Ultrasound-guided microwave ablation of hepatocellular carcinoma: Initial institutional experience

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Microwave ablation; Hepatocellular carcinoma; Thermal ablation; Ultrasound guided thermal ablation

Abstract  Background: Microwave ablation (MWA) is a new treatment modality for hepatocellular carcinoma (HCC) at our institution. The aim of this study is to evaluate the safety, procedure time and rate of complete ablation of this new modality.

Material and methods: Hospital medical ethics committee approval and informed consent were obtained. A total of 98 nodules in 72 patients (59 male, 13 female; mean age 57 (± 4.6) years, range 50–70 years) with HCC were treated with microwave ablation at our institution from June 2010 to February 2011. A 14 G cooled shaft Amica probe was introduced into the tumors under analgesic sedation and by US guidance. The patients were then followed up with contrast enhanced computed tomography (CT) and serum a-fetoprotein levels.

Results: One month after therapy, complete ablation was obtained in 96% (94/98) nodules. The complete ablation rate in tumors ≤3 cm and those >3 cm were 98%, and 94%, respectively. MW ablation success was higher with nodules ≤3 cm (57/58, 98.3%) in comparison to nodules

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1. Introduction

Hepatocellular carcinoma (HCC) is one of the most malignant tumors with a high mortality, aggressive growth behavior and a high recurrence rate (1). Hepatocellular carcinoma usually develops following chronic liver inflammation caused by hepatitis C (HCV) or B (HBV) virus (1). Egypt has the highest prevalence of HCV in the world and up to 90% of HCC cases in the Egyptian population were due to HCV (2). Therefore, HCC represents an important public health problem in Egypt and is the third among male cancers with > 8000 new cases predicted by 2012 (2).

Surgical resection has been recognized as the most potentially curative treatment for patients with HCC. Unfortunately, the majority of patients with primary HCC are frequently considered unresectable because of tumor number, location, or poor hepatic functional reserve due to underlying liver cirrhosis/hepatitis thus making resection of large volume of liver parenchyma unfeasible (3). Therefore, local ablative techniques have been developed to enable local destruction of tumors without damage of the healthy parenchyma (4). The tumors are destroyed in situ either by direct chemical application (ethanol ablation) or by cooling (cryotherapy) or by heating (radiofrequency or microwave ablation) (5).

Percutaneous MWA has been recently introduced at our institution and the aim of this study is to present our initial experience in the use of this new microwave technology as an alternative therapy for patients deemed inoperable for HCC, regarding its safety, procedure time and rate of complete ablation.

2. Materials and methods

2.1. Patients

From June 2010 to February 2011, a total of 99 patients with HCC, deemed unsuitable for hepatic resection were referred to our interventional radiology department from the hepatic surgery department at Ain Shams University Hospital. A total of 72 patients were recruited into this prospective study and treated with ultrasound-guided percutaneous MWA. The study group included 59 (81.9%) male and 13 (18.1%) female, with an average age (±SD) of 57 (±4.6) (range, 50–70 years). Exclusion criteria were: age older than 80 years, evidence of extra-hepatic involvement or extra-hepatic metastases, and severe bleeding diathesis (INR > 1.5) (6). The enrolled patients gave their written informed consent to enter the study after the procedure of thermal ablation was explained to them. The study was approved by the medical ethics committee of the hospital.

Diagnosis was settled by significant elevation of $\alpha$-fetoprotein > 200 µg/L and/or typical computed tomography (CT) criteria of HCC by triphasic spiral CT. The numbers of patients with single tumor nodule were 46 (63.9%) and those with two tumor nodules were 26 (36.1%). A total of 98 tumor nodules sized 2–5 cm with an average diameter (±SD) of 3.2 (±0.9) were treated. Fifty eight (59.2%) nodules were 3 cm or smaller and 40 (41.8%) nodules were larger than 3 cm.

Forty (55.6%) of the 72 patients had an increased serum $\alpha$-fetoprotein level (> 200 µg/L). Liver function status was classified as Child-Pugh class A in 24 patients (33.3%), B in 45 patients (62.5%), and C in 3 patients (4.2%). Standard pre-operative evaluation of patients included a triple phase computed tomography (CT) scan of the abdomen and pelvis, abdominal ultrasound, laboratory investigations, including; liver enzymes (SGOT, SGPT), serum albumin, coagulation profile (PT, PTT, INR), serum creatinine and complete blood picture (Table 1).

2.2. Ablation procedure

Microwave ablation was performed percutaneously under real-time ultrasound guidance using a GE LOGIQ 7 Pro US scanner (USA) with a 3.5–5 MHz probe.
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MWA was performed using as HS AMICA microwave delivery system (HS Hospital service S.P.A Roma, Italy). This microwave delivery system consisted of a MW generator named AMICA Gen., operating at frequency of 2450 MHz and a power output up to 100 W, and a 14 gauge (14G×150 mm and 14G×200 mm) cooled shaft electrode named AMICA-probe to deliver MW energy into liver tissue.

Before treatment began, a detailed plan for the placement of the electrode, the power output setting, and the emission time was established on a tumor-by-tumor basis. The aim of the treatment was to completely destroy the tumor, as well as the surrounding 0.5–1.0 cm normal appearing liver tissue. A pre-incision of the skin is done and a 14-gauge 15 cm guide needle with a sheath was inserted and positioned at the designated place of the tumor under sonographic guidance, then the stylet of the guide needle was pulled out. After the microwave electrode was introduced through the sheath of the guide needle, the sheath was withdrawn approximately 4–5 cm while keeping the electrode needle at its place to ensure that a portion of at least 4 cm from the tip of the electrode was exposed. Usually the tip of the electrode has to be placed at the bottom of the lesion about 0.5 cm inside the tumor margin. Being connected to the microwave generator, the energy application was then started.

In general a high power for a low time was used, i.e., an output setting of 60 W for 300 s. For some tumors, a prolonged application (300–800 s) of energy 60 W was used.

In lesions > 3 cm, after the first application we stop the treatment, then the needle can be just moved a bit backward, change direction of re-insert into the tumor, and start a further treatment session. This maneuver was repeated 2–4 times according to the size of the lesion. This ensues a bigger dimension of necrosis than applying the microwaves for the maximum time (25 min for 60 W), since during the last 5–10 min, the dimension of necrosis increases very slowly.

During each application of microwave energy, an expanding hyperechogenic area was produced which roughly judges the size of the ablation zone, i.e., necrotic zone. The necrosis length overcomes the tip of the electrode ahead by few mm (2–6 mm) depending on power and time of the treatment while the biggest increase occurs backwards and radially as the time goes over. These changes are visible on sonographic images but diminished rapidly as soon as the microwave generator was switched “off” and completely disappeared within 8 h. To minimize tumor seeding, the needle track was routinely ablated while withdrawing the antenna at about 2 cm/s. The power has to be set at 40 W.

2.3. Assessment of therapeutic efficacy

Local therapeutic efficacy was evaluated by contrast enhanced dynamic CT scanning (GE, Hi Speed Dual CT, USA) at 1 month after treatment. Complete ablation was defined as uniform hypo-attenuation without enhancement in the previous tumor area (7,8). However, contrast enhancement in the ablated zone indicated incomplete ablation or local recurrence when detected later on (9). Technical success was defined as complete ablation of the tumor, as determined at CT performed 1 month after MWA (10). Thereafter, CT examinations were performed once every 3 months interval up to the end of the study period.

Serum α-fetoprotein level was checked at 1 month after MWA. If the results showed an abnormal serum α-fetoprotein, subsequent checks were performed at an interval of 2–3 months.

Statistical analysis of the data was performed by using SPSS®15 software package under Windows7® operating system. Categorical data parameters were presented in the form of frequency and percent. Quantitative data were expressed in the form of mean, SD, range and median. Comparison was performed by Fisher exact test for categorical data and paired t-test for quantitative data. Probability level (P-value) was assumed significant if less than 0.05 and highly significant if P-value was less than 0.001. P-value was considered non-significant if greater than or equal to 0.05 Graphic presentation of data was done by using SPSS®15 software.

3. Results

The study included all cases referred from hepatic surgery department between June 2010 and 28th February 2011; that fulfilled the informed consent and inclusion criteria.

MW ablation was utilized to treat 98 hepatic tumor nodules in 72 patients. There were 59 men and 13 women with a mean age of 57 years (range: 50–70 years). Forty six patients had a single tumor nodule (Figs. 1–3) while 26 patients had two tumor nodules (Fig. 4), with a mean size of 3.2 cm. The locations of these tumors were evenly distributed for both the right and left lobes, with one tumor located within the caudate.

All patients completed the procedure safely and the median ablation time was 10 min (range: 5–15 min).

Technical success, as determined at dynamic CT performed 1 month after percutaneous MWA, was achieved in 94 (96%) of 98 nodules. The technical success rates for tumors 3 cm or smaller (Fig. 4) and those larger than 3 cm (Fig. 1–3) were 98.3% (57 of 58 nodules) and 92.5% (37 of 40 nodules), respectively. The four incompletely ablated tumors were treated with additional MWA sessions and technical success was achieved in all. MW ablation success was higher with nodules ≤3 cm (57/58, 98.3%) in comparison to nodules > 3 cm (37/40, 92.5%); however, the difference was non-significant (P = 0.301).

Follow-up for all cases extended for 10 months (from the start of the study till 31st March 2011) with a mean of 4 months (162 days ± 81); including the first follow-up step at 1st month after MWA then every 3 months; accordingly 26 (36.1%) patients were followed once, 22 (30.6%) patients were followed twice, and 24 (33.3%) patients were followed thrice (Table 2). During this limited period, none of the patients died, no local recurrence was detected up to the time of writing, however, new lesions at other sites of the liver occurred in 11 (15.3%) patients.

Alpha-fetoprotein (α-FP) was measured for all patients preoperatively, mean α-FP was 317.9 ± 235.1 (median = 231). Patients with values < 200 μg/L (n = 32) were excluded from follow-up with α-FP. Those patients were only evaluated by CT examination. Out of the 40 patients that had α-FP with values > 200 μg/L, 39 patients showed decreased level to within the normal range one month after ablation. The patient with increased α-FP showed a significant decrease in α-FP level at
Figure 1  Contrast-enhanced transverse CT scans in a 55-year old man with solitary HCC. (a) Pretreatment contrast enhanced scan reveals a 3×5 cm enhancing HCC (arrow) in segment V. (b) Scan obtained 1 month after PMCT depicts a non-enhancing hypoattenuating area (arrow head) with evident safety margin.

Figure 2  CT finding in 50-year old male with hepatocellular carcinoma. (a) Arterial phase CT scan obtained before microwave therapy shows a 5×5 cm hypervascular hepatoma (arrow) in segment VI of liver. (b) Arterial phase CT scan obtained 1 month after microwave therapy shows no enhancement within lesion.

Figure 3  Transverse CT images obtained in a 60-year old man with HCC treated with PMCT. (a) Pretreatment contrast enhanced image depicts a 4×5 cm enhancing (arrow). (b) Contrast enhanced scan 3 months after PMCT shows a non-enhancing hypoattenuating area (arrow).
4 month post-ablation, but was still above the normal range, then it dropped to the normal level at 7 months post-ablation (Table 2, Fig. 5).

Comparison between pre-operative versus follow-up alpha-fetoprotein values showed that values significantly decline by time ($t = 11.997, 12.023, 7.541; P < 0.001$ for 1 m, 4 m and 7 m comparisons, respectively). Moreover, there was significant decline on comparing alpha-fetoprotein at 4 m versus that at 7 m ($t = 2.342, P = 0.036$).

In our study, no complication occurred related to the ablation procedure. After percutaneous MWA, three patients whose tumors were located in the liver dome had severe right upper quadrant pain. The pain was relieved with the oral administration of analgesics. Forty-eight (66.6%) patients had a mild fever, which lasted 1–3 days. In two patients, a small discharge from the puncture wound occurred on the initial days after therapy and cleared up after local treatment. No other clinically relevant complications were observed.

4. Discussion

With the advantages of minimal invasiveness and predictability of therapeutic efficacy, thermal ablation has quickly gained a great deal of attention in the management of HCC [11,12].

Figure 4  Contrast-enhanced transverse CT scan in a 45-year old man with two HCC nodules. (a) Pretreatment scan reveals a $1 \times 3$ cm HCC (arrow) and $2 \times 2$ cm HCC (arrow head) in segment VIII and segment III, respectively. (b) Scan obtained 1 month after PMCT depicts a non-enhancing hypoattenuating areas at previously mentioned sites of tumor nodules (arrow and arrow head).

In recent years, the potential role of microwave ablation (MWA) has become increasingly apparent, micro-wave device and antenna had been greatly improved [13,14]. In microwave ablation an ultra-high-speed microwave (usually 2450 MHz) is emitted from exposed antenna of the electrode, causing the water molecules in the tissue to vibrate and rotate with similar frequency. Heat is generated and results in thermal coagulation of the target tissue [6].

In this study, a 2450 MHz internally cooled-shaft antenna was used. It has two channels inside the shaft lumen with distilled water circulated by a peristaltic pump to continuously cool the shaft. The low antenna shaft temperature can deliver more energy into the tissue without causing skin burn. In addition, low antenna shaft temperature can reduce higher temperature in the center to decrease tissue charring and improve energy transfer, which makes possible higher output and longer duration treatment [15]. As result, the ablation zone can be remarkably expanded.

Microwave ablation can be performed percutaneously, laparoscopically, thoracoscopically, or at laparotomy. Percutaneous treatment offers several advantages over other approaches [16]. The percutaneous approach is the least invasive, relatively expensive, can be performed on outpatient basis, and can be repeated to treat recurrent tumor, laparoscopic and thoraco-
This study reports the first initial utilization of this type of MW technology in the management of HCC at our institution. The ablation procedures were performed percutaneously with HS Amica probe. Percutaneous MWA appeared to be a well tolerated treatment in our patient group with no post-operative deaths and no complication occurred related to the ablation procedure. None of the patients in this series showed evidence of sepsis, bile duct damage, uncontrollable bleeding, or significant systemic upset. This compares very favorably with studies of alternative ablative modalities which have reported complications in up to 33% of the patients treated (17,18). Also, the study of Xu et al. (6), reported complications related to MW ablation in nine patients including pleural effusion in two liver failure in one, hepatic abscesses in two, skin burn in two and sub capsular hematoma in two.

In the present study, by using the cooled-shaft microwave antenna, and repeated probe re-insertion technique, the complete ablation rates for tumors 3 cm or less and those larger than 3 cm were 98.3% (57 of 58 nodules) and 92.5% (37 of 40 nodules), respectively. The four incompletely ablated tumors were treated with additional percutaneous MWA sessions and technical success was achieved in all. These results were comparable to those reported from Lu et al. (10) whose technical success rates for tumors 2 cm or smaller and those larger than 2 cm were 98% (45 of 46 nodules) and 92% (56% of 61 nodules), respectively, and after additional MW ablation sessions technical success was achieved in all his incompletely ablated tumors. However, our present results were quite superior to those of Kung et al. (14) who treated 90 patients with unresectable liver cancers. The complete ablation rates were 94%, 91%, and 92% for small (<3 cm), intermediate (3.1–5.0 cm) and large (5.1–8.0 cm) liver cancers. Additionally, in the study of Xu et al. (6) using multiple electrode insertion technique, the complete ablation rates at 1 month post-ablation in tumors 2.0, 2.1–3.9 and 4.0 cm in diameter were 93.1%, 93.8%, and 86.4%, respectively.

In our study, 39/40 patients with elevated α-FP showed decreased levels to within the normal range one month after ablation, and the remaining patient showed gradual decrease to reach the normal level at 7 months post-ablation. In the study of Lu et al. (10), 18/50 patients with elevated α-FP before ablation showed marked decrease at 1 month after MWA. Dong et al. (9), had in their study 139/234 patients with elevated α-FP level pre-ablation. At 1 month post-ablation 101/139 had decreased α-FP to normal level and 28/139 showed decrease in α-FP level although it did not drop to normal. The α-FP levels remained unchanged after MWA in 10 patients.

Though evaluating long term results and survival rates of percutaneous MWA is beyond our objective in this study, yet in our limited study period (10 months), the survival rate was 100%. This compares favorably with study of Lu et al. (10), where the 1 year survival rate for 36 patients was 96%, and that of Dong et al. (9), 1 year survival rate for 185 patients was 92.7%.

Limitation of our study; it was a short limited study and hence reliable long term results and survival rates could not be properly evaluated. It is a short term preliminary study focused on the technical efficacy and safety of this new MW technology rather than a long term follow-up study. However, further study with a larger patient sample and longer follow-up is suggested.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Treatment and follow-up.</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>72</td>
</tr>
<tr>
<td>Follow-up duration</td>
<td>162.1 ± 81.0 (36–299) [146.5]</td>
</tr>
<tr>
<td>Follow-up sessions</td>
<td>Once 26 (36.1%)</td>
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<td></td>
<td>Twice 22 (30.6%)</td>
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<td></td>
<td>Thrice 24 (33.3%)</td>
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<tr>
<td>Number of nodules</td>
<td>1 46 (63.9%)</td>
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<tr>
<td></td>
<td>2 26 (36.1%)</td>
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<tr>
<td>Size of nodules</td>
<td>3.2 ± 0.9 (2–5) [2.9]</td>
</tr>
<tr>
<td>≤3</td>
<td>58/98 nodule (59.2%)</td>
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<tr>
<td>&gt;3</td>
<td>40/98 nodule (41.8%)</td>
</tr>
<tr>
<td>MW ablation</td>
<td>Success 37/40 (92.5%)</td>
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<tr>
<td>Failure 1/40 nodule (2.5%)</td>
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<tr>
<td>Recurrence</td>
<td>11 (15.3%)</td>
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<tr>
<td>α-Fetoprotein</td>
<td>Pre 317.9 ± 235.1 (9–789) [231]</td>
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<tr>
<td></td>
<td>&lt;200 32 (44.4%)</td>
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<td></td>
<td>&gt;200 40 (55.6%)</td>
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<tr>
<td>Only patients with &gt;200 pre-operatively</td>
<td>1 m after 117.9 ± 78.1 (10–517) [117] a</td>
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<tr>
<td></td>
<td>&lt;200 39 (97.5%)</td>
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<td></td>
<td>&gt;200 1 (2.5%)</td>
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<tr>
<td>4 m after 106.0 ± 47.2 (21–176) [102] a</td>
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<td></td>
<td>&lt;200 24 (96.0%)</td>
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<td></td>
<td>&gt;200 1 (4.0%)</td>
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<tr>
<td>7 m after 85.8 ± 50.0 (10–165) [82] b,c</td>
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<td></td>
<td>&lt;200 14 (100%)</td>
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<td>&gt;200 0 (0%)</td>
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a P-value = 0.301 for comparison between size groups regarding success.

b P-value < 0.001 for comparison with pre-ablation.

c P-value = 0.036 for comparison with 4 months follow-up.

Figure 5 α-FP levels pre-ablation and during follow-up.
up period is needed to prepare for a subsequent long term follow-up and survival rate study.

5. Conclusion

This study suggests this new MW technology represents a safe, fast and efficacious way to perform hepatic ablation in patients with HCC. Initial results are encouraging, however, longer follow-up is needed for further classification of our results.

References


