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PHYSICS CONTRIBUTION

4D-IMAGING OF THE LUNG: REPRODUCIBILITY OF LESION SIZE AND DISPLACEMENT ON HELICAL CT, MRI, AND CONE BEAM CT IN A VENTILATED *EX VIVO* SYSTEM

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Purpose: Four-dimensional (4D) imaging is a key to motion-adapted radiotherapy of lung tumors. We evaluated in a ventilated *ex vivo* system how size and displacement of artificial pulmonary nodules are reproduced with helical 4D-CT, 4D-MRI, and linac-integrated cone beam CT (CBCT).

Methods and Materials: Four porcine lungs with 18 agarose nodules (mean diameters 1.3–1.9 cm), were ventilated inside a chest phantom at 8/min and subject to 4D-CT (collimation 24 × 1.2 mm, pitch 0.1, slice/increment 24×10^2/1.5/0.8 mm, pitch 0.1, temporal resolution 0.5 s), 4D-MRI (echo-shared dynamic three-dimensional-flash; repetition/echo time 2.13/0.72 ms, voxel size 2.7 × 2.7 × 4.0 mm, temporal resolution 1.4 s) and linac-integrated 4D-CBCT (720 projections, 3-min rotation, temporal resolution ~1 s). Static CT without respiration served as control. Three observers recorded lesion size (RECIST-diameters x/y/z) and axial displacement. Interobserver- and interphase-variation coefficients (IO/IP VC) of measurements indicated reproducibility.

Results: Mean x/y/z lesion diameters in cm were equal on static and dynamic CT (1.88/1.87; 1.30/1.39; 1.71/1.73; $p > 0.05$), but appeared larger on MRI and CBCT (2.06/1.95 [$p < 0.05$ vs. CT]; 1.47/1.28 [MRI vs. CT/CBCT $p < 0.05$]; 1.86/1.83 [CT vs. CBCT $p < 0.05$]). Interobserver-VC for lesion sizes were 2.54–4.47% (CT), 2.29–4.48% (4D-CT); 5.44–6.22% (MRI) and 4.86–6.97% (CBCT). Interphase-VC for lesion sizes ranged from 2.28% (4D-CT) to 10.0% (CBCT). Mean displacement in cm decreased from static CT (1.65) to 4D-CT (1.40), CBCT (1.23) and MRI (1.16).

Conclusions: Lesion sizes are exactly reproduced with 4D-CT but overestimated on 4D-MRI and CBCT with a larger variability due to limited temporal and spatial resolution. All 4D-modalities underestimate lesion displacement. **© 2009 Elsevier Inc.**

Computed tomography, Dynamic MRI, Cone beam CT, Lung nodules, Respiratory gating.

INTRODUCTION

Currently, radiotherapy of lung tumors compensates for respiratory motion by an expansion of the irradiated volume (1). The purpose of motion-adapted techniques is to minimize the volume of irradiated healthy tissue and to optimize tumor dose by limiting the target volume to certain positions of the tumor trajectory (gating) or by following its trajectory (tracking) (2–5). Recent technical developments have opened new perspectives in this field (6–8). Suitable systems use integrated kilovoltage or megavoltage imaging for the assessment of tumor positions throughout the respiratory cycle (9). Pretherapeutic four-dimensional (4D) imaging

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Conflict of interest: Carsten Thierfelder, Ph.D., is a company employee of Siemens Healthcare Sector.

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would serve to select patients who might profit from motion-adapted therapy and to quantify respiratory motion of the prospective target. This information would be integrated into a suitable treatment plan with final verification of the actual target volume positions at the linear accelerator with time-resolved imaging.

Either CT or MRI might be considered for a 4D workflow concept. Both principally allow definition of tumor size and its three-dimensional (3D) displacement during respiration (10–12). Four-dimensional CT with multidetector-row systems and short acquisition times permits a temporal resolution down to 250 ms (13,14). MRI with fast sequences such as two-dimensional (2D) gradient echo (GRE) or 2D fast steady-state GRE allows for lung-motion imaging with a temporal resolution between 3 and 10 images per second (15). Four-dimensional MRI with time-resolved 3D GRE sequences allows a temporal resolution of 1 s (16, 17). Integrated fluoroscopy and cone beam CT (CBCT) are available for the verification of tumor positions at the linear accelerator. The objective of this study was to evaluate 4D imaging with helical CT, MRI, and the integrated imaging system of a linear accelerator using an *ex vivo* system for the simulation of respiratory motion in inflated porcine lungs.

METHODS AND MATERIALS

The ex vivo system

Four porcine heart-lung specimens were obtained 4–8 hours before the experiments, lubricated with ultrasound gel (Aquasonic, Parker Laboratories, Fairfield, NJ), and collocated into the cavity of a dedicated chest phantom. A tracheal tube (Rüsch soft tracheal tube, 6.5 mm; Rüsch, Kernen, Germany) was introduced into the trachea and connected to an outlet through the chest wall. The lungs were then reinflated by continuous evacuation of the artificial pleural space at approximately –20 to –30 hPa. To simulate nodules, each specimen was prepared with six injections (1–4 mL) of hand-warm agarose (30 g/L Agarose, BD, Franklin Lakes, NJ) (18). To enhance MR signal and to adjust mean nodule density on CT to 20 ± 20 HU at 120 kVp, we added 0.125 mM/L Gd-DTPA (Gadolinium [III]-diethyltriaminepentaacetic acid, Magnevist, Schering, Berlin, Germany) and 1.5 g/L iodine (5 mL Ultravist 300, Schering) to the nodule matrix. A filling of the space between inner and outer shells of the phantom with 1.25 mg/mL of nickel sulfate hydrate ($NiSO_4$) solution was used to achieve realistic MR signal and radiation absorbance of a chest wall. The flexible ''diaphragm'' was inflated with water to simulate contractions and relaxations at a frequency of 8 per minute with a ratio of 1:2 for the duration of inspiration and expiration (14). Respiration was monitored with a commercial system (AZ-733V, Anzai Medical, Tokyo, Japan). It uses a load cell to convert changes in chest or abdomen diameter into an electric signal for the imaging system. For this study, the load cell was coupled to the pump unit with a proportionally distended spring.

Experimental design

The complete procedure included static helical CT (static CT) as baseline and time-resolved scans with CT (4D-CT), MRI with 3D GRE sequences (4D-MRI), and CBCT integrated into a linear accelerator (4D-CBCT). The phantoms were prepared and scanned at the 4D-CT site and then transported over a distance of 500 m to continue with MRI, CBCT, and a final static CT scan at the main facility. The final CT served to register changes of the specimen during the course of the experiment. Because a 4D mode was not available at this scanner, the final images were only performed under static conditions. For transport, the vacuum inside the artificial chest had to be disconnected for 15–20 min. Lung collapse was prevented by connecting a positive pressure of 30 hPa from a high-pressure flask to the tracheal tube. Duration of the complete procedure was approximately 2.5 hours. To reduce bias related to lung deterioration, the sequence of experiments was reversed for 2 of 4 preparations.

4D-CT scan settings

Scans of moving or static phantoms were acquired with a 40-slice CT scanner (Sensation Open, Siemens, Erlangen, Germany) at a pitch of 0.1 (defined as patient table feed per rotation and detector array width). The scan covered the complete artificial thoracic cavity using a standard technique for respiration frequencies of less than 12/min (120 kV, 400 effective mAs, collimation 1.2 mm, rotation time 1 s, 90-s scan time). Images were reconstructed with a 180° interpolation algorithm for 1.5/0.8 mm slice thickness/increment with a medium kernel (B50f). Six separate scans were performed for each study. Five scans were obtained at 0%, 25%, 50%, 75%, and 100% inspiration without motion but with a simulated respiration signal (hereafter ''static scans''). The sixth scan was obtained during ventilation at 8/min. It was retrospectively reconstructed corresponding to 0%, 25%, 50%, 75%, and 100% inspiration using the respiratory curve and the default software provided with the scanner.

CBCT imaging setup and data acquisition

For linac-integrated 4D-CBCT, the phantom was placed as a patient in prone position would be (Fig. 1). The scanner was a prototype system mounted at the gantry of a clinical linear accelerator (PRIMUS, Siemens OCS, Concord, CA) (19). It consists of an amorphous silicon flat panel detector (XRD, Perkin Elmer Optoelectronics, Fremont, CA) fixed directly below the multileaf collimator and a X-ray source (Optitop, Siemens Medical Solutions, Erlangen, Germany) mounted in the opposite direction. The axis of the imaging kV beam has a 180-degree offset to the therapeutic MV beam (20). This prototype was developed as precursor of a commercially available system (Artiste, Siemens OCS). The flat-panel detector provides images of 1024×1024 pixels with a pixel size of $0.4 \times 0.4\,mm^2$, and the source-to-detector distance is about 140 cm. Images were acquired for equidistant gantry rotation angles of 0.5°. Trigger pulse timestamps were stored for synchronization with the respiratory gating system. Within 2–3 min, 720 projections of one full rotation were acquired. Image reconstructions were performed using a Feldkamp algorithm for CBCT reconstructions with a voxel grid of $512 \times 512 \times 256$ (left-right/antero-posterior/cranio-caudal) and a voxel resolution of approximately $0.5 \times 0.5 \times 1.0$ mm (left-right/antero-posterior/cranio-caudal). Amplitude-based reconstructions were made with a 10% range of tolerance of the breathing signal, within which the radiograms were selected. Images were calculated for 0%–100% inspiration in 25% steps from the respiratory curve. Overall temporal resolution of the 4D-CBCT was approximately 1 s.

MRI

The MR examinations were performed on a clinical 1.5-T system (Magnetom Symphony, Siemens Medical Solutions) equipped with a high-performance gradient system (30 mT/m) and a six-channel phased array body coil. Images were acquired continuously during ventilation (8/min) and at static conditions using a dynamic 3D-GRE sequence with temporal interpolation (coronal time-resolved

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