3.0-T closed MR-guided microwave ablation for HCC located under the hepatic dome: a single-center experience

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\textbf{ABSTRACT}

\textbf{Purpose:} To analyze the clinical safety and efficacy of 3.0-T closed MR-guided microwave ablation (MWA) for the treatment of HCC located under the hepatic dome.

\textbf{Methods:} From May 2018 to October 2020, 49 patients with 74 HCCs located under the hepatic dome underwent MWA using 3.0-T closed MR guidance. The technical success rate, operative time, complete ablation (CA) rate, complications, local tumor progression (LTP), tumor-free survival (TFS) and overall survival (OS) were examined. Routine blood analysis, liver/kidney function and alpha fetoprotein (AFP) and protein induced by vitamin k absent or antagonist (PIVKA) levels were compared before and 2 months after MWA.

\textbf{Results:} All patients underwent MWA successfully, including 10 patients who underwent general anesthesia. The technical success rate was 100% without major complications. The CA rate was 95.9% (71/74) at the 2-month evaluation. The LTP rate was 2.7% during the median follow-up of 17.8 months (range: 4–43 months); the 6-, 12-, 18-month TFS rates were 97.8, 90.6, 68.1%, respectively, and the 6-, 12-, 18-month OS rates were 100, 97.6, 92.1%, respectively. There were no significant changes in routine blood tests and liver/kidney function (\(p > 0.05\)), while the AFP and PIVKA level decreased significantly at 2 months (\(p < 0.05\)).

\textbf{Conclusion:} 3.0-T MR-guided MWA is safe and feasible for HCC lesions located under the hepatic dome.

\section{1. Introduction}

In 2020, there were 910,000 cases of Hepatocellular carcinoma (HCC) worldwide, ranking it sixth among all malignant tumors with more than 830,000 deaths [1]. Ablation has become the first choice of radical and minimally invasive treatment for liver cancer \(\leq 3\) cm, and the long-term clinical efficacy is equivalent to that of surgery [2]. The connotation of precise ablation should include accurate positioning, precise puncture and fine evaluation, and the foundation of realizing these three core objectives is image visualization. It has been reported that the local recurrence rate of subphrenic HCC is as high as 29%, and the main reason may be the insufficient evaluation of the ablation zone [3]. At present, ultrasound (US) or CT are the main guidance and evaluation tools for MWA. However, US has poor display of small lesions under the background of severe liver cirrhosis, especially for lesions close to diaphragm because of the obstruction of lung tissue and ribs [4]; some small liver cancer lesions cannot be clearly displayed on CT, and the metal artifact of microwave antenna is large which is easy to cover the lesions; CT has irradiation damage to patients and the boundary of the ablation zone is a little ambiguous, which will affect precise evaluation [5]. With the development of imaging technology and MR-compatible materials, high-field MR-guided liver tumor ablation has become the latest academic field. Although the MR scanning time is relative long, MR-guided ablation should have the following technical advantages: lesion detection, intraoperative puncture and monitoring, and postablation evaluation [6]. The purpose of this study was to evaluate the efficacy and safety of MWA for HCC located under the hepatic dome with a 3.0-T closed MR system.

\section{2. Materials and methods}

\subsection{2.1. Patients}

This retrospective study was approved by the institutional review board of the First Affiliated Hospital of Zhengzhou University (approved protocol number: 2018-ky-207). All participants gave written informed consent that their data can be used for scientific purposes. From April 2018 to October 2020, 49 patients with 74 HCC lesions located under the hepatic dome underwent 3.0-T closed MR-guided MWA (Figure 1, Table 1). The inclusion criteria were as follows: (1) HCC diagnosed according to the European Association for the Study of the Liver; (2) distance between the lesion and diaphragm was \(\leq 5\) mm; (3) Child-Pugh grade A or B; (d) number...
of lesions ≤3; ④ maximum diameter of the tumor ≤5 cm without portal vein invasion; ⑤ Eastern Cooperative Oncology Group (ECOG) score ≤2; ⑥ China liver cancer staging IIb. The exclusion criteria were as follows: ① benign liver tumor; ② PLT ≤30 × 10^9/L or PT ≥25 s; ③ uncontrolled ascites; ④ Child-Pugh grade C; or ⑤ claustrophobia or MR-related contraindications.

### 2.2. Instruments

The MR scanner was a Magenetom Verio 3.0-T scanner with a 70-cm large aperture system (Siemens, Germany). The T1 scan sequence was T1-Vibe with the following parameters: TR 3.92 ms, TE 1.43 ms, FA 9, thickness 3.3 mm, and FOV 380 × 280 mm. The T2 scan sequence was T2-haste-fs with the following parameters: TR 1000 ms, TE 106 ms, FA 180, thickness 4.5 mm, and FOV 380 × 280 mm. Both of them were scanned with breath holding for 16 s. The microwave generator was an MR-compatible microwave therapeutic instrument with a voltage of 220 V, a frequency of 50 Hz, and an output power of 0–100 W (ECO-100E, Nanjing ECO Microwave System Engineering Co., Ltd.), which is placed outside the 5 Gauss line magnetic field to ensure safety. The size of the microwave applicator was 1.8 × 150 mm (ECO-100AI13), and the length of the microwave energy transmission line was 3.5 m.

### 2.3. Preoperative preparation

All patients underwent routine blood examinations, electrolyte level examinations, liver and kidney function testing, coagulation function testing, and cardiopulmonary function examinations within 3 days before MWA. Enhanced CT or MR should be performed within 1 week before MWA, and informed consent was signed. If the diameter of the lesion was more than 3 cm, TACE was performed within 2–4 weeks before MWA to reduce the ‘heat sink’ effect and improve the ablation efficiency [7].

### 2.4. MWA procedure

All punctures were performed by the same interventional radiologists (Jiao DC and Wang CY, who had 15 and 10-year experience on CT guided MWA, respectively). No solid food and water were allowed 4-6 h before MWA, and a holding breath exercise was done to facilitate the MR scan. The patient position was determined according to the tumor location and the puncture plan. Dexmedetomidine (0.5 l g/kg) and dezocine (10 mg) were used to achieve a satisfactory intravenous anesthesia effect, and general anesthesia could be used if the patients (especially for patients with small lesions close to the diaphragm) could not cooperate with breathing. General anesthesia is completed by the anesthesiologist (Tian C, who had 8-year experience on anesthesiology). After the T1WI and T2WI scans (each 16 s) were performed to locate the intrahepatic lesions, local anesthesia was administered with 2% lidocaine (100 mg) by operator himself. A 16-G microwave ablation applicator was inserted into the tumor by multiple MR scan guidance. The ablation parameters were selected according to the size of the lesion according to manufacturer’s recommendation. The applicator rod temperature was reduced by water cooling circulation system during the MWA. T1WI scanning was performed 3-5 min after ablation to evaluate the ablation zone (Figures 2–5). MWA was stopped, if the high-signal ring on T1WI completely covered the central low-

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**Table 1. Patient information.**

| Characteristics                  | Value (number/mean ± SD/range) |
|----------------------------------|--------------------------------|
| Total patients                   | 49                             |
| Age (mean±SD) (range)            | 59.2 ± 9.8 (34–78)             |
| Sex (male/female)                | 39/10                          |
| ECOG score (0/1)                 | 41/8                           |
| Child-Pugh (A/B)                 | 37/12                          |
| AFP level (>200 ng/ml)           | 14/35                          |
| Tumor location                   |                                |
| Segment 8                        | 31                             |
| Segment 7                        | 23                             |
| Segment 4                        | 15                             |
| Segment 2                        | 5                              |
| Tumor number (1/2/3)             | 29/15/5                        |
| Liver cirrhosis (Yes/No)         | 47/5                           |
| Hepatitis (B/C)                  | 44/5                           |
| Max diameter (cm) (range)        | 2.8 ± 0.9 (0.9–4.9)            |
| ≤ 2.5 cm (n = 28)                | 1.9 ± 0.4 (0.9–2.5)            |
| > 2.5 cm (n = 46)                | 3.4 ± 0.7 (2.6–4.9)            |
| Distance to hepatic dome (mm)    | 3.1 ± 1.5 (0–5)                |
| TACE assistance (yes/no)         | 31/18                          |
signal tumor and the peripheral 0.5 cm (the target sign), and the applicator was removed after puncture path ablation. The patient was sent back to the ward and given liver protection, acid suppression and symptomatic treatment.

2.5. Definition and follow up protocols

The technical success was defined as the successful completion of MR-guided MWA. Two months after the operation, 3.0-T upper abdomen plain and dynamic enhanced MR scans were performed to evaluate the tumor response. Complete ablation (CA) was defined as uniform hypoattenuation (on enhanced MR) without enhancement within the ablation zone. The lesion showed complete devascularization and incomplete complete ablation (ICA) was defined as local enhancement. Local tumor progression (LTP) was defined as local recurrence after more than 4 months of CA. Complications were assessed by Cardiovascular and Interventional Radiological Society of Europe (CIRSE) classification score system [7].

2.6. Statistical analysis

SPSS software version 21.0 (IBM, Chicago, USA) was used for statistical analysis. The data are expressed as the mean± standard deviation (SD). Kaplan–Meier survival curves were used to calculate the 6-, 12-, 24-month progression-free survival and overall survival rates.

3. Results

All patients underwent successful MWA, indicating 100% technical success. Only 4 patients adopted double microwave applicators ablation strategy, and the other patients used only single microwave applicator. Thirty-nine patients accepted intravenous anesthesia, while 10 patients (20.4%) underwent general anesthesia due to poor coordination of breath holding. Regarding the MRI manifestations, the ablation zone showed a high-signal area with clear boundaries, and the relatively low-signal area in the center was the initial tumor on T1WI (the target sign). The T2WI ablation zone showed a low signal, and a high-signal loop was seen.
The ablation and total procedure times were 15.7 ± 4.2 (range, 8.0–24.0) and 50.8 ± 15.3 (26.0–78.0) min, respectively. The CA rate was 95.9% (71/74) at the 2-month evaluation. Regarding tumor diameter stratification, the CA rate was 100% (28/28) and 93.5% (43/46) if tumor diameter was ≤ and >2.5 cm, respectively. Two lesions (diameter = 4.2 and 3.7 cm, S8 and S7, respectively) had a local residual tumor close to the pleural edge, and a third one (diameter = 4.2 cm, S7) had a residual tumor close to the inferior vena cava, these lesions underwent 125I seed.

Figure 3. A 62-year-old male with a 0.9-cm HCC lesion located in segment VIII. HCC can be shown on pretreatment MR on T2WI (A), cross section and (B) enhanced MR. (C) The microwave applicator is targeted gradually using tilting of the puncture path under coronal T1WI. (D) After the first circle of ablation (50 W/4 min), the hyperintensity zone on T1WI does not completely cover the low-intensity tumor. (F) The position of the microwave applicator was changed, aiming for complete ablation. (G) The lesion is completely overlapped by a rim of hyperintensity on T1WI (called the target sign) after second circle ablation. (H, I) Postablation MR after 2 months: The lesion is completely ablated on T2WI and enhanced MR.

Figure 4. A 52-year-old male with a 1.3-cm HCC lesion located in segment VIII. HCC can be shown on pretreatment MR on T2WI (A), cross section (B) and enhanced MR. (C) The microwave applicator is targeted gradually into the tumor (55 W/6 min). (E, F) The lesion is completely overlapped by a rim of hyperintensity on T1WI (called the target sign, D) and low intensity on T2WI and enhanced MR (E).
Brachytherapy for advanced treatment. There was no significant change in routine blood tests (white blood cells, platelets, hemoglobin) and liver/kidney function (alanine aminotransferase, aspartate aminotransferase, bilirubin, creatinine, urea nitrogen) (p > 0.05), while the alpha fetoprotein level decreased significantly at 2 months [preablation (262.4 ± 159.1) vs postablation (20.0 ± 10.8), p < 0.05]; more details are listed in Tables 2 and 3.

Regarding complications, there were no major ones such as massive hemorrhage, diaphragmatic perforation and liver abscission. Seventeen (34.7%) patients experienced minor complications (CIRSE grade 1), among whom 9 had right mild shoulder pain, 5 had pleural effusion, and 3 had a subcapsular hematoma (<5 ml). The LTP was 2.7% (2/74) during the median follow-up of 17.8 months (range: 4–43 months).

Table 2. Intra- and postoperative outcomes.

| Characteristics                          | Value (number/mean ± SD/range) |
|------------------------------------------|---------------------------------|
| Technical success for lesions (%)        | 74/74(100)                      |
| Intravenous/general anesthesia           | 39/10                           |
| Ablation time (min)                      | 15.7 ± 4.2 (8.0–24.0)           |
| Total procedure time (min)               | 50.8 ± 15.3 (26.0–78.0)         |
| Complications                            |                                 |
| Major complications (%)                  | 0                               |
| Minor complications (%)                  | 34.6%                           |
| Right shoulder pain                      | 9                               |
| Pleural effusion                         | 5                               |
| Subcapsular hematoma                     | 3                               |
| Hospital stay (week)                     | 2.9 ± 1.4 (1–7)                 |
| Local response at 2 months (CR/PR)       | 71/3                            |
| CA of diameter stratification ≤2.5 cm (n = 28) | 28 (100%)                     |
| >2.5 cm (n = 46)                         | 43 (93.5%)                      |
| 6-/12-/18-month overall survival (%)     | 100/97.6/92.1                   |

Table 3. Biochemical parameters and AFP levels before and 2 months after microwave ablation.

| Parameter                          | Pretreatment | Posttreatment | t Value | p Value |
|------------------------------------|--------------|---------------|---------|---------|
| White blood cells (× 10^9/L)       | 6.2 ± 1.3    | 6.0 ± 1.3     | 0.63    | 0.53    |
| Platelets (10^11/L)                | 96.5 ± 31.5  | 91.0 ± 28.5   | 0.87    | 0.39    |
| Hemoglobin (g/L)                   | 117.1 ± 15.9 | 121.5 ± 18.0  | -1.33   | 0.19    |
| Alanine aminotransferase (U/L)     | 34.5 ± 6.1   | 35.5 ± 5.6    | -0.31   | 0.76    |
| Aspartate aminotransferase (U/L)   | 35.9 ± 5.1   | 36.2 ± 5.0    | -0.99   | 0.32    |
| Bilirubin (μmol/L)                 | 19.6 ± 5.1   | 20.0 ± 4.1    | -0.77   | 0.44    |
| Creatinine (μmol/L)                | 71.0 ± 16.5  | 74.5 ± 15.2   | -1.16   | 0.25    |
| Urea nitrogen (mmol/L)             | 5.4 ± 1.1    | 5.5 ± 1.1     | -0.10   | 0.92    |
| Alpha fetoprotein (ng/ml)          | 262.4 ± 159.1| 20.0 ± 15.2   | 10.80   | 0.00    |
| PIVKA (mAU/ml)                     | 486.6 ± 21.5 | 413.5 ± 5.9   | 16.52   | 0.00    |

PIVKA: protein induced by Vitamin K absence or antagonist.
In total, five patients died, among whom 4 patients died due to tumor progression resulting in multiple organ failure, and 1 patient had acute gastrointestinal bleeding. The 6-, 12-, 18-month TFS and OS were 97.8, 90.6 and 68.1% and 100%, 97.6 and 92.1%, respectively.

4. Discussion

Since Seki firstly reported the success of US-guided ablation for the 21st treatment of HCC at 1994 [8], heat ablation had become an important part of minimally invasive treatment of HCC. However, it is considered to be the most technically challenging for tumors located under the hepatic dome due to the limitation of the puncture path affected by the ribs, diaphragm and lung tissue, leading to potential complications of referred pain, pneumothorax and diaphragm injury, with 0–23.6% occurrence in previous reports [9–12].

The precise ablation should include three technical requirements: positioning, monitoring and evaluation [13]. The basis of achieving these three objectives is image visualization. Due to the obstruction of lung tissue and the ribs, US cannot always show small lesions close to the diaphragm well, especially in patients with severe liver cirrhosis [14]. From our experience, the best benefit of MR comparing with US guided MWA for HCC located under the hepatic dome is that an oblique puncture from the caudal to the cranial side can decrease puncture complication and increase technical success without artificial ascites or effusion assistance in the vast majority of cases. CT can quickly carry out cross-sectional scanning, but some small HCC lesions cannot be clearly displayed on nonenhanced CT, what’s more, the large metal microwave antenna artifact can easily cover the lesion to some extent; furthermore, it is unable to quickly display oblique puncture from the caudal to the cranial side [15].

Theoretically, MRI has some unique advantages in guiding MWA [16–20]: 1) MR has no ionizing radiation or metal scattering artifact compared with CT; 2) MR has high resolution of soft tissue without being affected by bone or gas compared with US; 3) due to the ‘flow void effect’, blood vessels can be clearly displayed on MR images without contrast enhancement, which is convenient to technically predict the occurrence of a ‘heat-sink’ effect; 4) MR can display information along the whole microwave applicator showing the details of the three-dimensional relationship of the lesion, diaphragm and puncture path; 5) MR can provide an accurate local necrotic area on T1WI and T2WI without contrast medium injection. To our knowledge, after ablation, due to protein concentration and tissue hemorrhage, the ablation focus showed high signal on T1WI with clear edges; The dehydration effect of tissue after thermal injury leads to low signal on T2WI. It can also show the characteristic ‘target sign’; namely, the original tumor still shows a low signal after ablation, while the surrounding normal tissue shows a high signal. The ‘target sign’ allows detection of the surviving tumor tissue earlier than on CT and US [21], which is important for additional ablation decisions.

This study showed that 3.0-T closed MR has advantages in imaging, monitoring and evaluating the ablation zone with 100% technical success and without major complications. The CA rate was 95.9%, which falls within those of previous reports (84.2–100%) for MWA for tumors under the hepatic dome [11,12,22], and it is not unexpected; only the guidance tool was changed, while the other procedure were the same as with CT-guided ablation. The LTP rate was 2.7%, which is slightly lower than that in previous reports (5.5–18.8%) [11,12,22]; the sample size needs to be expanded to obtain more objective results. The preliminary experience is summarized as follows: 1) Image quality was influenced by respiratory control; therefore, general anesthesia (20.4% cases in this study) is recommended for patients with poor coordination of breath holding, especially for those with small lesions. 2) There is a delayed period on T1WI of the ablation zone, it is suggested that postablation evaluation be performed 3–5 min later. 3) The ‘target sign’ is very important to judge the ablation zone, and it is suggested that the high-signal ring should be more than 5 mm above the original low-signal tumor area on T1WI. 4) A large aperture of 70 cm provides relatively loose operating space for interventional operations, which can meet clinical needs. 5) It is suggested that an ablation strategy of ‘low power, short time and repeat’ can reduce the symptoms of discomfort among patients undergoing ablation under local anesthesia until the tumor and surrounding tissues are covered with high signal intensity on T1WI. 6) The study confirmed that the diagnostic advantage of MR can be transformed into a therapeutic advantage for small HCC lesions located under the hepatic dome (the smallest was 0.9 cm in this study, Figure 3); it may be the first choice for tumor ablation of lesions in challenging locations.

Early MR-guided ablation was mainly performed under low-field open MR. Morikawa et al. [23] first reported MWA for liver tumors under the 0.5-T MR guidance. Although the operation was a little cumbersome, but a ‘target sign’ was considered to have high clinical value. Considering the higher MR field strength has better soft tissue resolution, which means capable of finding smaller liver lesions, more and more scholars had tried using 1.5T and 3.0T MR as a guidance tool. Mahnken et al. [24] and Hoffmann et al. [25] reported the feasibility and effectiveness of 1.5-T closed MR guided radiofrequency ablation of liver tumors. Those authors believed that MR guidance can be used as the preferred tool for subphrenic, hilar and paravascular lesions, and our study came to the same conclusion. The core advantage of 3.0-T MR guidance is residual tumor localization and treatment evaluation. For example, in a 56-year-old patient with a 0.9-cm diaphragmatic small liver cancer (Figure 3), after the first ablation circle, the ablation area only covers part of the tumor area (possibly due to the patient’s breathing, the puncture needle retreats backward). After an immediate evaluation during the operation, the puncture applicator is adjusted again. Then, all the local lesions are completely destroyed. This is of great significance for the realization of real-time intraoperative evaluation, but it is difficult to complete with CT or US without enhancement.
Seventeen (34.7%) patients experienced minor complications, among whom 9 had right shoulder pain, and 5 had pleural effusion, indicating thermal damage to the diaphragm. In fact, the puncture path, ablation parameter (power/time) and imaging features were three main key factors contributing to complications. MR can display the information along an oblique puncture from the caudal to the cranial side to decrease damage to the lungs and diaphragm, the advantage of this approach is that the puncture path is parallel to the diaphragm and does not pass through the diaphragm and lung tissue.

However, MR guidance has its own limitations: (1) the existing MR equipment is mostly used for diagnosis, and the magnet, coil and scanning sequence are not fully suitable for MWA; (2) multiple long MR scans increase the total operative time; (3) an MR-compatible anesthesia machine, monitor and other ancillary equipment are relatively expensive; (4) this modality is contraindicated for patients with a cardiac pacemaker, metal implant and intraocular metallic foreign body. The limitation of the study was small sample size, short follow-up period, single center experience and diaphragm thermal injury was evaluated only by symptoms and imaging without pathological evidence.

On conclusion, 3.0-T MR-guided WMA of HCC lesions located under the hepatic dome is safe and feasible and can be used as the first choice for the ablation of small HCC lesions under the diaphragm in the future.

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Disclosure statement
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Data availability statement
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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