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Tumor motion

Frequency filtering based analysis on the cardiac induced lung tumor motion and its impact on the radiotherapy management

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ABSTRACT

Purpose/objectives: Lung tumor motion may be impacted by heartbeat in addition to respiration. This study seeks to quantitatively analyze heart-motion-induced tumor motion and to evaluate its impact on lung cancer radiotherapy.
Methods/materials: Fluoroscopy images were acquired for 30 lung cancer patients. Tumor, diaphragm, and heart were delineated on selected fluoroscopy frames, and their motion was tracked and converted into temporal signals based on deformable registration propagation. The clinical relevance of heart impact was evaluated using the dose volumetric histogram of the redefined target volumes.
Results: Correlation was found between tumor and cardiac motion for 23 patients. The heart-induced motion amplitude ranged from 0.2 to 2.6 mm. The ratio between heart-induced tumor motion and the tumor motion was inversely proportional to the amplitude of overall tumor motion. When the heart motion impact was integrated, there was an average 9% increase in internal target volumes for 17 patients. Dose coverage decrease was observed on redefined planning target volume in simulated SBRT plans.
Conclusions: The tumor motion of thoracic cancer patients is influenced by both heart and respiratory motion. The cardiac impact is relatively more significant for tumor with less motion, which may lead to clinically significant uncertainty in radiotherapy for some patients.
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Radiation therapy for thoracic cancer patients suffers from the constant motion of the tumor. Much research has been conducted to address respiration-induced tumor motion in radiotherapy with various approaches [1–7], such as voluntary breath control and the utilization of internal target volume (ITV) in treatment planning. In clinical implementation, most motion management approaches acquire tumor motion information through the respiration-correlated four-dimensional computed tomography (4DCT) [8]. These approaches, although attempting to tackle tumor motion, do not accurately account for the impact of cardiac motion.

Cardiac motion, along with the respiratory motion, cyclically alters the spatial locations of anatomic structures in the thoracic volume. Cardiac motion is involuntary, and with higher frequency compared to respiration. Due to the frequency and phase difference, the heart impact appears as inter-phase motion uncertainty in respiration-correlated 4DCT but cannot be fully captured as restricted by the relatively low sampling rate [9] and relatively short scanning time of CT. Research has been conducted on the impact of cardiac motion on lung tumors [10–12] using fluoroscopy imaging. In previous studies, to highlight the target motion in fluoroscopy images, a metal fiducial was implanted close to the tumor, and its motion was recorded as the tumor motion for analysis. The procedure is invasive and may not be applicable to many patients, plus the correlation between the surrogate and actual tumor motion was not fully investigated. Fortunately, the latest development of deformable image registration (DIR) and its clinical application has enabled the direct tracking of tumor motion without invasive implantation.

The objectives of this study were to (1) implement an object constrained DIR tool to extract the heart-induced tumor motion; (2) quantify the heart-induced tumor motion via frequency domain analysis; (3) conduct statistical study on the quantified cardiac impact, and (4) evaluate the potential clinical influence of cardiac motion on radiotherapy.

Methods and materials

Patients

30 patients who received external beam radiotherapy (EBRT) for thoracic cancer from October 2011 through May 2013 were

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enrolled onto a prospective Institutional Review Board approved study. Radiation was delivered to patients in 1.8 Gy or 2 Gy per day to a median dose of 62 Gy (min: 48.6 Gy, max: 66 Gy). To avoid using preliminary results to guide the clinical practice, we did not include SBRT patients in our study. However, for selected patients who met the criteria of SBRT, we generated experimental SBRT plans following the clinical protocol at the institute. These experimental plans were used for the evaluation of the potential cardiac impact in clinical cases.

Image acquisition

Patients underwent respiration correlated retrospective 4DCT scanning for treatment planning purposes using a GE Lightspeed™ 16 CT scanner (Waukesha, WI) equipped with the Advantage 4DCT system. The 4DCT images were generated retrospectively by acquiring images in the cine mode at the interval determined by $(t_{resp}+1)/20)$, where t_{resp} was the length of patient's respiratory cycle. The generated images were sorted into 10 different image sets corresponding to different respiratory phases, denoted as from 0% to 90%.

For all patients, 15-s fluoroscopy was acquired weekly in the anterior–posterior (AP) direction at 8 frames per second as part of the pre-treatment patient setup procedure. All fluoroscopy was acquired by the kilo-voltage On Board Imaging (OBI) system of Varian© (Palo Alto, CA) using the same imaging protocol. The overall radiation dose from fluoroscopy was estimated and deemed clinically negligible.

Terminology

The definition of GTV (gross tumor volume), CTV (clinical target volume), ITV, and PTV (planning target volume) complied with ICRU62 [7] and the clinical practice at the facility where the proposed study was conducted.

The tumor motion definition used in this study accounts for the intra-fractional shape, size, and location change of the tumor. We assumed the tumor self-deformation was ignorable compared to the respiration and cardiac impact. The motion between any two give time points was defined as the displacement of the center of mass (COM) of the tumor between the corresponding images.

Image processing

4DCT images were transferred to the Eclipse treatment planning system (TPS) (Varian Medical Systems, Palo Alto, CA). All target volumes were manually delineated for treatment planning.

The motion information in the fluoroscopy images was analyzed with a software package driven by the in-house deformable registration propagation algorithms [13,14]. The software interface and the structures we used to retrieve the motion signals were illustrated in Supplementary Fig. 1. First DIR was performed between the digitally reconstructed radiograph (DRR) of the corresponding 4DCT phase and a fluoroscopy frame f_0 to project the tumor into the 2D domain of fluoroscopy images, forming the initial tumor template G_0. To propagate, one frame was registered non-rigidly to its direct neighbors, i.e., f_i to f_{i-1} and f_{i+1}, constrained by G_i. The registration generated a displacement map d_{ij} between the source (f_i) and target ($f_{i\pm1}$). By deforming G_i using d_{ij}, we derived $G_{i\pm1}$ in the target frames, and the propagation continued until displacement between all neighboring frames had been calculated.

Cardiac motion analysis

For patients included in this study, the average respiratory frequency was 0.2 s^{-1}, while the average heartbeat frequency was 1.4 s^{-1}. The frequency difference enabled the separation of cardiac motion signals from the respiratory motion through frequency domain analysis.

In the first step of the decoupling process we retrieved the cardiac motion signal by depriving the respiration impact from heart motion. The respiratory motion frequency w_{resp} was determined directly using right diaphragm motion signal $r(t)$. The heart motion (in form of heartwall motion) in fluoroscopy images was usually a combination of the heartbeat and the respiration motion. To derive the cardiac motion frequency, we performed Fourier transformation of the motion signal of the heart, and filtered out the low frequency component in heart motion using a tentative cutoff frequency. The cardiac motion without respiratory impact was reconstructed using the filtered frequency signal.

The choice of the cutoff frequency affected the decoupling process. To effectively decouple the motion, we performed correlation analysis between the respiratory motion, and heart motion with and without the respiratory impact. We evolved the value of the cutoff frequency based on the analysis result until the reconstructed heart motion was no longer correlated with the respiratory motion. The heartbeat frequency w_{heart} was determined from the filtered heart motion signal $f'(t)$.

In the second step of the decoupling process, we defined the patient specific cutting off frequency w_{cutoff} for tumor motion decoupling as

$$\frac{2}{w_{cutoff}}=\frac{1}{w_{heart}}+\frac{1}{w_{resp}} \tag{1}$$

The tumor motion $\vec{m}_{target}$ observed on the fluoroscopy images were decoupled into two components $\vec{m}_{heart}$ and $\vec{m}_{resp}$ corresponding to the heartbeat and the respiratory impact, respectively, and the amplitude of both components of tumor motion was calculated. In Fig. 1 the tumor motion and the separated respiratory and cardiac impact signals were presented.

To verify the magnitude of the tumor motion, two experienced radiation oncologists manually contoured the tumor in both 4DCT and selected frames of the fluoroscopy. The tumor motion magnitude was also derived from the manual contours to verify the motion magnitude calculated from DIR.

Statistics

We calculated both the correlation coefficient and the probability of the no-correlation between the tumor motion and the cardiac motion. We define the two motions as correlated if the probability of no-correlation $p < 0.05$; highly correlated if the correlation coefficient value was >0.67. The average and standard deviations of the correlation-coefficient and cardiac impact amplitude for different lobes and tumor sites have been calculated and studied respectively to determine whether the cardiac impact was location-dependent for lung tumor. In Supplementary Fig. 3 the separated cardiac impact signal was overlaid to the corresponding heart wall motion signal to verify the correlation.

Clinical relevance study

First we conducted a linear regression fit of the cardiac motion impact ratio to the overall tumor motion as a function of the tumor motion amplitude.

Secondly, we regenerated ITVs for each of the patients by expanding the GTVs at the 50% phase with motion margin computed as the sum of the maximum magnitudes of the corresponding cardiac and respiratory induced motion. The volumes of new ITVs were compared with the ones in the original plans. To evaluate the impact of the cardiac motion, the dose coverage of the newly redefined PTVs (ITVs plus setup margin) was computed

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