Comparison of Semi-automatic Volumetric VX2 Hepatic Tumor Segmentation from Cone Beam CT and Multi-detector CT with Histology in Rabbit Models

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Rationale and Objectives: The purpose of this study was to compare tumor volume in a VX2 rabbit model as calculated using semiautomatic tumor segmentation from C-arm cone-beam computed tomography (CBCT) and multidetector computed tomography (MDCT) to the actual tumor volume.

Materials and Methods: Twenty VX2 tumors in 20 adult male New Zealand rabbits (one tumor per rabbit) were imaged with CBCT (using an intra-arterial contrast medium injection) and MDCT (using an intravenous contrast injection). All tumor volumes were measured using semiautomatic three-dimensional volumetric segmentation software. The software uses a region-growing method using non-Euclidean radial basis functions. After imaging, the tumors were excised for pathologic volume measurement. The imaging-based tumor volume measurements were compared to the pathologic volumes using linear regression, with Pearson's test, and correlated using Bland-Altman analysis.

Results: Average tumor volumes were 3.5 ± 1.6 cm^3 (range, 1.4–7.2 cm^3) on pathology, 3.8 ± 1.6 cm^3 (range, 1.3–7.3 cm^3) on CBCT, and 3.9 ± 1.6 (range, 1.8–7.5 cm^3) on MDCT ($P < .001$). A strong correlation between volumes on pathology and CBCT and also with MDCT was observed (Pearson's correlation coefficient = 0.993 and 0.996, $P < .001$, for CBCT and MDCT, respectively). Bland-Altman analysis showed that MDCT tended to overestimate tumor volume, and there was stronger agreement for tumor volume between CBCT and pathology than with MDCT, possibly because of the intra-arterial contrast injection.

Conclusions: Tumor volume as measured using semiautomatic tumor segmentation software showed a strong correlation with the "real volume" measured on pathology. The segmentation software on CBCT and MDCT can be a useful tool for volumetric hepatic tumor assessment.

Key Words: Tumor segmentation software; C-arm cone-beam CT; multidetector CT; VX2 hepatic tumor.

A change in tumor volume as a response to local therapy such as transcatheter arterial chemoembolization is a prognostic indicator of therapeutic success. Tumor size is the only component of the Response Evaluation Criteria in Solid Tumors (RECIST) (1). First described in 2000, RECIST is based on tumor diameter measurement, in which the longest diameter of a given target lesion, or the sum of the longest diameters for a set of target lesions, is measured and compared before and after chemoembolization on cross-sectional imaging (either computed tomography or magnetic resonance imaging. It is a one-dimensional measurement that often poorly represents true tumor response after chemoembolization and is subject to high interobserver variability (2,3). Although RECIST was appropriate at the time of its introduction, the simplicity of RECIST now makes insufficient use of the sophisticated advances in modern imaging units. With the advent of multidetector computed tomography (MDCT) and improved detectors, the ability to assess tumor volume using three-dimensional (3D) metrics has become much more feasible. Furthermore, with the

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advent of C-arm cone-beam computed tomography (CBCT), tumors can be assessed during the procedure for planning or for efficacy of treatment (4). However, before volume-based metrics can supplant RECIST, these methods must be shown to be accurate and precise. This was recognized in version 1.1 of RECIST (released in 2009): the importance of studying volumetric anatomic assessment in greater detail is necessary before anatomic unidimensional assessment of tumor burden can be abandoned (1).

The purpose of this study was to evaluate the accuracy of semiautomatic tumor segmentation software with CBCT and MDCT and compare these measurements to pathologic volume-based measurements in a VX2 rabbit hepatic tumor model.

MATERIALS AND METHODS

This study was an ancillary study. The aim of the primary study was to explore the performance of drug-eluting beads in terms of tumor penetration and pharmacokinetics. All animal studies were approved by our institution's animal care and use committee. All procedures were conducted under their guidelines.

Animals

Twenty adult male New Zealand white rabbits weighing between 3.8 and 4.3 kg (Myrtle's Rabbitry, Thompson Station, TN) were used for this study. All rabbits were implanted with VX2 liver tumors, as described in previous work (5). These animals were used for another study (doxorubicin-eluting bead treatment).

Anesthesia

The tumor-bearing animals were anesthetized twice: once for tumor implantation and once for tumor treatment. For tumor implantation, induction was achieved with 5% isoflurane (Hospira, Lake Forest, IL) and 95% oxygen (Air Gas, Salem, NH) and then sustained with 2.5% isoflurane and 97.5% oxygen. For treatment, the animals were premedicated with an intramuscular injection of acepromazine (2.5 mg/kg; Phoenix, St Joseph, MO) and ketamine hydrochloride (Ketaject 44 mg/kg; Phoenix). Sedation was maintained with propofol 10 mg/mL (APP Pharmaceuticals, Schaumburg, IL) in monitored boluses of 2 mg (0.25 mL) intravenously via the right marginal ear vein. After the procedure, analgesic buprenorphine (0.02–0.05 mg/kg) was injected intramuscularly for pain relief.

MDCT

All animals underwent multidetector biphasic computed tomographic scans before the embolization and treatment procedure, which was 7 days after tumor implantation. At 7 days, the aggressively growing VX2 tumors were close to spherical in shape and without necrotic cores as seen in larger sized tumors (>3 cm in diameter). This was required for the primary study. Imaging was performed using a conventional multidetector computed tomographic unit (Toshiba Aquilion ONE; Toshiba Corporation, Tokyo, Japan). MDCT was performed using tube voltage of 120 kVp and tube current of 80 mA, a rotation time of 0.5 seconds, and a scan time of 60.5 seconds. The matrix used was 512 × 512 × 200, with a 492 × 492 × 192 mm reconstructed field of view. The arterial and portal acquisitions were respectively performed at 12 and 30 seconds after contrast injection (2 ml Oxilan 300 mg I/mL; Guerbet LLC, Roissy, France).

Drug-eluting Bead Transarterial Chemoembolization (DEB-TACE) Procedure

For all rabbits, an incision was made in the skin and subcutaneous structures after shaving, disinfecting, and draping the right inner thigh and groin. Blunt dissection was performed to expose the right femoral artery. A 3-F introducer (Check-Flo; Cook, Bloomington, IN) was introduced over a guide wire through the femoral arterial access. Next, the hepatic artery was catheterized using a 2-F JB1 catheter (Cook) and a 0.014-inch guide wire (Transend; Boston Scientific Corporation, Miami, FL). Chemoembolization was performed using 100 to 300 μm drug-eluting beads (LC Beads; Biocompatibles, Oxford, CT) loaded with doxorubicin (these animals were used for another study, as described above).

C-arm CBCT

All animal imaging was performed using a commercial C-arm system (Allura FD20 with XperCT option; Philips Healthcare, Best, The Netherlands). C-arm CBCT was performed using tube voltage of 80 kVp, tube current of 85 mA, tube exposure time of 5 ms, with a 5-second scan time, and a frame rate of 60 frames/s. The images were reconstructed immediately after image acquisition using the commercially available 3D algorithm on the scanner to a 256 × 256 × 192 matrix with a voxel size of 0.98 mm^3. All cone-beam computed tomographic images were acquired before embolization with a simultaneous contrast injection (2 ml Oxilan 300 mg I/mL).

Animal Sacrifice, Histology, and Tumor Volume Measurement

All animals were sacrificed under deep anesthesia by intravenous injection of 100 mg/kg intravenous thiopental 7 days after the DEB-TACE procedure. Necropsy was done on all animals. Rabbit livers were dissected, carefully removed, and placed in a container containing 5% formaldehyde. Two weeks later, 5-mm tumor slices were taken for gross examination. Tumor shape was classified as an oblate or a prolate spheroid by the primary investigator. Tumor volume was calculated along the spheroid volume as $V = (\pi A^2 B)/6$. For prolate and oblate spheroids, the equatorial diameters were,