



# Long-Term Survival of Large ( $\geq 3$ CM) Hepatocellular Carcinoma Treated with Microwave Ablation

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## Abstract

**Purpose:** To evaluate the long-term Overall Survival (OS) rate in patients with large ( $\geq 3$ cm) Hepatocellular Carcinoma (HCC) treated with Microwave Ablation (MWA).

**Materials and Methods:** 19 patients with HCC with tumors size ranging from 3cm-9.5cm were treated with MWA. 15 of the 19 patients had single tumor, 4 patients had multiple tumors. 23 tumors were identified. Lesions were evaluated at 1-, 3-, and 6-months post ablation using the mRECIST criteria. 12 of the 19 patients had Transhepatic Arterial Chemoembolization (TACE), 8 patients had repeat MWA, and 3 patients had liver transplant subsequently. OS rate was analyzed.

**Result:** The mean follow up period was  $22.8 \pm 12.8$  months, and the range was 2-40 months by the end of study. Out of 23 tumors, 10 tumors had Partial Response (PR), 8 tumors had Complete Response (CR), 3 tumors had Stable Disease (SD), and 2 tumors had Progressive Disease (PD). The 6-month, 1-year and 2-year OS rates were 94.4%, 94.4%, and 85.7% respectively.

**Conclusion:** MWA is an effective treatment for HCC  $\geq 3$ cm given its favorable long-term OS rate.

**Keywords:** Microwave ablation; Large hepatocellular carcinoma; Long-term survival

## Introduction

Liver cancer is one of the most commonly diagnosed cancers in the world. It is the fifth most frequently diagnosed cancer worldwide with the incidence rate of 8 per 100,000 and the second most frequent cause of cancer death [1,2]. Out of all the primary liver cancers, 70%-90% are Hepatocellular Carcinoma (HCC) [3].

According to the Barcelona Clinic Liver Cancer (BCLC) staging and treatment strategy for HCC and the European Association for the Study of the Liver recommendation (EASL), very early- stage and early-stage HCC should be managed with surgical resection or liver transplantation when the criteria are met [4,5]. However, less than 20% of patients are surgical candidates [6]. Current American Association for the Study of Liver Disease (AASLD) and Society of Interventional Radiology (SIR) guidelines recommend Percutaneous Thermal Ablation (PTA), with Radiofrequency Ablation (RFA) as the ablative modality, for patients who are not suitable to undergo surgical treatment for HCC with BCLC stage 0 and A [7,8]. RFA has shown to be effective with its Complete Response (CR) rate and long-term Overall Survival (OS) rate that were comparable to the ones of surgical treatments [4,7,9]. Recent studies have even shown potential effectiveness of ablation in treating larger tumors (size  $\geq 3$ cm) [10,11]. However, only a few studies have reported on the long-term survival rate for HCC  $\geq 3$  cm treated with Microwave Ablation (MWA). Therefore, the present study evaluated long-term survival rate of patients, with large HCC ( $\geq 3$ cm), who were treated with MWA.

## Materials and Methods

Institutional review board approval was obtained for this retrospective review, and written informed consents were obtained from every patient before treatment. Data was collected from the electronic health records on patients treated.

### Patients

From July 2011 to December 2014, a total of 19 patients with 22 tumors  $\geq 3$  cm underwent Computed Tomography (CT) guided MWA. Of the 19 patients, there were 13 male and 6 female; 15 had solitary lesion, 4 had multiple lesions. The mean age was  $63 \pm 8.6$  years (range: 54-86 years). The mean diameter of the tumors was  $4.1\text{cm} \pm 1.7\text{cm}$  (range: 3cm-9.5cm). The demographic data of the patients is shown in Table 1.

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HCC was diagnosed by histological evidence, by contrast-enhanced CT, or by Magnetic Resonance Imaging (MRI). The inclusion criteria for patients eligible for MWA were as follows: 1) no more than 3 tumors with at least 1 tumor  $\geq 3$ cm; 2) absence of vascular invasion, distant metastases, and lymph node involvement; 3) liver function status at Child-Pugh A or B; 4) no contraindication for MWA; and 5) the patient was not a surgical candidate at the time of the procedure.

### Ablation procedures

MWA was performed percutaneous under CT guidance with the MicroThermX (Perseon Med, formerly BSD Medical Corp. Salt Lake City Utah, USA). The ablation system consists of a microwave generator with frequency of 915 MHz and provides output from 0-180watts (maximum 60watts per channel), with the capability of using 3 antennas at the same time. Microwave was delivered through a 14 G cooled shaft SynchroWave Antenna (Perseon Med.).

All procedures were performed under general anesthesia. Triple phase CT of the liver was performed to identify and locate the lesion(s). Using CT guidance, the lesion(s) was accessed using the ablation antenna. Size of the antenna and the length of time of microwave delivery was selected following manufacturer protocol to achieve a target 1 cm ablation margin around the lesion. Overlapping ablative technique was required for larger tumor(s). Follow-up CT was done immediately to ensure ablation at the intended site. The antenna was then removed and the tract was ablated to prevent bleeding from the liver surface.

### Assessment of therapeutic efficacy

Contrast-enhanced CT or MRI of the abdomen was performed 1-, 3-, and 6-month post ablation to evaluate therapeutic efficacy using m-RECIST criteria. Complete Response (CR) was defined as disappearance of all target lesions. Partial Response (PR) was defined as 30% decrease in sum of the longest diameter of target lesions. Progressive Disease (PD) was defined as 20% increase in the sum of the longest diameter of target lesions. And Stable Disease (SD) was defined as small changes that do not meet above criteria.

The patients were followed in outpatient setting at 1-, 3-, 6-month and every 3 months thereafter to monitor clinical response and to obtain specimens for laboratory evaluation.

All patients were monitored for the development of local and distant recurrence with contrast-enhanced CT, MRI, or ultrasound of the abdomen every 3 months. Due to multifaceted reasons such as patient condition and disease progression, timing and modality of follow-ups and image studies were at the patient's primary care team's discretion and the patient's availability. Patients with recurrence, PR, PD, SD were treated with repeat MWA and/or TACE.

### Statistical analysis

Continuous variables were expressed as mean  $\pm$  standard deviation. Survival rates were analyzed using the Kaplan-Meier method. Statistical analysis program, IBM SPSS Statistics 24, was utilized to perform data analysis.

## Result

### Long-term survival

Survival rate was measured from the day of initial MWA treatment until the day of last follow-up or the day of patient death. Nineteen patients with 22 tumors were followed. The mean follow-up period was  $22.8 \pm 12.8$  months with range 2-40 months by the end

of study. Out of 22 tumors, 10 tumors had PR, 7 tumors had CR, 3 tumors had SD, and 2 tumors had PD radiologically. At the time of analysis 17 patients were alive at the last known follow up, 12 patients were confirmed to be alive at the end of the study with mean survival length  $31.17 \pm 6.34$  months, 2 patients were deceased at 4-month and 17-month due to various causes, and 5 patients were lost to follow-up at 2-, 6-, 7-, 7-, and 16- month. At 6-month mark, 1 patient was lost to follow-up, 1 patient was deceased, therefore a total of 18 patients were used to analyze OS rate. At 1-year mark, 3 more patients were lost to follow-up. There was no new death during the time period, and a total of 15 patients were used to analyze OS rate. And at 2-year mark, a total of 5 patients were lost to follow-up, 2 patients were deceased, and 14 patients were used to analyze OS rate. OS rates were 94.4%, 94.4%, and 85.7% for 6-month, 1-year, and 2-year, respectively (Figure 1).

## Discussion

Although liver transplant and resection remain the first line treatment for very early and early-stage HCC per EASL guideline [5], ablation using RFA is the first choice in treating HCC with BCLC stage 0-A when the patient is not a surgical candidate [7]. Recently, some studies have demonstrated comparable result in ablation and surgical therapy for early stage HCC. Lü "et al". [12]. Reported complete tumor free rate of 100% vs. 94.7% for resection and ablation, respectively, with local recurrence rate to be 0. Furthermore, Chen "et al". [9] reported no statistically significant difference in OS in RFA and resection group for solitary tumor  $< 5$ cm. The 1-, 2-, 3-, and 4-year OS rates were 95.8%, 82.1%, 71.4%, 67.9% and 93.3%, 82.3%, 73.4%, 64.0% for RFA and resection, respectively. Despite recent positive reports in patients with HCC treated with RFA, some studies reported lower recurrence and better survival rate in HCC patients who were treated with resection. Current EASL and AASLD guidelines recommend RFA as the ablative modality because it has been the most evaluated technology [5,7]. But MWA, a relatively newer technology, has started to gain more acceptances with recent improvements in technology, which increased the ablation zone. Kuang "et al". [13] reported CR rates of 94%, 91%, and 92% in small ( $\leq 3.0$ cm), intermediate (3.1cm-5.0cm), and large (5.1cm-8.0cm) liver tumors, respectively, treated with MWA. Similarly, Liu "et al". [14] reported CR rates of 94.2% for 3cm-5cm tumors and 75% for 5cm-8cm tumors. Also, Yin "et al". [11] reported CR rates of 95.4% and 80% for tumors sizes of 3cm-5cm and 5cm-7cm, respectively, and reported no statistically significant difference in the mortality of RFA and MWA. Furthermore, Huo "et al". [15] reported in a meta-analysis that there was no clear difference in RFA and MWA, and that both are suitable option to treat HCC. Given the advantage of MWA such as high intra-tumoral temperature, faster ablation, larger ablation volume, and less susceptibility to heat-sink effect, MWA may be considered as a more attractive choice of therapy than RFA [16]. Few studies have been published to evaluate the long-term OS for large tumors treated with MWA. Yin "et al". [11] used both RFA and MWA to treat patients with HCC with tumors measuring from 3cm to 7cm and reported OS rates of 76%, 47%, 31%, and 15% for 1-, 2-, 3-, and 5-year, respectively. Median survival length was 19 months vs. 30.3 months,  $p = 0.0846$ , for RFA and MWA, respectively. Liu "et al". [13] studied HCC patients treated with MWA reported 1-, 2-, 3-, and 5-year OS rates of 92.3, 80.2, 66.1, and 46.5%, respectively, for tumors size 3-5 cm; and 1-, 2-, 3-, and 5-year OS rates of 60.7, 46.4, 39.3, and 13.1% for tumors size 5-8 cm. While Poon "et al". [17] studied large HCC ( $> 3$ cm) patients who were treated with RFA and reported 6-, 12-, and 18-months OS of 85%, 81%, and 76%, respectively. Present study found OS rates of 94.4%, 94.4%, and 85.7% for 6-month, 1-year,

and 2-year, respectively, for tumors  $\geq 3$  cm (range: 3cm-9.5cm). The two deceased patients had tumor sizes of 4.9cm and 9cm. This observation was expected given the knowledge that larger tumors have a negative impact on patient outcome [18,19]. At the same time present study also demonstrated that there is a survival benefit to 2 years for tumors  $\geq 3$ cm treated with MWA.

The limitations of this study included its retrospective and nonrandomized study design, small sample size, patients lost to follow-up, and absence of comparison of mortality data with small tumors and different treatment modalities. A prospective randomized study with larger sample size and longer follow-up period is required to provide a more conclusive data on the long-term OS of patients with large ( $\geq 3$ cm) HCC treated with MWA.

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