INTERVENTIONAL RADIOLOGY

Microwave ablation assisted by three-dimensional visualization system as local therapy for relapsed hepatoblastoma: a small pilot study

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Abstract

Purpose We aimed to explore the feasibility of microwave ablation (MWA) assisted by three-dimensional visualization system for relapsed HB in children.

Methods From August 2014 to February 2017, five patients with relapsed HB were enrolled. A total of 12 liver tumors were treated with MWA assisted by a three-dimensional visualization system. Follow-up data were obtained in all patients. The residual liver volume, local tumor progression, new intrahepatic tumors, survival outcome, and complications were analyzed.

Results All tumors were completely ablated in a single session. The mean ablation time per tumor was 9.7 ± 8.6 min, and the median ablation/liver volume ratio was 2.37%. No local tumor progression was observed during a follow-up period of 9–39 months. All patients were still alive at the end of the follow-up. The median progression-free survival time after ablation was 9 months, and the median survival time after ablation was 12 months. No other complications were observed except for fever.

Conclusions MWA assisted by three-dimensional visualization system appears to be a safe and feasible local treatment for recurrent HB in pediatric patients.

Keywords Microwave · Ablation techniques · Hepatoblastoma · Children

Introduction

Hepatoblastoma (HB) is the most common primary pediatric liver tumor [1], with an annual incidence rate of 1–5 per 1 million population worldwide [2]. Despite improvements in chemotherapy protocol and surgical techniques, approximately 12% of patients who achieve complete response relapse with dismal outcomes [3–5]. Unfortunately, no standard treatment protocol for relapsed HB has been established to date.

A second surgical resection seems to be a critical intervention, but the optimal surgical technique for reoperation remains challenging [6]. Multiple lesions in different liver segments, limited volumes of the remaining liver, and tumor proximity to major vascular structures make reoperation almost impossible. In addition, for patients with multiple recurrence, the "rescue transplants" are not as effective as expected and could not be regarded as a safety net [7–9]. Therefore, it is necessary to explore other strategies to reduce the local tumor burden of patients with recurrent HB.

Recently, percutaneous thermal ablation, mainly including radiofrequency ablation (RFA) and microwave ablation (MWA), has received increasing attention as a treatment modality for unresectable liver tumors or for patients ineligible for surgery [10]. However, for pediatric patients with relapsed HB who underwent previous liver resection, the residual liver volume is limited, and the normal anatomic relationship between the liver and surrounding structures has changed. Therefore, it is crucial to analyze the spatial

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relationship between tumors and adjacent structures comprehensively and develop a substantial pre-procedure plan on the ablation procedure.

A three-dimensional (3D) visualization software system developed by our group has been proven to be effective in improving the precision of MWA in treating adult hepatic and renal tumors [11, 12]. This system can not only provide a pre-procedure plan for ablation, but also post-procedure assessment of the ablation zone. However, to the best of our knowledge, no studies about MWA aided by 3D visualization system for pediatric tumors have been published. Thus, we conducted this study to preliminarily explore the feasibility of MWA aided by 3D visualization system for relapsed HB in children. In this paper, we report our initial experience about this treatment modality.

Materials and methods

Patients

This is a retrospective case series study. Written informed consent for the procedure was obtained from each child's parents and the study protocol was approved by the local ethics committee. From August 2014 to February 2017, five patients with a total of 12 tumors were treated. The criteria for enrollment were: (1) diagnosis of relapsed HB confirmed via ultrasound-guided biopsy or on the basis of newly identified tumors on contrast-enhanced magnetic resonance imaging (MRI) and a high level of serum alpha-fetoprotein; (2) refusal of or ineligibility for reoperation; and (3) stable hematogenic parameters (no anemia, normal coagulation parameters, and no active infection). The median ages of the patients were 11 years (range 3.3–16 years). The median maximum diameter of the recurrent HBs was 1.6 cm (range 1.0–3.5 cm). Table 1 shows the detailed baseline characteristics of the five patients. Before initial surgery, the tumors had been classified according to the PRETEXT system [13] as stage II, III, or IV hepatoblastoma. All patients had undergone surgical resection and postoperative chemotherapy. Three patients received neoadjuvant chemotherapy prior to the initial surgery. During the follow-up period, a total of 12 recurrent tumors were detected.

Methodology of the procedure

3D visualization system

A computer-assisted 3D visualization system was developed by our group. As previously reported [11, 14], it is an integrated system with functions including tumor segmentation, thermal field simulation, puncture path planning, and image registration.

For pre-procedure planning, enhanced MRI imaging within 1 week prior to MWA was imported into the system. Then, via semiautomatic image segmentation and the 3D visualization quantitative calculations, the anatomic relationships between index tumor and surrounding structures were displayed, the access path was planned, and the thermal field distribution was simulated. To ablate the tumor completely and safely, several principles for the pre-procedure planning should be followed simultaneously: (1) simulative thermal field covering the target tumor and a 5 mm circumferential ablative margin, (2) minimizing the number of antenna insertions, and (3) no vital structures in the insertion path.

After MWA, this system was used to assess and calculate the volume of the ablation zone and the residual liver. The processes are based on post-procedure (3 days after MWA) contrast-enhanced MRI. MRI images with DICOM format data were imported into our 3D visualization software system for processing and analysis. By segmenting the tumor and ablation zone, a 3D image of the ablation zone was displayed and the ablation volume after MWA was computed (Fig. 1).

Microwave ablation

Patients were placed in the left lateral position or supine position according to the tumor location. Under general anesthesia, MWA was performed using the microwave unit (KY-2000, Kangyou Medical, Shanghai, China), which consists of a microwave generator, a needle antenna, and a cooling system. The microwave antenna was percutaneously inserted into the tumor under continuous ultrasound guidance. During MW ablation, a power output of 50 W was routinely used until the heat-generated hyperechoic water vapor completely encompassed the entire tumor and the predetermined safety margin. When the ablation was completed, the needle track was coagulated with the antenna being withdrawn.

Artificial ascites technique during the MWA procedure

For hepatic tumors adjacent to the gastrointestinal tract, artificial ascites was introduced before MWA. After the administration of local anesthesia with 1% lidocaine, an 18-gauge catheter (BD Angiocath; Sandy, UT, USA) was inserted into the peritoneal cavity between the edge of the liver and the adjacent gastrointestinal tract. Then, 0.9% saline solution was injected slowly into the catheter. The induction of artificial ascites was judged to be successful once the distance between the tumor and adjacent gastrointestinal tract was widened to at least 0.5 cm; the MWA procedure was then performed. A drip infusion of saline solution was continued during MWA to maintain the tumor–gastrointestinal tract distance of at least 0.5 cm.

Table 1 Clinical characteristics of the patients

Patient no.	Age	Sex	Size and locations of the tumor (cm)	Interval time between surgery and relapses (months)	Previous treatment	PRE-TEXT stage	AFP values (µg/L) at diagnosis
1	11 years	Female	1.2 × 1.2 (S7)	8	Lobectomy + post-surgery chemotherapy (4 cycles)	III	575600
			1.6 × 1.5 (S7)				
			1.6 × 1.5 (S7)				
			1.0 × 1.0 (S7 and S8)				
2	13 years 6 months	Male	2.3 × 2.1 (S2, adjacent to the stomach)	6	Pre-surgery chemotherapy (4 cycles) + lobectomy + post-surgery chemotherapy (4 cycles)	IV	26000
			1.4 × 0.8 (S2)				
3	16 years	Female	2.4 × 2.1 (S8, adjacent to the inferior vena cava)	50	Segmentectomy + post-surgery chemotherapy (8 cycles)	II	< 100
			1.1 × 0.9 (S7)				
			1.2 × 0.8 (S1)				
4	3 years 3 months	Female	3.5 × 2.4 (S2 and S3)	6	Pre-surgery chemotherapy (6 cycles) + segmentectomy + post-surgery chemotherapy (5 cycles)	III	540000
5	3 years 6 months	Female	3.1 × 2.7 (S7 and S8)	10	Pre-surgery chemotherapy (6 cycles) + lobectomy + post-surgery chemotherapy (6 cycles)	III	43000
			1.9 × 1.8 (S7)				

S segment of the liver according to Couinaud's system of segmentation of the liver

Post-procedure observation and follow-up

All patients underwent close post-procedure monitoring for possible complications and side effects, including fever, skin burn, abdominal pain, hepatic dysfunction, pleural effusion, and intraperitoneal hemorrhage. One day after MWA, contrast-enhanced ultrasound (CEUS) examination was performed. Treatment response was assessed based on the modified Response Evaluation Criteria in Solid Tumors (mRECIST), in which complete response (CR) was defined as the disappearance of any arterial enhancement in the lesion. Patients with CR underwent the follow-up protocol that consists of the contrast-enhanced MRI and/or CEUS at 1, 3, and 6 months after the treatment and every 6 months thereafter. For patient whose treatment response was not evaluated to be CR, an additional session of MWA was performed. Local tumor progression was defined as the appearance of tumor foci at the edge of the ablation zone after at least one contrast-enhanced follow-up has documented adequate ablation and an absence of viable tissue in the target tumor and surrounding ablation margin by using the imaging criteria [15]. The survival time was defined as the period from the completion of MWA treatment to death or last follow-up. All patients underwent chemotherapy after MWA according to individual condition and previous chemotherapy protocols.

Statistical analysis

All data reported were expressed as median or mean ± SD. Statistical analysis was performed via SPSS 17.0 statistical software package (Chicago, IL, USA).

Results

The data about ablation procedures and outcomes of all five patients are given in Table 2. All 5 patients with 12 tumors underwent MWA assisted by 3D visualization
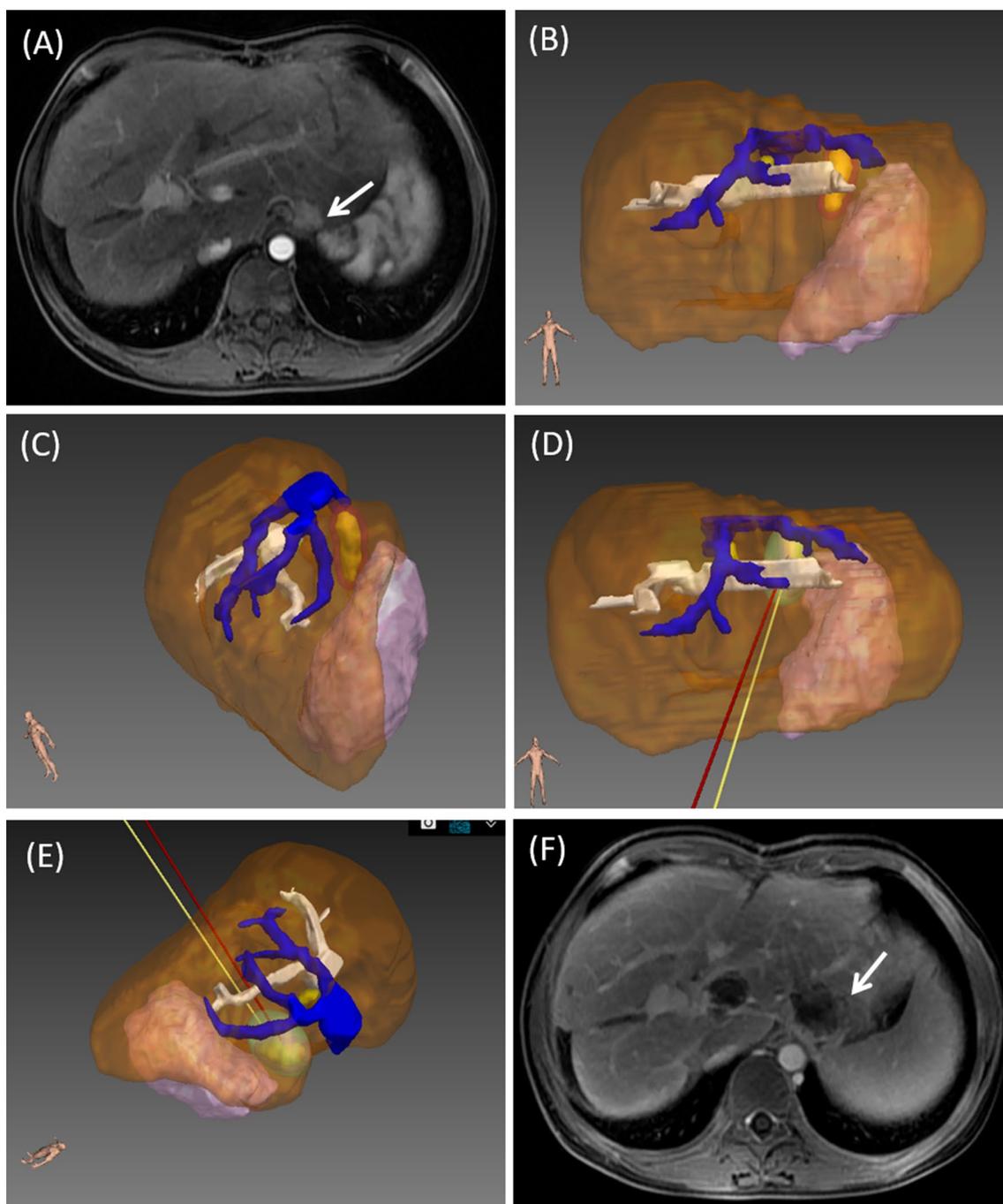
Fig. 1 Images of a tumor locating in SII in the left lobe of No.2 patient. **a** Pre-procedure contrast-enhanced MRI imaging showed that the tumor was close to the stomach. **b**, **c** The pre-procedure 3D visualization images of the spatial relationship of tumor and the surround-ing vital structure (yellow—the tumor, red—a 5 mm circumferential ablative margin). **d**, **e** The simulated thermal field distribution of the intended access path. **f** The contrast-enhanced MRI showed complete tumor necrosis after microwave ablation

system, and 2 patients (No. 1 and 2) with 2 tumors received artificial ascites assistance during ablation. The mean ablation time per tumor was 9.7 ± 8.6 min, and the mean number of antenna insertions was 2 ± 1.2 per tumor. CEUS and contrast-enhanced MRI within 3 days after MWA showed that all the 12 tumors were completely ablated. The post-procedure tumor volume and ablation volume were computed via the 3D visualization system (Table 3). The median ablation/liver volume ratio was 2.37%.

The resting time for all patients after MWA did not exceed 6 h. Elevated aminotransferase levels (alanine aminotransferase (ALT), 191.7 ± 97.1 U/L; aspartate

Table 2 Ablation procedures and outcomes of patients

Patient no.	Size of the tumor (cm)	Number of antenna insertions	Ablation power (W)	Total ablation time (min)	Complications	Local tumor progression	New hepatic metastasis/ location of metastasis	Recurrence-free interval (months)	Survival time after ablation (months)
1	1.2 × 1.2	1	50	3	Fever	No	Yes/S2, S5	5	12
	1.6 × 1.5	2	50	8					
	1.6 × 1.5	2	50	8					
	1.0 × 1.0	1	50	2					
2	2.3 × 2.1	2	50	10	–	No	No	–	9
	1.4 × 0.8	1	50	3.5					
3	2.4 × 2.1	2	50	10	Fever	No	Yes/S3, S6	18	39
	1.1 × 0.9	1	50	2					
	1.2 × 0.8	1	50	2.5					
4	3.5 × 2.4	5	50	32	–	No	Yes/S4	6	16
5	3.1 × 2.7	4	50	19	–	No	No	–	12
	1.9 × 1.8	2	50	16					

aminotransferase (AST), 385.2 ± 236.7) were tested after MWA in all patients, but it reverted to near normal value (ALT, 63.7 ± 23.1 U/L; AST, 50.8 ± 12.7) at discharge. Only two patients developed fever with a temperature higher than 39 °C, and it was resolved via conservative therapy within 5 days. No any other immediate or periprocedural major complications were found in any patient. All patients were discharged from the hospital within 3 days after the treatment.

The last follow-up of all patients in the study was in December 2017. During a follow-up period of 9–39 months, no local tumor progression was observed in any patient. However, multiple new intrahepatic tumor foci were detected in three patients (No. 1, 3, and 4), and all foci were remote from the ablation zone (Table 2). Due to their ineligibility for reoperation, they received combination treatment of chemotherapy, trans-arterial chemoembolization, and MWA. All patients were still alive at the end of the follow-up. The median progression-free survival (PFS) and overall survival (OS) after ablation was 9 months (range 5–18 months) and 12 months (range 9–39 months), respectively.

Discussion

Thermal ablation, as an effective minimally invasive therapy, has been used in treating adult hepatic malignancies for more than 25 years [16–18]. In recent years, a number of researches have reported the safety and efficacy of RFA in treating liver tumors of pediatric patients [19–23]. However, up to now, there is no report regarding MWA for pediatric malignant hepatic tumors. In fact, MWA, as a relatively recent technology applied in treating various types of tumors in adults [24–26], has shown multiple theoretical advantages compared with RFA, including the capability to achieve larger ablation volume, more rapid heating, and lower susceptibility to heat-sink effects [27, 28]. The higher thermal efficiency of MWA makes it possible to shorten the ablation time. In this study, the mean ablation time per tumor was 9.7 ± 8.6 min (range 3–32 min). While, the ablation time of RFA reported in another similar study was 12.8 min [29]. Thus, MWA seems to have a potential in shortening the procedure duration, which may make it more suitable for pediatric patients who cannot tolerate long procedures. However, according to a recent randomized controlled trial on the efficacy of MWA versus RFA for hepatocellular carcinoma,

Table 3 The volume ratio before and after MWA

Patient no.	Total liver volume (mL)	Tumor volume before MWA (mL)	Tumor/liver volume ratio (%)	Ablation volume (mL)	Ablation/liver volume ratio (%)
1	831.89	8.60	1.03	21.93	2.64
2	1013.18	9.01	0.89	12.59	1.24
3	719.18	5.13	0.71	17.08	2.37
4	409.62	2.83	0.69	8.82	2.15
5	485.40	15.49	3.19	32.24	6.64

there is no difference between these two treatment modalities in terms of the duration for the entire procedure [30]. Hence, whether MWA is a timesaving treatment modality needs to be further proved.

Moreover, a residual liver volume (RLV) is an essential safety component of MWA in treating pediatric liver neoplasms [31]. A small RLV% conventionally predicts severe hepatic dysfunction after the procedure [32]. For pediatric patients who had previously undergone hepatectomy, conserving as much RLV as possible with complete tumor necrosis is even more important. Hence, thermal ablation for relapsed HB remains challenging in this patient population. On one hand, excessive ablation may result in unnecessary loss of liver volume; on the other hand, insufficient coverage of the ablation zone may lead to the emergence of residual unablated tumor or local tumor progression. Thus, for pediatric patients with recurrent HB, it is essential that the tumors are ablated completely and conformally. The 3D visualization system was demonstrated to be effective in displaying anatomic relationships between index tumor and surrounding structures, planning access path, simulating the thermal field distribution, and predicting the residual liver volume [11, 13], which is important in realizing conformal tumor ablation. In this study, although two tumors were adjacent to the stomach and the inferior vena cava, via pre-procedure planning using the 3D visualization system, all tumors were completely ablated in a single session without injury to surrounding structures. Moreover, the mean number of antenna insertions was only 2 ± 1.2 per tumor, and the median ablation/liver volume ratio was less than 3%. Apparently, this modality achieved effective ablation without excessive loss of liver volume.

In this study, we applied ultrasound to guide the ablation procedure because of the following reasons. First, ultrasound provides real-time imaging to facilitate the whole interventional procedure and ensure the ablation antenna to be placed on the prespecified site. Second, ultrasound guiding is free of ionizing radiation. Hence, it is a safe way in guiding ablation for pediatric tumors. Third, compared with CT and MRI, ultrasound costs less [33]. For pediatric patients, ultrasound is quite qualified in clear imaging, so it is unnecessary to increase medical expense to choose CT or MRI.

In terms of patient recovery, although the post-procedure level of ALT and AST increased to ninefold and 17-fold, respectively, it reverted to relatively normal levels within 1 week. Moreover, all patients were on bed rest for only less than 6 h after the procedure and were discharged within no more than 3 days after the treatment, indicating prompt recovery.

Although new intrahepatic tumor foci were detected in three patients in the follow-up, the new foci were not located in the same liver segment with previous tumors. We considered that the progression depends not only in the pathology

of the tumor, but also in the combination protocol of local treatment and chemotherapy. At the end of the follow-up, the OS rate was 100%. In a similar study on RFA in treating recurrent HB [29], the OS rate was 80%. Hence, MWA appeared to have more potential in prolonging the survival time of patients.

There are a few limitations in this study. First, due to the low incidence of HB, only a limited number of pediatric patients with recurrent HB were enrolled. Second, because MWA assisted by a 3D visualization system is a relatively new technique, the follow-up period after ablation was relatively short. Third, the treatment effects of different chemotherapy regimens combined with MWA should be observed and compared, which was not done in this study.

In conclusion, MWA assisted by a 3D visualization system preliminarily appears to be a safe and feasible technique for local treatment of recurrent HB in pediatric patients. However, prospective studies with sufficient sample size, comparative evaluation, and appropriate inclusion criteria are needed to verify our findings.

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