CLINICAL STUDY

Three-Dimensional Measurement of Hepatocellular Carcinoma Ablation Zones and Margins for Predicting Local Tumor Progression

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ABSTRACT

Purpose: To propose a postprocessing technique that measures tumor surface with insufficient ablative margins ($\leq$ 5 mm) on magnetic resonance (MR) imaging to predict local tumor progression (LTP) following radiofrequency (RF) ablation.

Materials and Methods: A diagnostic method is proposed based on measurement of tumor surface with a margin $\leq$ 5 mm on MR imaging. The postprocessing technique includes fully automatic registration of pre- and post–RF ablation MR imaging, a semiautomatic segmentation of pre–RF ablation tumor and post–RF ablation volume, and a subsequent calculation of the three-dimensional exposed tumor surface area. The ability to use this surface margin $\leq$ 5 mm to predict local recurrence at 2 years was then tested on 16 patients with cirrhosis who were treated by RF ablation with a margin $\leq$ 5 mm in 2012: eight with LTP matched according to tumor size and number and α-fetoprotein level versus eight without local recurrence.

Results: The error of estimated tumor surface with a margin $\leq$ 5 mm was less than 12%. Results of a log-rank test showed that patients with a tumor surface area $>$ 425 mm^2 had a 2-year LTP rate of 77.5%, compared with 25% for patients with a tumor surface area $\leq$ 425 mm^2 (P = .018).

Conclusions: This proof-of-concept study proposes an accurate and reliable postprocessing technique to estimate tumor surface with insufficient ablative margins, and underscores the potential usefulness of tumor surface with a margin $\leq$ 5 mm to stratify patients with HCC treated by RF ablation according to their risk of LTP.

ABBREVIATIONS

AFP = α-fetoprotein, DSC = DICE similarity coefficient, HCC = hepatocellular carcinoma, LTP = local tumor progression, RF = radiofrequency, ROI = region of interest, 3D = three-dimensional, THRIVE = T1 high resolution isotropic volume excitation

Percutaneous thermal ablation, especially radiofrequency (RF) ablation, is a safe and effective treatment for hepatocellular carcinoma (HCC) (1,2), providing similar outcomes to surgical resection (2). However, despite progress in RF devices (3–6), the prognosis of cirrhotic patients with HCC treated by RF ablation as first-line is still impaired by local tumor progression (LTP) occurring within 2 years after RF ablation (7).

LTP occurs in 10%–21% of patients and is associated with poor prognosis (2,6). The likelihood of local progression increases with tumor size as a result of satellite nodules (8), which is why a 5-mm minimum ablation margin is recommended by several studies (9,10). However, some of these studies (9,11,12) used a rigid registration that is not optimal for the liver because of significant deformations by respiratory movements

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Figure E1 and Appendices E1–E3 are available online at *www.jvir.org*.

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and the ablation zone (13). Moreover, these studies assessed only two-dimensional minimal margins, failing to take into account the heterogeneous shape of the ablative volume around the tumor and that the minimal margin is not necessarily indicative of the margin sizes all around the tumor. This could explain the fact that LTP occurred in "only" as many as 30%–50% of patients with an ablation margin ≤ 5 mm (14). As illustrated in **Figure 1**, two patients with an identical minimal ablation margin can have different zones at risk of LTP. A measure of the tumor surface with insufficient ablative margins that represents the three-dimensional (3D) ablation margin therefore may be a better way to assess RF ablation accuracy during the procedure and follow-up and to improve the prognosis.

The aim of the present study is to propose a full post-processing technique designed to measure the tumor surface with insufficient ablation margin ≤ 5 mm and to assess its potential to predict LTP at 2 years after RF ablation.

MATERIALS AND METHODS

Patients

Institutional review board approval was obtained, and consent was waived for this retrospective study. From our hospital database, we retrospectively included patients with cirrhosis who underwent RF ablation in 2012 for a single HCC with minimum ablative margins ≤ 5 mm and experienced LTP (n = 8). Based on propensity score (15), according to tumor size and number and α-fetoprotein (AFP) level, we matched a control group of eight patients treated in our institution in 2012 with no LTP and a minimum treatment margin ≤ 5 mm. Overall, 16 patients with cirrhosis were included to test our postprocessing technique, eight in each group (with and without LTP). All tumors met the Milan criteria (16), so the maximum tumor size was 5 cm.

Diagnosis and Staging of HCC and RF Ablation

Noninvasive criteria of the European Association for the Study of the Liver were used to diagnose HCC (16). All RF ablation procedures were performed percutaneously under general anesthesia. Real-time ultrasound (US) with a 4-MHz probe was chosen as the first-line guidance modality for all patients. A senior interventional radiologist (at least 5 y of experience) performed RF ablation with use of monopolar expandable LeVeen needles (RF 3000; Boston Scientific, Marlborough, Massachusetts). Thermal ablation was performed according to the manufacturer's instructions. RF ablation was performed under US surveillance to determine sufficient overlap of the hyperechoic ablation zone on the HCC lesion. Follow-up after ablation was performed with MR imaging at 1 month.

LTP (17) describes the appearance of tumor foci at the edge of the ablation zone after at least one contrast-enhanced follow-up study has documented adequate ablation and an absence of viable tissue in the target tumor and surrounding ablation margin based on imaging criteria. This term applies regardless of whether tumor foci were discovered early or late in the course of imaging follow-up.

Experimental Setup

MR imaging acquisition. Pre- and post–RF ablation MR imaging was performed on a 1.5-T clinical unit (Tesla Archiva 1.5; Philips, Best, The Netherlands). MR protocol consisted of axial T2-weighted sequences with and without fat saturation, a T1-weighted in- and out-of-phase sequence, and a 3D T1-weighted sequence with fat

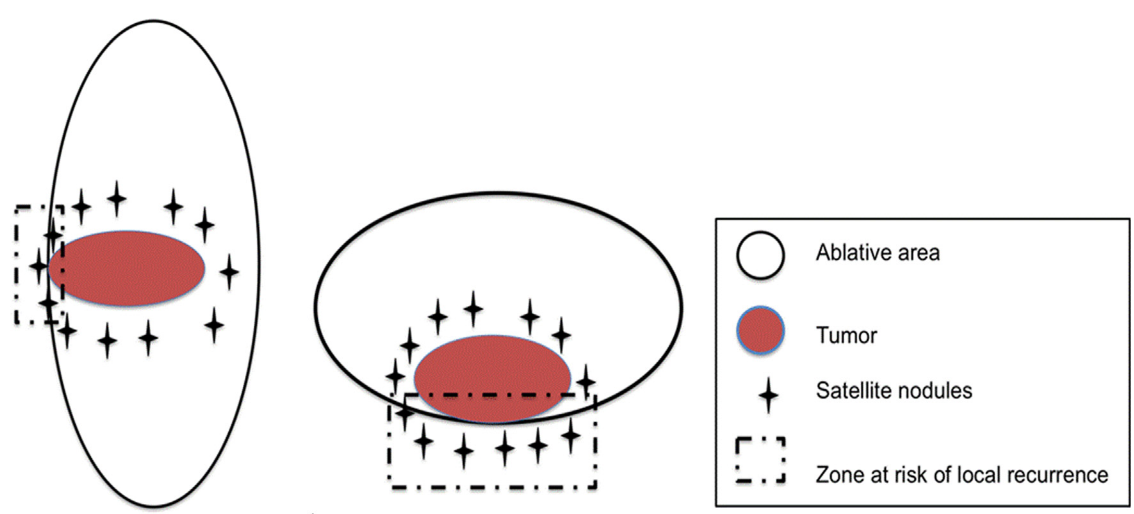

Figure 1. Schematic illustration of two typical ablative surfaces depicts similar minimal margins but different tumor areas exposed to insufficient margins. Minimal margins equal to 0 mm are shown with a small **(a)** and large **(b)** tumor area exposed to insufficient margins. Note that the probability of untreated satellite nodules is higher in the second case **(b)**.