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PHYSICS CONTRIBUTION

ANALYSIS OF PROSTATE PATIENT SETUP AND TRACKING DATA: POTENTIAL INTERVENTION STRATEGIES

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Purpose: To evaluate the setup, interfraction, and intrafraction organ motion error distributions and simulate intrafraction intervention strategies for prostate radiotherapy.

Methods and Materials: A total of 17 patients underwent treatment setup and were monitored using the Calypso system during radiotherapy. On average, the prostate tracking measurements were performed for 8 min/fraction for 28 fractions for each patient. For both patient couch shift data and intrafraction organ motion data, the systematic and random errors were obtained from the patient population. The planning target volume margins were calculated using the van Herk formula. Two intervention strategies were simulated using the tracking data: the deviation threshold and period. The related planning target volume margins, time costs, and prostate position "fluctuation" were presented.

Results: The required treatment margin for the left–right, superoinferior, and anteroposterior axes was 8.4, 10.8, and 14.7 mm for skin mark-only setup and 1.3, 2.3, and 2.8 mm using the on-line setup correction, respectively. Prostate motion significantly correlated among the superoinferior and anteroposterior directions. Of the 17 patients, 14 had prostate motion within 5 mm of the initial setup position for $\geq$91.6% of the total tracking time. The treatment margin decreased to 1.1, 1.8, and 2.3 mm with a 3-mm threshold correction and to 0.5, 1.0, and 1.5 mm with an every-2-min correction in the left–right, superoinferior, and anteroposterior directions, respectively. The periodic corrections significantly increase the treatment time and increased the number of instances when the setup correction was made during transient excursions.

Conclusions: The residual systematic and random error due to intrafraction prostate motion is small after on-line setup correction. Threshold-based and time-based intervention strategies both reduced the planning target volume margins. The time-based strategies increased the treatment time and the in-fraction position fluctuation. © 2011 Elsevier Inc.

Patient setup, Intrafraction motion, Tracking, Planning target volume, PTV margin, Intervention strategies.

INTRODUCTION

In external beam prostate radiotherapy (RT), target position uncertainty can affect the treatment efficacy (1, 2). Uncertainty arises from inaccuracies in the daily setup procedure, daily movement of the prostate with respect to the setup landmarks, and intrafraction motion. To mitigate its effect, a margin is added to the clinical target volume to define the planning target volume (PTV). A well-defined margin should reflect the anticipated prostate position variations relative to the intended target position for the particular setup procedure in use. For example, if the setup has been determined using daily alignment to skin marks, the margin should accommodate the daily and intrafraction prostate motion relative to those marks. In contrast, if internal fiducial markers have been used for daily image-guided setup, the margin should accommodate the intrafraction organ movement after the initial alignment. The correct margin should be determined from actual observations of the prostate movement for each setup scenario and also should incorporate the intrinsic instrumental and measurement uncertainties of the setup procedure itself.

The prostate position for a particular patient can change systematically during the complete treatment course while fluctuating randomly around its mean daily position. Similar systematic and random variations can occur during a single fraction. By observing and measuring these patterns of fluctuation in a population of patients, one can establish the expected target position uncertainty for any given setup procedure. Appropriate margins can then be estimated from population-based rules that ensure acceptable target coverage for, for example, 90% of the patients.

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It is now possible to track the position of the prostate continuously during each treatment fraction using the Calypso four-dimensional (4D) localization system (Calypso Medical Technologies, Seattle, WA). This system is a wireless electromagnetic system that uses a radiofrequency source/receiver array to localize implanted transponders. Several investigators (3–7) have evaluated the Calypso system localization accuracy in a phantom or have analyzed prostate motion data acquired using this system. Balter *et al.* (3) concluded that the Calypso system has submillimeter localization accuracy in both stationary and moving phantoms. Litzenberg *et al.* (6) analyzed data from 11 prostate cancer patients implanted with Calypso transponders and demonstrated the influence of intrafraction prostate motion on the PTV margin.

We used the Calypso system to perform a clinical study of interfraction and intrafraction prostate movement during RT for a cohort of 17 patients. We then used our observations to estimate the appropriate margins for various daily patient alignment scenarios. Finally, we used our data to simulate various intervention strategies to improve the alignment accuracy and reduce the margins, while accounting for the time costs (increase in treatment time) and potential increases in prostate position fluctuations for some patients.

METHODS AND MATERIALS

The Calypso 4D localization system localizes and tracks electromagnetic transponders implanted in the patient's target volume. The overall system components and operating principles have been described by Balter *et al.* (3). This system can measure the target position with submillimeter accuracy at a rate of 10 Hz. As a part of the research agreement between the Virginia Commonwealth University and Calypso Medical, the digital tracking data were exported from the 4D tracking station and converted into readable format using a software program provided by Calypso Medical.

Patient information

The present study, using an institutional internal review board-approved protocol, analyzed the tracking data from 17 consecutive prostate cancer patients who had undergone treatment with implanted Calypso transponders between 2007 and 2008 at the Virginia Commonwealth University. All patients were educated about transponder implantation and the Calypso System operation during RT. For each patient, three transponders were implanted into the prostate gland at the right base, left base, and apex, using a transrectal ultrasound-guided procedure. Computed tomography (CT) simulation was performed 1 week after implantation to minimize the influence of transponder drift. Permanent skin marks for localizing the isocenter using room lasers were placed at simulation. The CT images were imported into the Pinnacle treatment planning system (Philips Medical Systems, Fitchburg, WI). The coordinates of the transponders and the planned treatment isocenter point, usually the centroid of the transponders, were obtained from the treatment planning system and manually transferred to the Calypso 4D tracking station computer.

Patient setup and tracking

At the start of each treatment fraction, the patient initially underwent treatment setup using the skin marks placed during CT simulation. Next, the patient position was localized using the Calypso system. The treatment target deviation from the machine isocenter was determined from the detected transponder positions in the left–right (LR), superoinferior (SI) and anteroposterior (AP) directions and reported as a translational displacement (Δx, Δy, Δz) of the isocenter position from that measured during simulation CT. The radiation therapists then manually adjusted the treatment table position by that translational displacement (Δx, Δy, Δz) to approximately zero of the deviation before treatment.

During each treatment fraction, the Calypso system continued monitoring the position of the planned isocenter point. Whenever the intrafraction position deviated >5 mm from the setup position for >25 s on any axis, our policy was to interrupt treatment and adjust the treatment couch. However, this procedure was not uniformly implemented. Our analysis was able to identify only 14 treatment sessions that had intrafraction couch adjustments. To avoid bias in our analysis, the data sets of these patients were processed to recover the patient's original prostate motion trajectories as if no adjustments had been made.

During the processing of the tracking data for the present study, some of the tracking files were corrupted. Each patient had an average of about 28 tracking sessions, each about 8 min long. Population histograms of the intrafraction prostate motion along each axis were obtained. The cumulative probabilities of prostate deviating from the initial setup positions in three-dimensional (3D) distances and along each axis were also calculated.

To evaluate the directional properties of prostate motion for each tracking session, we calculated the correlation coefficients among the position data of the three axes using the following equation:

$$Corr(X,Y) = \frac{Cov(X,Y)}{\sqrt{Var(X)^{*}Var(Y)}} \tag{1}$$

where X and Y represent the prostate position history along the LR, SI, or AP axis in each treatment fraction, $Cov(X,Y)$ is the covariance between the two histories, and $Var(X)$ and $Var(Y)$ are their individual variances, for each pair of coordinate axes. To investigate the prostate displacement trend with time, the fraction of time in each minute bin that the prostate was displaced beyond distance threshold (*i.e.,* 3, 5, 7, or 10 mm) was analyzed as a function of monitoring the elapsed time since the initial interfraction setup.

Statistical analysis of inter- and intrafraction position data and their reduction to margin estimates

During treatment session i of patient j, tracking measurement k was obtained from the Calypso system. If we denote patients as $j \in \{1,2,\cdots,N\}$ and each patient's treatment session as $i \in \{1,2,\cdots,M_j\}$ and each tracking measurement as $k \in \{1,2,\cdots,O_{ij}\}$, during a treatment, the clinical target volume location would be as follows:

$$\mathrm{L}_{ijk} = \mathrm{S}_{ij} + \mathrm{X}_{ij}(t_k) \tag{2}$$

where S_{ij} is the setup error and $\mathrm{X}_{ij}(t_k)$ is the organ motion error for Patient j and fraction i at the kth moment. From this, we obtained the following:

$$\overline{\mathrm{L}}_j = \left(1/M_j\right)\sum_{i=1}^{M_j}\left(\mathrm{S}_{ij} + 1/O_{ij}\sum_{k=1}^{O_{ij}}\mathrm{X}_{ij}(t_k)\right)$$

$$\text{mean setup and organ motion error : j} - \text{th patient} \tag{3}$$