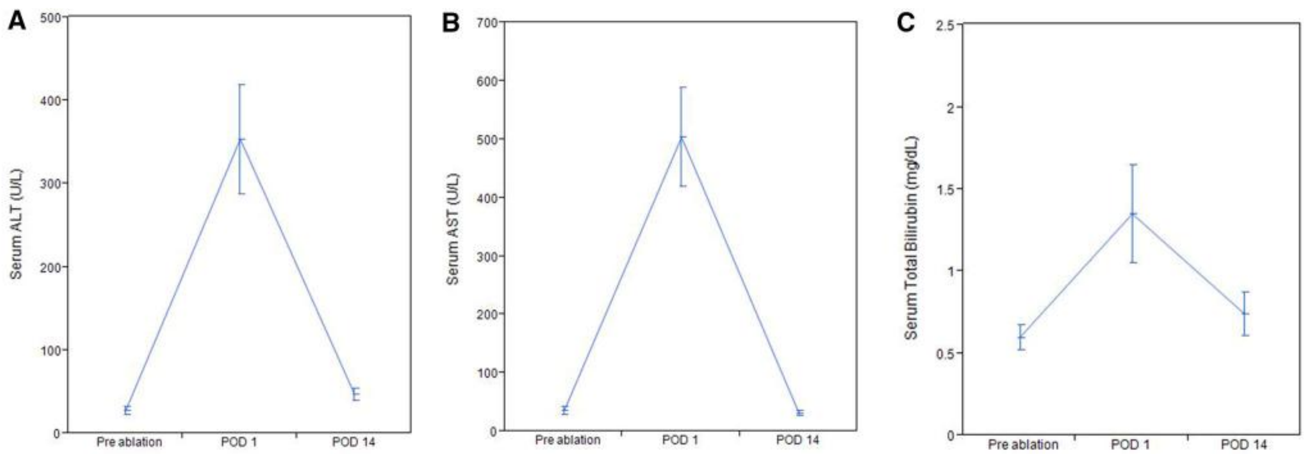

Fig. 5 Perioperative changes in serum alanine transaminase (ALT) (**A**), aspartate transaminase (AST) (**B**) and bilirubin (**C**) in the study patients. There was an elevation seen on postoperative day (POD) 1, with a return to baseline at 2 weeks

zones of certain sizes. Overall, the experience was favorable, with no adverse consequences encountered in the perioperative period. This study is continuing, with the patients scheduled for their subsequent follow-up to determine the local tumor control rate of this technology.

In order to perceive the advantages of MWA over RFA the mechanism and physics behind this technology need to be understood. Microwave uses frequencies between 915 and 2450 MHz, which are much higher than RFA (400 kHz), thereby omitting the need to use grounding pads [12]. Microwaves diffuse better in tumoral than normal tissue [13]. Microwaves agitate water molecules and create frictional heat. Although RFA also creates frictional heat, with microwave, tissue temperatures of 160–180 °C are created, in contrast to 100 °C achieved with RFA, which is limited to the boiling temperature of tissue [14]. The rise in temperature is also faster with MWA. The tissue temperature 5 mm adjacent to the MW antenna tip is 100 °C, in contrast to 70 °C with RFA. Owing to the better thermal properties, the heat-sink effect is less compared to RFA [15]. However, because of rapid heating along the antenna, cooling systems are required to be able to run at high power settings (100 W, rather than 60 W).

During the learning curve, important lessons were learned. The first is that, despite the ablation power of the current antenna system, it is less stiff compared to an RFA catheter. Although it was introduced through the skin in the first patients, its fragility was recognized and a 3- to 5-mm trocar was used in the subsequent procedures to minimize the trauma to the antenna. It is also not possible to steer the antenna once inside the parenchyma. For this reason as well, the additional trocar becomes useful to achieve the angle of entry to the liver parenchyma, without bending the needle. Using this technique, lesions distributed across all liver segments were successfully targeted.

The second is that the antenna diameter is larger than the RFA needle, which requires more meticulous hemostasis during the withdrawal from the liver tissue. This was achieved by using 50–100 W of power and staying a certain depth for longer, if bleeding does not stop. By using this technique, no perioperative bleeding was experienced in the study.

Since the system produces significant power, ablation of superficial lesion should proceed with the application of a lower power for 30 s and subsequent increase in the power to 75 or 100 W, to prevent a rupture of the liver parenchyma. The ablation zone should be monitored with intraoperative ultrasound to ensure that the whole lesion is encompassed by the ablation zone. Although this was more difficult to assess with this technology, it was still possible to assess the lesion for complete coverage with the ablation defect (due to nitrogen outgassing) with laparoscopic ultrasound. Any uncovered part of the lesion should be retreated with repeat ablation. Using this ultrasound guidance, there were no residual untreated lesions at 2-week imaging. Overall, the ablations were created in shorter time compared to the author's experience with RFA. For instance, a 5-cm ablation may take up to 25–30 min with the RFA technology. In the current study, a 5-cm spherical ablation zone was created in 15 min.

With RFA, in order for an ablation zone to cover the tumor completely, the needle needs to be placed exactly at the center of the tumor. Nevertheless, this is different for the MWA antenna. Since the ablation develops away from the antenna, ablation zones can encompass the tumor even if the antenna is not positioned exactly at the center of the tumor. This is a significant advantage in terms of needle placement. In addition, for RFA technology, ablation algorithms are set for certain needle deployments (i.e., 2, 3, 4 or 5 cm), whereas for MWA, the generator can be programmed to achieve any predicted ablation size (up to 5 cm), adding more precision and variability to the procedure.

In the literature, different authors have reported on open [7, 16–18], percutaneous [6, 19] and laparoscopic [20, 21] applications of MWA for various malignant liver tumors. The morbidity in these studies has ranged from 0 to 60 % and mortality 0–2 % [6, 19–21]. The current study, with no morbidity or mortality via a predominantly laparoscopic approach, compares favorably with these reports.

The spherical indices calculated in the current study were very close to 1, validating the ability of the MWA system used to create spherical zones of ablation. This feature overcomes the limitations of previous microwave systems.

In conclusion, this is the first clinical report of a new MWA technology capable of creating spherical ablation zones with a single antenna. The predominantly laparoscopic technique described resulted in favorable outcomes, with no perioperative morbidity or mortality. The important question of whether these advantages will translate into better local tumor control rate than RFA will be answered by future studies.

Disclosures Eren Berber has no conflict of interest or financial ties to disclose.

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