Usefulness of the Extracted-Overlay Function in CT/MR-Ultrasonography Fusion Imaging for Radiofrequency Ablation of Hepatocellular Carcinoma

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Key Words

Extracted-overlay function · Hepatocellular carcinoma · Radiofrequency ablation · Volume Navigation · Fusion imaging

Abstract

Objectives: We developed a novel technique of the extracted-overlay function in CT/MR-ultrasonography (US) fusion imaging for radiofrequency ablation (RFA), in which only a tumor extracted from CT/MR images with a virtual ablative margin of arbitrary thickness is overlaid on US. The usefulness of this function is investigated in this preliminary report.

Methods: The volume data of the extracted tumor with a virtual ablative margin were created on an image-processing workstation, and transported into a US unit equipped with a CT/MR-US fusion imaging system. After the positional registration of US and transported images, the extracted tumor with an ablative margin could be overlaid on US. In RFA, using this function, an electrode was inserted targeting the overlaid tumor with an ablative safety margin of 5 mm on US, and the treatment effect was evaluated by dynamic CT. Treatment results of 23 consecutive hepatocellular carcinomas (HCCs) that underwent RFA using this function were retrospectively analyzed. **Results:** Complete tumor ablation was achieved in 22 (95.7%) and 1 (4.3%) HCCs in 1 and 2

treatment sessions, respectively. **Conclusions:** Due to the visualization of an extracted tumor with an ablative safety margin on a US image, even during and after ablation, this function is useful for treatment planning and guidance of RFA.

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Introduction

The CT/MR-ultrasonography (US) fusion imaging system has recently been reported to be useful for radiofrequency ablation (RFA) of hepatocellular carcinoma (HCC) [1–5]. In this system, any cross-sectional multiplanar reconstruction images of CT or MR are synchronously displayed as reference images, side-by-side with US. This system has enabled RFA of HCCs with poor conspicuity on US and made it easy to evaluate the treatment effect at the bedside [1–4]. The CT/MR-US fusion imaging system is also capable of the overlay display of reference images on US, which directly indicates the location of the target tumor. However, it is difficult to perform RFA on the overlaid images, since background US usually becomes quite obscured [2, 3]. To solve this problem, we developed a novel technique which we call the extracted-overlay function, in which only the target tumor is ex-

tracted from reference images and overlaid on US, together with a virtual safety ablative margin of arbitrary thickness around the tumor. This preliminary study aimed to investigate the feasibility and efficacy of this function for RFA.

Materials and Methods

Patients and Tumors

Our institutional review board approved this retrospective study and informed consent was waived. From November 2012 to January 2013, we conducted RFA with the extracted-overlay function for 18 consecutive patients with 23 HCCs diagnosed based on the typical imaging features or biopsy [6]. In this period, this function was used for all cases that underwent RFA.

CT and MRI Acquisition

Dynamic CT and CT angiography was conducted with the 64-channel multidetector row helical CT, MDCT (Discovery CT 750HD, GE Healthcare, Milwaukee, Wisc., USA) with slice thicknesses of 1.25 and 0.675 mm, respectively. For dynamic CT, patients were intravenously administered 2.0 ml/kg of nonionic contrast material with a concentration of 300 mg iodine (mgI)/ml, which was injected with a fixed duration of 30 s using an automatic injector. The arterial-, portal- and equilibrium-phase images were obtained at approximately 35–45, 65–80 and 190–205 s, respectively, after the initiation of the contrast material injection [7].

For CT angiography, two catheters were selectively placed, one in the superior mesenteric artery for CT during arteriportography (CTAP) and the other in the common hepatic artery for CT during hepatic arteriography (CTHA). CTAP images were obtained 30–33 s after injection of 66–80 ml of 150–160 mgI/ml non-ionic contrast medium, at a rate of 2.0 ml/s. CTHA images were obtained 5–8 s after administration of 20–33 ml of 150–160 mgI/ml nonionic contrast material, at a rate of 1.0 ml/s [8].

Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced MR images were acquired with a 1.5-tesla MR system (Signa Excite HD 1.5T, GE Healthcare). At first, an unenhanced MR imaging was obtained using a T1-weighted gradient-echo sequence (dual echoes; in-phase and out-of-phase). Then, unenhanced-, arterial-, portal-, late- and hepatobiliary-phase images were acquired just before, 25, 70, 180 s and 20 min, respectively, after bolus injection of 25 µmol/kg body weight (0.1 ml/kg) of Gd-EOB-DTPA at a rate of 2.0 ml/s, using a T1-weighted high-resolution sequence in a single breath hold (18–20 s) [6, 7]. Dynamic- and hepatobiliary-phase images were acquired with three-dimensional gradient-echo sequences (Liver Acquisition with Volume Acceleration, LAVA, GE Healthcare). The slice thickness of dynamic- and hepatobiliary-phase images were 5 and 3 or 5 mm, respectively.

The Extracted-Overlay Function

For the extracted-overlay function, the imaging modality in which a tumor was most clearly depicted was used as a reference (fig. 1a). CT or MR imaging data for a reference were imported into an image processing workstation (Advantage Workstation Volumeshare 4, GE Healthcare). At first, the contour of the tumor was traced on each slice by an operator of RFA and the tumor was ex-

tracted from the original images. Then, by tracing around the extracted tumor circumferentially using a virtual brush, we added a virtual safety margin to the extracted tumor. Since the thickness of the virtual brush can be freely modified, we can add a virtual ablative margin of arbitrary thickness. In this study, the thickness was set at 5 mm, which has been reported to be related with a low local tumor progression rate [9–11] (fig. 1b). The volume data of the extracted tumor and the tumor with a virtual ablative safety margin were saved in the digital imaging and communication in medicine, DICOM, format. Subsequently, these volume data were transported into a US unit (LOGIQ E9, GE Healthcare) equipped with a CT/MR-US fusion imaging system (Volume Navigation, GE Healthcare), together with the original CT or MR imaging data, and used as reference images. After the positional registration of US and the original images [1], these three data sets could be displayed together or separately as references, simultaneously with US. The color of each reference could be modified for clear discrimination.

Subsequently, by means of the overlay display, these three data sets were overlaid on US, together or individually. In this way, since only an extracted tumor, with or without a virtual ablative safety margin, could be overlaid, the background US images did not get obscured (fig. 1d).

RFA Procedure

RFA was performed by 1 of 3 operators with more than 10 years of experience, using a cool-tip single electrode with a 2- or 3-cm exposed tip (Cool-tip RF Ablation System, Covidien, Boulder, Colo., USA). We used artificial ascites when necessary.

Using the extracted-overlay function, an extracted tumor with a virtual ablative safety margin was overlaid on US. Targeting the overlaid tumor, an electrode was inserted and ablation was conducted. To achieve complete ablation of the tumor, together with a virtual ablative safety margin when possible, ablation was repeated.

After the ablation, we evaluated whether the overlaid tumor was completely encompassed with the spreading hyperechoic bubbling area [12, 13]. If an overlaid tumor was protruding from the bubbling area, additional ablation was performed until it was completely within the bubbling area.

Treatment Evaluation of RFA

The treatment effect was evaluated by the consensus of 2 radiologists with more than 10 years of experience, who were blind to the clinical information. We defined complete ablation as meeting all of the following conditions on dynamic CT performed within 7 days after RFA: (i) no sign of tumor stain was present around the coagulated area on the arterial phase and (ii) the coagulated area circumferentially extended beyond a tumor boundary in the portal and equilibrium phases. When residual tumor was suspected, additional ablation was conducted until these conditions were satisfied.

Results

All 18 patients with 23 HCCs were treated without major complications. The profiles of these patients are listed in table 1. The time required for the preparation of the extracted-overlay function was less than 30 min in all cases.

Fig. 1. A 68-year-old man with hepatitis C-related cirrhosis and HCC underwent RFA with the extracted-overlay function using artificial ascites. **a** The arterial phase of dynamic CT showed hyper-vascular HCC (arrow), 15 mm in diameter, in segment VIII, which was used as a reference for CT/MR-US fusion imaging (Volume Navigation, GE Healthcare). **b** On an image-processing workstation (Advantage Workstation Volumeshare 4, GE Healthcare), the tumor was extracted from original data of the arterial phase of dynamic CT (white portion), and an ablative safety margin of 5 mm was added to the extracted tumor by tracing around it circumferentially with a virtual brush of 5 mm thickness (green portion). When a portion of the added margin protruded beyond the edge of the liver, it was trimmed. After the volume data of the extracted tumor

and the tumor with a virtual ablative safety margin were imported into a US unit (LOGIQ E9, GE Healthcare), they were used as a reference for Volume Navigation, together with the original CT data. **c** Side-by-side display of real-time grayscale US and original CT images, in which the target tumor (arrow) was depicted as a hypoechoic nodule on grayscale US. **d** The extracted-overlay function, in which the tumor (pink portion) and a virtual ablative safety margin (blue portion) were overlaid on US. Since only the tumor with a virtual ablative safety margin was overlaid, the background US images did not become obscured. Aiming at the overlaid tumor with a virtual ablative safety margin, a cool-tip electrode was inserted and ablation was carried out. **e** The portal-phase image of dynamic CT 3 days after RFA showed complete ablation of the tumor.

All 23 HCCs were judged to be completely encompassed with the surrounding hyperechoic bubbling area just after the first treatment session, and 22 (95.7%) HCCs were revealed to be completely ablated on dynamic CT. The 1 remaining HCC was located in segment VIII beneath the diaphragm, which was considered to be a

difficult location to conduct RFA [14]. However, complete ablation was also achieved after the second treatment session, using the extracted-overlay function. The procedure of the extracted-overlay function in RFA is demonstrated through the presentation of 2 cases in figures 1 and 2.

Table 1. Characteristics of 18 patients with 23 HCCs

Characteristics	Value
Age, years	75 (60–83)
Gender (male/female)	9/9
Etiology (HBV/HCV/other)	1/15/2
Tumor diameter, mm	14.8 (7.0–31.4)
Segmental location of tumor (2/3/4/5/6/7/8)	1/2/5/3/3/1/8
Tumor vascularity (hypervascular/hypovascular)	20/3
Imaging modalities used for the extracted-overlay function (arterial phase of dynamic CT/portal phase of dynamic CT/CTHA/CTAP/hepatobiliary phase of Gd-EOB-DTPA-enhanced MR imaging)	4/2/5/1/11
Size of exposed tip of cool-tip needle (2/3 cm)	22/1
Treatment sessions per tumor before complete ablation (1/2), n	22/1
Ablations per tumor, n	2 (1–4)

Data are presented as median (range) or number. HBV = Hepatitis B virus; HCV = hepatitis C virus.

Fig. 2. The extracted-overlay function during RFA of HCC in a 65-year-old man with hepatitis C-related cirrhosis. The hepatobiliary phase of Gd-EOB-DTPA-enhanced MR imaging was used as a reference and the tumor (yellow portion) with a virtual ablative safety margin (blue portion) was overlaid on US. Although the tumor usually becomes invisible due to spreading hyperechoic bubbles during ablation, it remains visible using the extracted-overlay function. Therefore, the depth of the inserted electrode can be adjusted so that the extracted tumor, together with a virtual ablative safety margin when possible, becomes completely encompassed by the spreading hyperechoic bubbling area.

Discussion

Although the CT/MR-US fusion imaging system is considered to be useful for RFA [1–4], misregistration is inevitable in the conventional side-by-side display of US and reference images. Although registration accuracy should be originally confirmed by the overlay display, background US images often become too obscure for practical use, because of the simple overlaying of different imaging modalities. Although we can use the global positioning system (GPS) tool of Volume Navigation for indicating the tumor location of CT/MR reference images on US images, the GPS marker cannot indicate the tumor three-dimensionally [1, 3, 15]. On the other hand, the extracted-overlay function could overlay an entire tumor extracted from CT/MR images on US, and background

US images did not become indistinct, leading to good treatment results of RFA in this study.

The extracted-overlay function has two other significant advantages. First, the visualization of an extracted tumor from reference images, with a virtual ablative safety margin, on real-time US enables effective treatment planning since the site, angle, depth and number of times of electrode insertion can be efficiently planned before RFA puncture. This advantage is considered to be especially apparent in HCCs which are not conspicuous on US [1, 2, 4, 15]. Second, the tumor remains visible, despite spreading hyperechoic bubbles, during and after ablation. During ablation, by comparing an overlaid tumor with the bubbles, the depth of an electrode can be adjusted so that the overlaid tumor becomes completely encompassed by the bubbles (fig. 2). In addition, the treatment effect can

be evaluated three-dimensionally, simply by comparing an overlaid tumor with spreading hyperechoic bubbles, or more accurately, by using contrast-enhanced US [1, 3, 12, 13]. Besides, by adding a virtual margin to the extracted tumor, an ablative margin can be evaluated quantitatively. Even if a tumor is protruding from the ablation zone, the target point of additional ablation is clear, since the tumor remains visible even after ablation.

One of the limitations of the extracted-overlay function lies in the registration accuracy of CT/MR-US fusion imaging. In addition to respiratory movement and nonrigid characteristics of the liver [2, 3, 10], the lack of intrahepatic landmarks makes registration difficult. This might be one of the causes of the only case of incomplete ablation after the first treatment session, since the tumor was located just beneath the diaphragm where there were few intrahepatic landmarks suitable for registration, such as branches of large blood vessels. Another

limitation remains in terms of the accuracy of the manual process of extracting the tumor and adding a virtual ablative safety margin. Also, the outline of cranial and caudal portions of the tumor may be somewhat inaccurate when an imaging modality with a thick slice is used as a reference.

In conclusion, the extracted-overlay function in the CT/MR-US fusion imaging system is useful for treatment planning and guidance of RFA. This is due to the visualization of a tumor extracted from CT/MR reference images with an ablative safety margin on US images.

Disclosure Statement

The authors declare that no financial or other conflict of interest exists in relation to the content of the article.

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