

# Multimodality 3D Tumor Segmentation in HCC Patients Treated with TACE

Zhijun Wang, MD, PhD, Julius Chapiro, MD, Rüdiger Scherthaner, MD, Rafael Duran, MD, Rongxin Chen, MD, PhD, Jean-François Geschwind, MD, MingDe Lin, PhD

**Rationale and Objectives:** To validate the concordance of a semiautomated multimodality lesion segmentation technique between contrast-enhanced magnetic resonance imaging (CE-MRI), cone-beam computed tomography (CBCT), and multidetector CT (MDCT) in patients with hepatocellular carcinoma (HCC) treated with transarterial chemoembolization (TACE).

**Materials and Methods:** This retrospective analysis included 45 patients with unresectable HCC who underwent baseline CE-MRI within 1 month before the treatment, intraprocedural CBCT during conventional TACE, and MDCT within 24 hours after TACE. Fourteen patients were excluded because of atypical lesion morphology, portal vein invasion, or small lesion size which precluded sufficient lesion visualization. Thirty-one patients with a total of 40 target lesions were included into the analysis. A tumor segmentation software, based on non-Euclidean geometry and theory of radial basis functions, was used to allow for the segmentation of target lesions in 3D on all three modalities. The algorithm created image-based masks located in a 3D region whose center and size were defined by the user, yielding the nomenclature “semiautomatic”. On the basis of that, tumor volumes on all three modalities were calculated and compared using a linear regression model ( $R^2$  values). Residual plots were used to analyze drift and variance of the values.

**Results:** The mean value of tumor volumes was  $18.72 \pm 19.13 \text{ cm}^3$  (range, 0.41–59.16  $\text{cm}^3$ ) on CE-MRI,  $21.26 \pm 21.99 \text{ cm}^3$  (range, 0.62–86.82  $\text{cm}^3$ ) on CBCT, and  $19.88 \pm 20.88 \text{ cm}^3$  (range, 0.45–75.24  $\text{cm}^3$ ) on MDCT. The average volumes of the tumor were not significantly different between CE-MRI and DP-CBCT, DP-CBCT and MDCT, MDCT and CE-MRI ( $P = .577, .770, \text{ and } .794$ , respectively). A strong correlation between volumes on CE-MRI and CBCT, CBCT and MDCT, MDCT and CE-MRI was observed ( $R^2 = 0.974, 0.992 \text{ and } 0.983$ , respectively). When plotting the residuals, no drift was observed for all methods showing deviations of no  $>10\%$  of absolute volumes (in  $\text{cm}^3$ ).

**Conclusions:** A semiautomated 3D segmentation of HCC lesions treated with TACE provides high volumetric concordance across all tested imaging modalities.

**Key Words:** Tumor segmentation; MRI; C-arm cone-beam CT; MDCT; hepatocellular carcinoma; TACE.

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Locoregional therapies (ie, conventional transarterial chemoembolization [cTACE]) represent the mainstay of therapy for patients with unresectable primary and some secondary liver malignancies. Because treatment recommendations are usually based on measurements made on cross-sectional imaging, accurate and workflow-efficient

evaluation of tumor size on baseline imaging and radiologic tumor response assessment on follow-up imaging constitute important aspects of the therapeutic concept (1–3). There are three accepted methods to assess tumor response to TACE: Response Evaluation Criteria in Solid Tumor [RECIST], European Association for the Study of the Liver [EASL] guidelines, and modified RECIST [mRECIST]. The diameter-based RECIST is used to measure changes in overall tumor size. The bidimensional EASL is used to measure the area of enhancement, and the more recently introduced unidimensional mRECIST measures the maximal diameter of tumor enhancement (4,5). The advent of workflow-efficient and clinically practicable segmentation-based 3D quantification of tumor volumes has been confirmed as technically feasible, highly reproducible, and reader independent. However, no evidence exists until today for the intermodality concordance between these systems. Before their full clinical introduction, these methods must be shown as accurate and reproducible across all cross-sectional imaging modalities. The purpose of our study was

Acad Radiol 2015; ■:1–6

From the Division of Vascular and Interventional Radiology, Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins Hospital, Sheikh Zayed Tower, Ste 7203, 1800 Orleans St, Baltimore, MD 21287 (Z.W., J.C., R.S., R.D., R.C., J.-F.G.); Interventional Radiology Department, Chinese PLA General Hospital, Beijing, China (Z.W.); and U/S Imaging and Interventions (UII), Philips Research North America, Briarcliff Manor, New York (M.L.). Received May 9, 2014; accepted March 8, 2015. Funding Sources: Support for this work was provided by National Institutes of Health/National Cancer Institute (R01 CA160771 and P30 CA006973); Philips Research North America, Briarcliff Manor, NY; the Rolf W. Guenther Foundation for Radiological Science; and the Beijing Nova Program (Z121107002512127). **Address correspondence to:** J.-F.G. e-mail: [jfg@jhmi.edu](mailto:jfg@jhmi.edu)

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<http://dx.doi.org/10.1016/j.acra.2015.03.001>

thus to validate the concordance of a semiautomated multimodality lesion segmentation technique on contrast-enhanced magnetic resonance imaging (CE-MRI), C-arm cone-beam computed tomography (CBCT), and multidetector CT (MDCT) in patients with hepatocellular carcinoma (HCC) treated with TACE.

## MATERIAL AND METHODS

### *Patient Study Selection*

This was a single-institution retrospective study. Health Insurance Portability and Accountability Act compliant and institutional review board approved the study. All patients were provided with informed consent before cTACE in the study. Diagnosis of HCC was confirmed by liver biopsy or the lesion presented with typical features on dynamic contrast-enhanced CT or MR cross-sectional imaging (hypervascularity in the arterial phase and washout in the venous phase) and an  $\alpha$ -feto-protein level of  $\geq 200$  ng/mL. Patients with unresectable HCC were evaluated and treated with cTACE after discussion at the multidisciplinary liver tumor conference. Eligibility criteria for cTACE were as follows: focal or multifocal unresectable HCC; Child-Pugh classification A or B; Eastern Cooperative Oncology Group performance status was 0 or 1, and no contraindication to contrast medium. Patients with tumor burden of  $>70\%$  presence of extrahepatic disease or complete tumor occlusion of the portal vein were excluded. The eligibility criteria for assessment of the treated target lesions included all patients 1) with dynamic CE-MRI within 4 weeks before cTACE, intraprocedural dual-phase CBCT (DP-CBCT), and MDCT 24 hours after cTACE; 2) with well visualized target lesion in all the three modalities; 3) with clear border between tumor and liver tissue. Targeted lesions that were not visualized well (ie, atypical lesion morphology like that found in infiltrative disease) or with insufficient imaging on any modality were excluded from our study.

### *Preprocedural CE-MRI Technique*

All patients underwent baseline CE-MRI using a 1.5-T MR unit (CV/I; GE Medical Systems, Milwaukee, WI) and a phased-array torso coil within 4 weeks before the TACE. The imaging protocol included 1) axial T2-weighted fast spin-echo images (repetition time [TR]/echo time [TE], 5000/100 milliseconds; matrix size,  $256 \times 256$ ; slice thickness, 8 mm; interslice gap, 2 mm; receiver bandwidth, 32 kHz); 2) axial single-shot breath-hold gradient-echo diffusion-weighted echo-planar images (TR/TE, 5000–6500/110 milliseconds; matrix size,  $128 \times 128$ ; slice thickness, 8 mm; inter slice gap, 2 mm;  $b$  value, 500 sec/mm<sup>2</sup>; receiver bandwidth, 64 kHz); and 3) axial breath-hold unenhanced and contrast-enhanced (0.1 mmol/kg intravenously of gadodiamide, Omniscan; General Electric, Princeton, NJ) T1-weighted 3D fat-suppressed spoiled gradient-echo images (TR/TE, 5.1/1.2 milliseconds;

field of view, 320–400 mm<sup>2</sup>; matrix size,  $192 \times 160$ ; slice thickness, 4–6 mm; receiver bandwidth, 64 kHz; flip angle, 15) in the arterial and portal venous phases (20 and 70 seconds after intravenous contrast administration, respectively). The arterial and venous phase of the CE-MRI imaging was used for the study.

### *Intraprocedural Dual-Phase CBCT Technique*

The intraprocedural dual-phase CBCT was performed to visualize the target lesion and its feeding arteries before chemoembolization. The imaging was performed using a commercially available angiographic system (Allura Xper FD20; Philips Healthcare, Best, The Netherlands). This system was equipped with the XperCT option, enabling C-arm CBCT acquisition and volumetric image reconstruction (Feldkamp back projection). For each CBCT scan, the area of interest was positioned in the system isocenter, and over approximately 5 seconds, 312 projection images (60 frames/s) were acquired with the motorized C-arm covering a 200° clockwise arc at 40° per second rotation speed (matrix size,  $384 \times 384 \times 296$ ; field of view,  $25 \times 25 \times 19$  cm). As the images were being acquired, the projections were transferred to the reconstruction computer to produce volumetric data. Isotropic images of 0.6 mm were reconstructed from the DP-CBCT scans. The dual-phase prototype feature allowed for the acquisition of two sequential multiphase CBCT scans using only one contrast injection. The same contrast injection protocol was applied to all cases: the contrast injection was done through the catheter placed into the proper hepatic artery, and the scan was triggered after contrast was injected for 3 seconds (amount 18 mL; rate 2 mL/s; Oxilan 300 mgI/mL; Guerbet LLC, Bloomington, IN). The patients were instructed to be at end-expiration apnea during each of the CBCT scans with free breathing between the early and delayed arterial phase scans. If needed, oxygen was administered to patients during the acquisition to minimize the discomfort of breath-holding. In this work, the second phase was used because the tumors were best visualized at that phase (6,7).

### *Transcatheter Arterial Chemoembolization*

cTACE was performed according to our standard institutional protocol, and all procedures were performed by an interventional radiologist (J.-F.G.) with 15 years of experience in hepatic interventions. With use of the Seldinger technique, a 5F vascular sheath was placed in the right common femoral artery over a 0.035-in guide wire (Terumo Medical, Somerset, NJ). Under fluoroscopic guidance, a 5F glide Simmons-1 catheter (Cordis, Miami, FL) was advanced into the aortic arch and then used to select the celiac axis. The catheter was advanced into the desired hepatic artery over the guidewire. Using a 3F Renegade HI-FLO catheter coaxially over a 0.014-in Transcend wire (Boston Scientific, Natick, MA), selective catheterization was performed to achieve lobar or segmental

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