RESEARCH ARTICLE

# Therapeutic efficacy of radiofrequency ablation in hepatocellular carcinoma evaluated with MRI and serum alpha-fetoprotein

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## Abstract

**Objective:** To investigate the feasibility of combined magnetic resonance imaging and serum alpha-fetoprotein for evaluating the therapeutic efficacy of radiofrequency ablation in patients with hepatocellular carcinoma.

**Methods:** The retrospective cohort study was conducted at Affiliated Hospital of North Sichuan Medical College, Sichuan, China and comprised patients with pathologically confirmed hepatocellular carcinoma lesions who underwent percutaneous radiofrequency ablation between January 1, 2018, and October 31, 2023. Magnetic resonance imaging scans were performed at baseline and seven days after radiofrequency ablation, and the subsequent follow-up magnetic resonance imaging was regularly carried out in line with the Expert Consensus on the Standardised Clinical Application of Image Guided Hepatic Tumour Thermal Ablation. Clinical data, including serum alpha-fetoprotein level, was collected at the same time points as magnetic resonance imaging. Sensitivity, specificity and accuracy were calculated to evaluate the therapeutic efficacy. Data was analysed using SPSS 22.

**Results:** Of the 83 patients with mean age 54.78±11.43 years, 62(74.7%) were male and 21(25.3%) were female. There were 96 lesions, and 72(75%) of them had maximum diameter <3cm, while 24(25%) had maximum diameter ranging from 3cm to 4.95cm. The mean maximum diameter of the lesions was 3.16±0.92cm, while the volume ranged from 0.15cm3 to 78.15cm$^3$. Serum alpha-fetoprotein levels decreased significantly after radiofrequency ablation ($p<0.05$). The sensitivity, specificity, and accuracy of magnetic resonance imaging in the assessment of therapeutic efficacy were 90.32%, 92.31% and 91.67% for complete ablation; 83.33%, 92.31% and 90.63% for tumour residual; 89.47%, 94.37% and 93.33% for local tumour progression; and 93.55%, 95.24% and 94.68% for new tumours, respectively.

**Conclusion:** The combination of magnetic resonance imaging and serum alpha-fetoprotein was found to be a reliable and practical tool for evaluating the therapeutic efficacy of percutaneous radiofrequency ablation in hepatocellular carcinoma patients.

**Keywords:** Hepatocellular carcinoma, Radiofrequency ablation, Magnetic resonance imaging, Serum alpha-fetoprotein, Therapeutic efficacy. (JPMA 76: 1220; 2026) **DOI: https://doi.org/10.47391/JPMA.21152**

## Introduction

Hepatocellular carcinoma (HCC) is the predominant form of liver cancer, and accounts for >90% of primary liver malignancies.[1] According to World Health Organisation WHO) data, HCC ranks as the fourth most common cancer globally and the sixth leading cause of tumour-related mortality worldwide.[2,3] The primary treatment modality for HCC is surgical resection, but only 10-30% of HCC patients are eligible for it, depending on favourable size and location of lesions.[4,5] Radiofrequency ablation (RFA), as a complementary treatment modality, is a minimally invasive therapeutic technique that aims at desiccating tumour tissue and inducing coagulative necrosis by delivering high frequency via electrodes placed within the lesions.[6,7] RFA has been widely used for HCC treatment and has exhibited promising therapeutic efficacy, especially for small liver cancer and locoregional treatment for unresectable HCC.[8]

However, HCC lesions after RFA are still at risk of residual tumour, local tumour progression, and new tumour development due to multiple contributing factors.[9] Therefore, timely and accurate evaluation of HCC lesions after RFA is particularly important. Magnetic resonance imaging (MRI) offers superior spatial resolution and soft-tissue resolution compared to ultrasound and computed tomography (CT). Simultaneously, multi-sequence, multi-parameter, multi-phase enhancement and functional imaging of MRI scans can provide comprehensive and accurate depiction of HCC lesions. However, the specific evaluation methods and clinical value of MRI for HCC patients after RFA therapy have not been systematically clarified or fully validated in existing literature.[10] Additionally, serum alpha-fetoprotein (AFP), which serves as one of the main oncofoetal antigens and diagnostic markers for primary HCC, also holds significant value in the monitoring of primary HCC, and can complement the MRI-

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based evaluation.

The current study was planned to investigate the feasibility of combined MRI and serum AFP for evaluating the therapeutic efficacy of RFA in HCC patients.

## Patients and Methods

The retrospective cohort study was conducted at Affiliated Hospital of North Sichuan Medical College, Sichuan, China and comprised patients with pathologically confirmed HCC lesions who underwent percutaneous RFA between January 1, 2018, and October 31, 2023. Approval as obtained from the institutional ethics review committee, which waived the requirement for informed consent because of the retrospective design of the study.

Data was retrieved for all HCC patients who had been pathologically confirmed and received RFA treatment in line with the Standards for the Diagnosis and Treatment of Primary Liver Cancer 2022, and the Expert Consensus on the Standardised Clinical Application of Image-Guided Hepatic Tumour Thermal Ablation for RFA treatment.[11,12] Those included were patients with maximum diameter of the lesion less than or equal to 5.0cm in patients with single tumour, or the number of lesions in patients with multiple tumours was less than or equal to three, with a maximum diameter of less than or equal to 3.0cm, Besides, the patients had no contraindication to RFA therapy, such as Child-Pugh C liver function or uncorrectable coagulation dysfunction. Data was excluded if the image quality was too poor to clearly depict the lesions, as assessed by the signal-to-noise ratio and motion artefact grading criteria, and if the follow-up MRI had not been performed according to the relevant guidelines[11,12] or if MRI data was incomplete,[12] Cases were also excluded if RFA had been used only for palliative ablation, which aimed at local tumour control and alleviation of complications, or if the there were complications related to other tumours in the liver. RFA had been performed percutaneously using single or multiple electrodes of a radiofrequency generator, and overlapping ablations were determined according to the size of the tumour. The radiofrequency electrode was cooled by a water circulation pump, which infused cold saline into the electrode lumen to maintain the active tip temperature <30°C. The ablation route and range of HCC were determined by preoperative MRI and ultrasound. Radiofrequency electrodes were percutaneously inserted into the tumour tissue. Driven by high-frequency alternating current (375-500kHz), intratumoral ions underwent vigorous oscillation and frictional heating, rapidly raising the temperature of peri-electrode-tract tumour tissue to 60-120°C and inducing tumour cell coagulative necrosis.[13] RFA procedures were continued until complete tumour ablation was achieved. To ensure adequate ablation of the tumour margin, the range of ablation was required to cover the tumour margin from 0.5cm to 1.0cm under ultrasound guidance.[13] The first follow-up MRI was conducted seven days after RFA to assess whether or not the treatment had been technically successful.

The follow-up MRI post-RFA was done in accordance with the Expert Consensus on Standardised Clinical Application of Image-Guided Thermal Ablation of Liver Tumours.[12] Within seven days post-RFA, the first follow-up MRI was performed, including T1-weighted imaging, T2-weighted imaging with fat suppression, contrast-enhanced T1-weighted imaging, and diffusion-weighted imaging (DWI). Subsequent follow-up MRI scans were repeated monthly in the first three months post-RFA, and then the follow-up interval was adjusted to once every three months. A negative result was determined when the previous follow-up MRI did not show residual tumour, local tumour progression, or new tumour, and serum AFP was <20μg/L in patients without drug or alcohol abuse, or with chronic liver diseases, such as hepatitis. A positive result was defined as the presence of any of the following manifestations on follow-up MRI: residual tumour, local tumour progression, or new tumour. Additionally, a high level of serum AFP level or a post-RFA elevation in AFP level was indicative of a positive result. For the positive cases, RFA or other suitable treatments were adopted, and subsequent follow-up was performed in accordance with the relevant protocol.[12] Moreover, serum AFP levels were obtained for all the patients before and during the follow-up post-RFA to analyse and compare the effectiveness of RFA. All the patients were followed up in accordance with the relevant protocols.[11,12]

Preoperative and follow-up MRI scans were performed using a Signal 3.0-T scanner (Discovery MR 750; GE Medical Systems, Slough, United States) equipped with a 32-channel body phased-array coil for abdominal imaging with respiratory and cardiac gating. All patients were required to fast for six hours prior to each examination. During the abdominal MRI examination, each patient was required to lie on the scanning bed in the supine position. The scanning sequences included conventional axial T1-weighted imaging (repetition time [TR]/echo time [TE] 4/2ms, field of view [FOV] 320mm×320mm, slice thickness 4mm and slice interval 1mm), conventional axial T2-weighted imaging with fat suppression (TR/TE 6316/73ms, FOV 320mm×320mm, slice thickness 4mm and slice interval 1mm). DWI scan used the following scanning parameters: TR/TE 4600/81ms, slice thickness 4mm, slice interval 1mm, FOV 320mm×320mm, number of excitation

3 times, and matrix 192×192, while the diffusion-sensitive gradient b-values of DWI were 400s/mm$^2$, 600s/mm$^2$, 800s/mm$^2$ and 1,000s/mm$^2$.[14] After the routine conventional scans, axial multiple-phase contrast-enhanced T1-weighted imaging with three-dimensional (3D) liver acquisition with volume acceleration (LAVA) was acquired using the following scanning parameters: (TR/TE 4/2ms, FOV 360mm×360mm, slice thickness 3mm), after elbow intravenous (IV) injection of 15mL gadodiamide (Omniscan; GE Healthcare, Little Chalfont, US) at the flow rate of 2-3mL/s for a total dose of 0.2mmol/kg bodyweight, followed by a 20mL saline solution flush with a high-pressure injector system (Spectris MR Injector System; Bayer, Leverkusen, Germany). The early arterial phase, late arterial phase, portal venous phase and delayed phase images were obtained at 18s, 25s, 60s and 180s, respectively, after the contrast agent was injected.

MRI data was independently analysed by two abdominal radiologists, with the first reader having 12 years of experience in abdominal MR imaging, and the second reader having 10 years of experience. They were blinded to patients' clinical and laboratory data. This was done to ensure inter-observer reliability. MRI and serum AFP levels before and after RFA were used to judge the therapeutic efficacy of RFA, and pathology was used to determine the viable tumour eventually. The viable tumour in ablation area in serial follow-up MRI was presented as slight hypo-intensity in T1-weighted imaging, slight hyper-intensity in T2-weighted imaging, hyper-intensity in high b-value DWI with a low apparent diffusion coefficient value on quantitative maps compared to background liver. Additionally, it showed hyper-enhancement in the hepatic arterial phase and washout appearance in the portal venous and/or delayed phases relative to the background liver.

The efficacy of HCC after RFA was classified into four categories based on relevant standards[11,12] as follows: complete ablation meant no viable tumour was observed within the ablation area during a series of follow-up MRI scans after RFA, and the range of ablation extended from 0.5cm to 1.0cm beyond the tumour margin; tumour residual meant viable tumour was observed in the ablation area in the first follow-up MRI after RFA; local tumour progression meant viable tumour was observed in the ablation area during any subsequent follow-up MRI scan after the initial follow-up; and new tumour meant viable tumour was located within the liver outside the ablation area during any follow-up MRI scan after RFA (Figure).

Data was analysed using SPSS 22. Continuous data with normal distribution was expressed as mean ± standard deviation (SD), while non-normally distributed data was presented as median with interquartile range (IQR). The inter-observer agreement of image evaluation was assessed using Kappa test, where Kappa values <0.40, 0.41-0.75, and >0.75 represented poor, good and excellent reliability, respectively. The agreement between the follow-up clinical results and MRI findings were tested using the chi-square test. Wilcoxon signed-rank test was used to compare pre- and post-RFA serum AFP levels. Complete ablation, residual tumour, local tumour progression, and new tumours were categorised as categorical data. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of MRI evaluation were calculated using diagnostic analytics. P<0.05 was considered statistically significant.

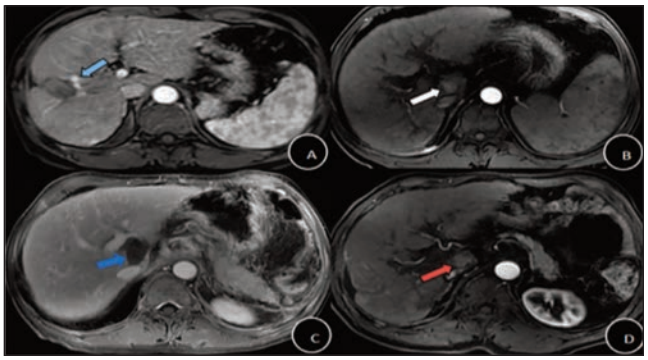


**Figure:** Seven days after RFA, the first follow-up MRI identified viable tumour at the ablation border, arterial-phase hyper-enhancement on CE-T1WI indicated residual tumour tissue (A). Preoperative MRI showed HCC with arterial-phase hyper-enhancement (CE-T1WI; B). Initial post-RFA MRI revealed no viable tumour in ablation area (C). At 30 months after RFA, viable tumour with arterial-phase hyper-enhancement was identified in the ablation area on follow-up MRI (D), and pathology confirmed it as local tumour progression.
*HCC: Hepatocellular carcinoma, RFA: Radiofrequency ablation, MRI: Magnetic resonance imaging*

## Results

Of the 83 patients with mean age 54.78±11.43 years, 62(74.7%) were male and 21(25.3%) were female. The follow-up period ranged 6-42 months. The mean maximum diameter of the lesions was 3.16±0.92cm (range: 0.5-4.95cm), while the volume ranged from 0.15cm$^3$ to 78.15cm$^3$. There were 96 lesions, and 72(75%) of them had maximum diameter <3cm that received RFA using a single electrode, while the remaining 24(25%) had maximum diameter ranging from 3cm to 4.95cm, and underwent RFA using 2-4 electrodes.

Median serum AFP level at baseline was 51.17µg/L (IQR: 1.5-96,700µg/L) which went down significantly to 7.845µg/L (IQR: 1.02-48,100µg/L) post-RFA ($p$<0.05).

Before RFA, the inter-observer agreement of Kappa value for HCC diagnosis was 0.791. During the follow-up after RFA, the inter-observer agreement of Kappa values for

**Table-1:** MRI-based evaluation of therapeutic efficacy in HCC after RFA.

| Diagnosis method | Complete ablation (n=96) | | Tumour residual (n=96) | | Local tumour progression (n=90) | | New tumour (n=94) | |
|---|---|---|---|---|---|---|---|---|
| | Y | N | Y | N | Y | N | Y | N |
| **Pathology confirmed** | 65 | 31 | 18 | 78 | 19 | 71 | 31 | 63 |
| **MRI diagnosis** | | | | | | | | |
| **Consistency** | 60 | 28 | 15 | 72 | 17 | 67 | 29 | 60 |
| **Misdiagnosis** | 5 | 3 | 3 | 6 | 2 | 4 | 2 | 3 |

HCC: Hepatocellular carcinoma, RFA: Radiofrequency ablation, MRI: Magnetic resonance imaging, Y: Yes, N: No.

**Table-2:** MRI performance in evaluating HCC therapeutic efficacy after RFA during serial follow-up.

| Therapeutic efficacy | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) | Kappa value (95% CI) |
|---|---|---|---|---|---|---|
| Complete ablation | 92.31 | 90.32 | 84.85 | 95.24 | 91.67 | 0.81 (0.69-0.94) |
| Tumour residual | 83.33 | 92.31 | 71.43 | 96.00 | 90.63 | 0.71 (0.54-0.88) |
| Local tumour progression | 89.47 | 94.37 | 80.95 | 97.10 | 93.33 | 0.81 (0.66-0.97) |
| New tumour | 93.55 | 95.24 | 90.63 | 96.77 | 94.68 | 0.88 (0.78-0.98) |

HCC: Hepatocellular carcinoma, RFA: Radiofrequency ablation, MRI: Magnetic resonance imaging, PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval.

determining complete ablation, residual tumour, local tumour progression, and new tumours were 0.813, 0.711, 0.807 and 0.881, respectively. Therefore, the results evaluated by the first radiologist were used for further analysis.

The therapeutic efficacy of the lesions post-RFA based on the follow-up MRI findings, serum AFP levels, and pathology was noted (Table 1). The sensitivity, specificity, PPV, NPV and accuracy of MRI findings in the detection of complete ablation, residual tumour, local tumour progression, and new tumour post-RFA were noted in detail (Table 2).

## Discussion

HCC is the most prevalent form of liver cancer worldwide, and is associated with a significantly high mortality rate. It primarily occurs in patients diagnosed with chronic liver diseases, such as cirrhosis or severe fibrosis.[3] The majority of patients in the current study exhibited chronic liver disease resulting from persistent infection with hepatitis B and C viruses or metabolic liver disorders, such as non-alcoholic steatohepatitis or alcoholic liver disease.

The serum AFP, serving as a key oncofoetal antigen and a diagnostic biomarker for primary HCC, holds significant value in the surveillance of primary HCC. According to studies, serum AFP is utilised not only for the diagnosis of HCC and assessment of prognostic efficacy in HCC patients, but is also implicated in promoting malignant transformation of liver cells and the occurrence and progression of HCC, with >70% of HCC patients exhibiting elevated serum AFP levels, which typically indicates a high risk of HCC development and a poor prognosis.[15-18] Serum AFP is produced by foetal hepatocytes, yolk-sac cells, and normal gastrointestinal cells, and it gradually decreases to <10µg/L within 300 days after birth.[15-19] For normal adults, serum levels of AFP are always <20µg/L, but for patients with drug or alcohol abuse or chronic liver diseases, such as hepatitis or cirrhosis, it may increase to 100µg/L.[15-20] The Italian guidelines and the American Association for the Study of Liver Diseases guidelines consider serum AFP >200µg/L to be diagnostic for HCC.[16] Besides, studies have also suggested using a serum AFP level >400µg/L to confirm HCC.[21] The current study also observed a significant correlation between serum AFP levels and the therapeutic efficacy of HCC ablation. Prior to RFA, 73.5% of HCC patients exhibited serum AFP exceeding 20µg/L, while 26.5% had AFP levels below this threshold. This observation can be attributed to AFP-secreting HCC, a subtype of HCC characterised by aberrant AFP overexpression. In the follow-up period after RFA, most of the patients with complete ablation lesions underwent a substantial decrease in serum AFP, whereas patients with residual tumour, local tumour progression, or new tumour experienced sustained high serum AFP or even further increases. Therefore, serum AFP holds significant value in the assessment of viable tumour of HCC after RFA.

MRI exhibits promising performance in the evaluation of therapeutic efficacy of HCC after RFA, owing to the advantage of high resolution, multi-parametric imaging and the combination with function imaging.[22] Therapeutic efficacy for HCC after RFA includes complete ablation, residual tumour, local tumour progression, and new tumour. Previous studies on the therapeutic efficacy of HCC after RFA mainly focused on tumour residual.[23] Whereas, the current study showed that incomplete ablation for HCC after RFA was associated with the occurrence of local tumour progression and new tumour. A previous report indicated that incomplete ablation for HCC after RFA was mainly caused by factors such as large size, irregular shape, invasive growth of tumour, and proximity to large vessel and important organs.[24] Furthermore, conventional MRI scans are difficult to accurately depict residual tumour or

local tumour progression within three months after RFA due to the small range, lower viability and inflammatory reaction of lesions. The current study found that using conventional MRI combined with contrast-enhanced T1-weighted imaging and DWI could significantly improve the accuracy in evaluating viable tumour after ablation. The underlying pathological mechanism postulates that RFA induces cellular membrane damage in tumour cells, leading to unrestricted diffusion of water molecules and subsequent alterations in apparent diffusion coefficient values between the tumour tissue and coagulative necrosis.[25] Therefore, MRI functional imaging and contrast-enhanced T1-weighted imaging have important value in determining the viable tumour of HCC after RFA.

In the current study, misdiagnosis on MRI after RFA included residual tumour, local tumour progression, and new tumour. For tumour residual and local tumour progression, the inflammatory reaction, congestion and oedema in the operation area after RFA made the ablation boundary obscure. Besides, the inflammatory reaction exhibited similar manifestations to HCC on MRI, characterised by slight hyper-intensity in T2-weighted imaging and hyper-enhancement in contrast-enhanced T1-weighted imaging at the boundary of the ablation area. Hepatocyte-specific contrast medium can be used to distinguish viable tumours from postoperative inflammatory changes. For new tumour in follow-up MRI, a few lesions were eventually confirmed as dysplastic nodules of cirrhosis. The use of hepatocyte-specific contrast medium and needle biopsy could help accurately differentiate between new tumour and dysplastic nodules after RFA.

The current study has several limitations. First, the sample size is relatively small, which may lead to outcome data bias and compromise generalisability of the findings. Second, given the retrospective, single-centre design of the study and non-uniform follow-up protocols, the potential selection bias may exist, and the generalisability of the results is inevitably limited. Future prospective, multicentre studies with standardised follow-up procedures are recommended to address these limitations.

## Conclusion

The combination of MRI and serum AFP was found to be a reliable and practical tool for evaluating the therapeutic efficacy of percutaneous RFA in HCC patients. This approach could provide valuable references for clinical decision-making regarding post-ablation follow-up strategies and treatment adjustments, thereby optimising patient management.

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**Author Contribution:**

**JMC, ZQM, JW, LQY, JQY:** Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.