

AbstractID: 10123 Title: Effects of breathing variation on internal target volume (ITV) in respiratory gated radiation therapy

**Introduction:** Accuracy of 4DCT reconstruction depends on reproducible patient breathing during scans and highly synchronized external surrogates. Studies have been conducted to investigate the effects of breathing variation on the motion information extracted from 4DCT (1, 2). Our previous study showed that tumor ITV can be underestimated by 4DCT maximum intensity projection (MIP)-based measurement by up to 50% due to breathing variation (1). In respiratory-gated radiation therapy, the planning target volume (PTV) is composed of the ITV in the gated window ( $ITV_{GW}$ ) and a setup margin (SM):  $PTV_{GW}=ITV_{GW}+SM$ . Similarly, due to the breathing variation of patients,  $ITV_{GW}$  determined from 4DCT can also be erroneous. It is the objective of this study to investigate the effects of breathing variation on  $ITV_{GW}$  in the respiratory gated radiation therapy.

**Methods and Materials:** 7 healthy volunteers (mean age 39.8) and 5 lung cancer patients (mean age 68.4) were included in this study. All MR images were acquired on a 1.5T MRI scanner (Avanto, Siemens, Germany) using a TrueFISP sequence. A single sagittal plane, in the middle right lung for volunteers and across the center of the tumor for patients, was scanned for a continuous 5-minute for each subject. All subjects were instructed to breathe normally during the scan. Imaging parameters (TR/TE: 3.7/1.13 ms; FOV: 384×312 mm; Flip angle: 52°; Slice thickness: 7 mm; Matrix: 256×208) were used so that the acquisition rate (0.3 seconds per frame) is similar to that of 4DCT. Motion trajectories of tumor (for patients) or a pulmonary vessel (for volunteers) were determined from dMRI and used in 4DCT simulation. A MATLAB program was written to simulate cine-mode 4DCT acquisition by segmenting and rebinning the dynamic MR images. The simulation method has been described in details previously (1) and will not be repeated here.

**Phantom study:** Image motion phantoms were created to mimic lung motion, with a solid disk to represent the “tumor” (1). The density of the “lung” and “tumor” was set to 0 and 1 respectively. The “tumor” was initially placed at the center of the image and then moved with given motion trajectories determined from dMRI. Dynamic phantom images generated in such manner were then used to reconstruct simulated 4DCT images (sCT). Subsequently a single-breathing-cycle motion trajectory of the “tumor” is determined from the 10-bin sCT. An exhalation gating window was determined as the phases within which the residue motion of the “tumor” is less than 5 mm. If the gating window contains more than 5 phases, then only the 5 phases with the smallest residual motion were selected. sCT images in the gating window were then grouped to generate a MIP image, from which the gated window internal target area ( $ITA_{GW}$ , 2D counterpart of  $ITV_{GW}$ ) was determined. Similarly, the 5-minute dynamic phantom images in the gating window were also grouped. Instead of a MIP image, an average intensity of projection (AIP) image was generated in this case, and  $ITA_{GW}$  was determined as the area in the AIP image where the intensity is greater than 0.05. In another word, locations where the “tumor” presented less than 5% of its entire moving time were not included in  $ITA_{GW}$ . This is to avoid potential errors induced by sudden breathing changes. Area ( $ITA_{GW}$ ), major axis ( $L1$ ) and minor axis ( $L2$ ) of the  $ITA_{GW}$  were determined for each of the  $ITA_{GW}$ , as shown in Fig. 1d. Measurements from sCT were compared with those from dMRI. In addition, Dice coefficient of similarity ( $DSC$ ) between the two  $ITA_{GW}$  was calculated. Our simulation method was validated with hypothesized 5-minute sinusoidal trajectory (period=5s; amplitude=10mm). Ideally, results from sCT and dMRI should be the same in this case.

**Patient study:** Similar study was performed on the dynamic MR images of lung cancer patients. Exhalation gating window was determined in the same manner as described above. MIP images in the gating window were generated for both sCT and dMRI, from which the  $ITA_{GW}$  was determined. Unlike in the phantom study,  $ITA_{GW}$  were manually contoured by experienced oncologist in this case. Measurements of  $ITA_{GW}$ ,  $L1$ ,  $L2$  and  $DSC$  were also performed.

**Results:** Phantom study with the sinusoidal trajectory showed identical measurements of  $ITA_{GW}$ ,  $L1$ ,  $L2$  between sCT and dMRI (not shown), with a  $DSC$  of 1. The results validated our simulation. Fig. 1 shows an example of the phantom study. Gating window of 20% to 60% was chosen based on the single-breathing-cycle trajectory determined from sCT (Fig. 1b). Gated window MIP images generated for sCT and dMRI are substantially different (Fig. 1c). Fig. 2 shows an example of the patient study. Gated window AIP images showed apparent difference between sCT and dMRI, as well as the  $ITA_{GW}$  indicated by red arrows (Fig. 2b), primarily due to the large breathing variation of this patient (Fig. 2a). Over all, in the phantom study with 3cm ‘tumor’ (Fig. 3b), measurements in dMRI are significantly ( $p$ -value<0.001) greater than those in sCT ( $ITA_{GW}=992.9\pm 121.7\text{mm}^2$ ,  $L1=38.1\pm 3.8\text{mm}$ ,  $L2=33.1\pm 1.0\text{mm}$  in dMRI;  $ITA_{GW}=836.7\pm 66.6\text{mm}^2$ ,  $L1=34.1\pm 2.4\text{mm}$ ,  $L2=31.2\pm 0.7\text{mm}$  in sCT). These differences are even greater in the phantom study with 1cm ‘tumor’ as shown in Fig. 3a ( $ITA_{GW}=189.9\pm 44.7\text{mm}^2$ ,  $L1=18.7\pm 4.0\text{mm}$ ,  $L2=13.0\pm 0.7\text{mm}$  in dMRI;  $ITA_{GW}=131.7\pm 13.8\text{mm}^2$ ,  $L1=15.0\pm 1.5\text{mm}$ ,  $L2=11.4\pm 0.5\text{mm}$  in sCT).  $ITA_{GW}$  similarity is  $0.91\pm 0.05$  and  $0.79\pm 0.10$  for the 3cm and 1cm ‘tumor’ respectively. Similar results were found in the patients study ( $ITA_{GW}=1554.4\pm 822.5\text{mm}^2$ ,  $L1=49.9\pm 11.3\text{mm}$ ,  $L2=38.5\pm 11.9\text{mm}$  in dMRI;  $ITA_{GW}=1319.0\pm 852.7\text{mm}^2$ ,  $L1=43.2\pm 14.0\text{mm}$ ,  $L2=36.8\pm 12.0\text{mm}$  in sCT), with an  $ITA_{GW}$  similarity of  $0.83\pm 0.09$ . In addition, these differences between sCT and dMRI are more substantial when lung motion range is larger than 1cm, as shown in Fig. 4, independent of the ‘tumor’ size.

**Discussion:** Our results showed that  $ITV_{GW}$  can be underestimated by 4DCT, suggesting an additional margin to account for breathing variation may be necessary in defining  $PTV_{GW}$  for respiratory-gated radiation therapy. Explicitly, we propose  $PTV_{GW}=ITV_{GW}+VM+SM$ , where VM is the breathing variation margin. If the margin can be approximated as  $(L1_{dMRI} - L1_{sCT})/2$  and  $(L2_{dMRI} - L2_{sCT})/2$  in the two axis respectively, then the margin size is about 3 mm and 1 mm in the major axis and minor axis respectively. This margin is expected to be larger when tumor motion is greater than 1 cm. There are several

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limitations of this study, including potential simulation errors and over-simplified patient selection criteria for gated therapy. In addition, the dosimetry effects of breathing variation in the reparatory gated treatment require further investigation. Some respiratory gating systems (such as Varian’s RPM system) have self-correction algorithm to minimize the effects of breathing variation during the treatment. Irregular breathing can be automatically detected and radiation beam will be automatically turned off that period, which may diminish the dosimetry effects of breathing variation.

**Conclusion:** Our simulation study demonstrated that 4DCT-based measurement may underestimate the gated window ITV in respiratory gated radiation therapy. An addition margin to account for the breathing variation may be necessary in determining the gated window PTV.

**References:**

1. Cai J, *et al.* Estimation of the error in maximum intensity projection (MIP) based internal volume (ITV) of lung tumors: a simulation and comparison study based on dynamic MRI. *Int J Radiat Oncol Biol Phys* 2007;69:895-902.
2. Simon L, *et al.* Initial evaluation of a four-dimensional computed tomography system using a programmable motor. *J Appl Clin Med Phys* 2006;7:50-65.

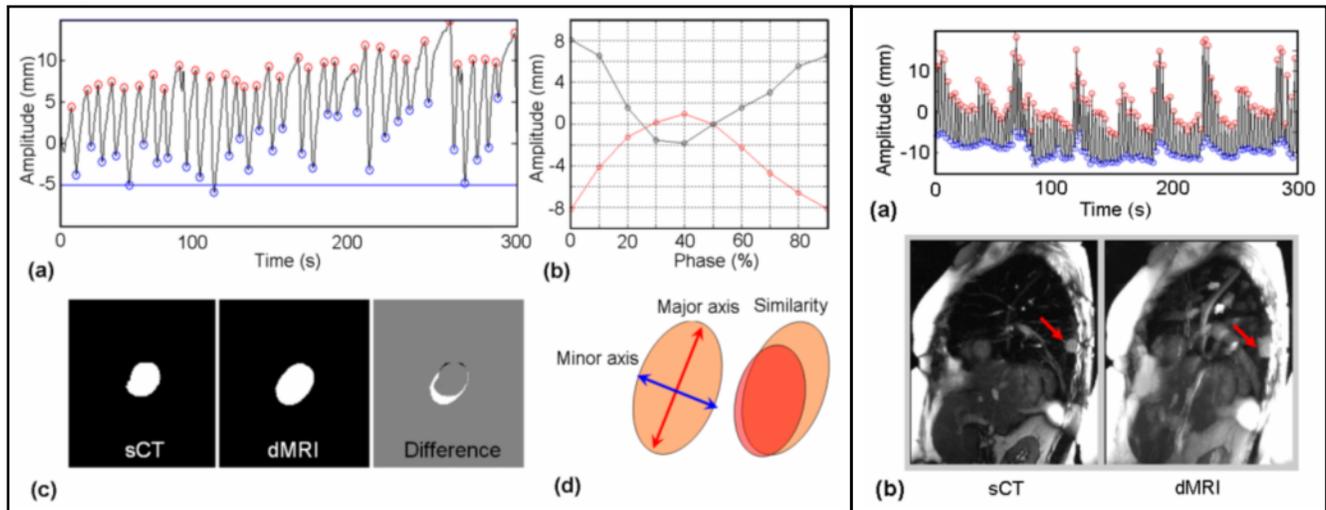


Figure 1: (a) Motion trajectory in the SI direction determined from dMRI and used to generate motion phantom images. (b) Single-breathing-cycle trajectories determined from simulated 4DCT. Gating window is 20%-60% in this case. (c) Gated window ITAs determined from sCT and dMRI, and the difference between the two. (d) Sketches explaining the measurements of major axis, minor axis and similarity.

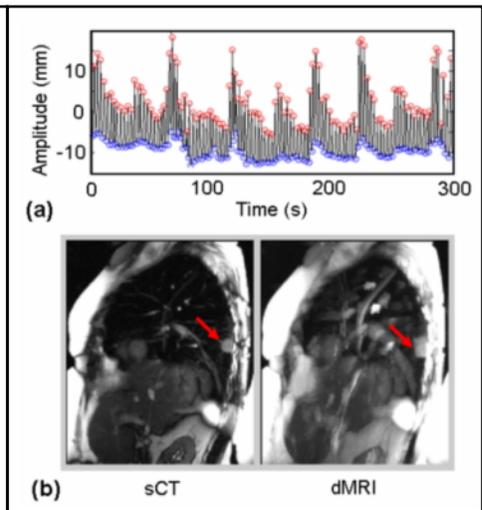


Figure 2: (a) Motion trajectory in the SI direction determined from dMRI of a lung cancer patient. (b) Gated window MIP images showing the gated window ITAs determined from sCT and dMRI, indicated by red arrows.

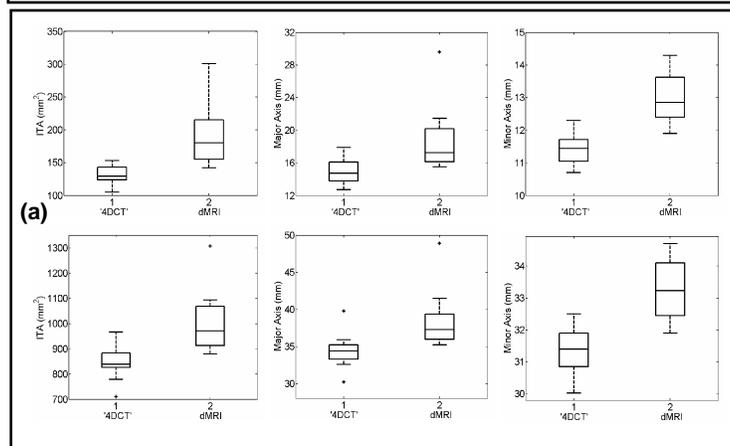


Figure 3: Comparisons in gated window ITA, major axis and minor axis between sCT and dMRI. (a) The hypothesized ‘tumor’ is 1 cm in diameter. (b) The hypothesized ‘tumor’ is 3 cm in diameter. (p-value<0.001).

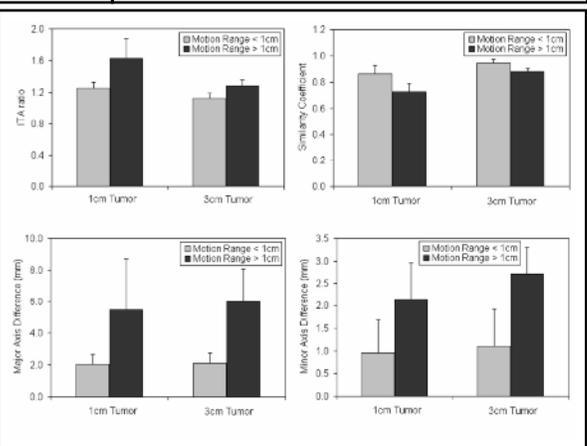


Figure 4: Comparisons in ITA ratio, major axis difference, and similarity between subjects with lung motion range < 1cm and those with lung motion range > 1cm. (p-value<0.05)