International Journal of Radiation Oncology biology • physics

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Clinical Investigation: Genitourinary Cancer

Relationship of Imaging Frequency and Planning Margin to Account for Intrafraction Prostate Motion: Analysis Based on Real-Time Monitoring Data

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Received Sep 6, 2011, and in revised form May 9, 2012. Accepted for publication May 30, 2012

Summary

One thousand forty-five fractions of real-time prostate tracking data from 31 patients were used to assess the relationship of repositioning frequency and planning margins on geometric coverage of the prostate. Results showed comparable magnitude of intrafraction prostate motion between the superior-inferior and anterior-posterior directions. Under ideal circumstances, 1-, 2-, and 3-mm vector planning margins require an imaging frequency of every 15, 60, and 240 seconds to account for intrafraction prostate motion, respectively.

Purpose: Correction for intrafraction prostate motion becomes important for hypofraction treatment of prostate cancer. The purpose of this study was to estimate an ideal planning margin to account for intrafraction prostate motion as a function of imaging and repositioning frequency in the absence of continuous prostate motion monitoring.

Methods and Materials: For 31 patients receiving intensity modulated radiation therapy treatment, prostate positions sampled at 10 Hz during treatment using the Calypso system were analyzed. Using these data, we simulated multiple, less frequent imaging protocols, including intervals of every 10, 15, 20, 30, 45, 60, 90, 120, 180, and 240 seconds. For each imaging protocol, the prostate displacement at the imaging time was corrected by subtracting prostate shifts from the subsequent displacements in that fraction. Furthermore, we conducted a principal component analysis to quantify the direction of prostate motion.

Results: Averaging histograms of every 240 and 60 seconds for all patients, vector displacements of the prostate were, respectively, within 3 and 2 mm for 95% of the treatment time. A vector margin of 1 mm achieved 91.2% coverage of the prostate with 30 second imaging. The principal component analysis for all fractions showed the largest variance in prostate position in the midsagittal plane at 54° from the anterior direction, indicating that anterosuperior to inferoposterior is the direction of greatest motion. The smallest prostate motion is in the left-right direction.

Conclusions: The magnitudes of intrafraction prostate motion along the superior-inferior and anterior-posterior directions are comparable, and the smallest motion is in the left-right direction. In the absence of continuous prostate motion monitoring, and under ideal circumstances, 1-, 2-, and 3-mm vector planning margins require a respective imaging frequency of every 15, 60, and 240 to account for intrafraction prostate motion while achieving adequate geometric target coverage for 95% of the time.

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This research is supported in part by the United States Army Medical Research and Materiel Command (USAMRMC, W81XWH-080-0358).

Conflict of interest: none.

Int J Radiation Oncol Biol Phys, Vol. 85, No. 3, pp. 700–706, 2013
0360-3016/$ - see front matter
http://dx.doi.org/10.1016/j.ijrobp.2012.05.044

Introduction

Modern radiation therapy for prostate cancer, imaging-guided radiotherapy in particular, has significantly improved our ability to localize the prostate prior to each treatment. With daily imaging guidance, the reduction of planning margins from 1.0-1.5 cm to 0.5-0.8 cm in intensity modulated treatment plans permits dose escalation with tolerable treatment toxicities in the rectum and bladder (1-5). Hypofractionated treatment regimens may further increase efficacy of radiation therapy according to the increasing evidence of a low alpha-beta ratio in prostate cancer (2). Further reduction of the planning margins in hypofractionated stereotactic body radiation therapy (SBRT) demands more precise prostate localization before treatment and more frequent imaging guidance during treatment. Furthermore, because the higher dose per fraction may prolong the treatment time, the probability of intrafraction prostate motion is greater than in conventional treatments. Using an electromagnetic device (Calypso, Calypso Medical, Seattle WA), monitoring the prostate motion and intervention during treatment is possible at a frequency of 10 Hz. If real-time monitoring at such a high frequency is not available, the relationship between the frequency of intrafraction monitoring and planning margins is not clear. The purpose of this study was to determine the magnitude of intrafraction prostate motion using real-time positioning data and to assess the idealized relationship between the planning margins and frequency of imaging guidance during treatment in the absence of continuous monitoring of the prostate location during treatment.

Methods and Materials

Thirty-one patients with prostate cancer were treated using intensity modulated radiation therapy (IMRT). They underwent real-time monitoring using an electromagnetic tracking system (Calypso) at our institution, and data from these patients were retrospectively analyzed. All patients underwent implantation of 3 beacon transponders within the prostate before simulation. A typical IMRT course consisted of 38-39 fractions. In our clinical practice, we used a threshold action level of 3 mm in any direction lasting >30 seconds to interrupt the treatment for repositioning. Thus, some daily treatments were split into 2-3 fractions. These split fractions were considered independent fractions for this analysis but only fractions with a treatment time >120 seconds of data available were included. The mean fraction length was 7 minutes and 23 seconds (±94.1 seconds), and 1045 fractions were analyzed with a mean of 34 fractions (range 2-41) per patient.

Clinical alignment protocol

Pinnacle 8.0m treatment planning software (Philips, Amsterdam, the Netherlands) was used to identify the transponders and treatment isocenter coordinates. The coordinates of the transponders were manually entered by the therapists to the Calypso System and checked by a physicist to prepare for daily patient setup and real-time tracking during treatment.

Before the CT simulation, patients were instructed to have a bowel movement and to drink 20 oz of fluid, 30-45 minutes before the simulation. Patients were advised to follow the same instructions before each daily treatment to attempt to maintain the same anatomic relationship between the prostate and organs at risk. No other interventions, such as enemas or rectal balloons, were used. Before each daily treatment, the patient was initially aligned to skin marks and then aligned to the target as defined by the Calypso isocenter. During treatment, the Calypso system continuously tracked the positions of the prostate. When the center of the transponders moved outside of the predetermined tolerance (3 mm displacement in any direction >30 seconds), the radiation beam was paused to reposition the patient. The operation and accuracy of the Calypso has been described previously with evidence in patients showing a mean (SD) agreement between Calypso and kV X-ray localization within 1.5 mm (0.9) and 1.9 mm (0.9) (4, 6-8). Data in phantoms has shown a mean (SD) agreement between X-ray and Calypso of 0.5 mm (0.1 mm) (7). These numbers only represent the difference between the KV X-ray and Calypso system as the ground truth is unknown. Of the 1045 fractions analyzed, 9 fractions in 8 patients had treatment interrupted.

Data process and analysis

Daily prostate localization and tracking data for each patient was stored on the Calypso workstation and was exported from the workstation onto individual spread sheets within Microsoft Excel (Microsoft, Seattle, WA). A Matlab (Mathworks, Natick, MA) tool was written to process the data efficiently.

The Calypso tracking data of each fraction contained a series of points composed of x, y, and z coordinates as a function of treatment time. The x, y, z in centimeters represents the prostate displacement relative to the isocenter at time zero with a sampling frequency of 10 Hz. The magnitude of the prostate displacement at a given time was calculated as the Euclidean distance from the initial position as given by Eq. (1).

$$D(t) = \sqrt{x(t)^2 + y(t)^2 + z(t)^2} \quad (1)$$

D(t) is the magnitude of displacement and x(t), y(t), and z(t) are the displacements in each of 3 orthogonal directions.

To simulate an ideal imaging and position correction of the prostate back to the isocenter, the displacement of x_i, y_i, and z_i at the time of correction, i, was set to zero by subtracting x_i, y_i, and z_i from the subsequent displacements of the fraction. For all fractions, to simulate different imaging protocols, this correction procedure was repeated at different intervals during each fraction (once every 10, 15, 20, 30, 45, 60, 90, 120, 180, and 240 seconds). Thus, for each fraction, the data was analyzed 10 times with a different simulated imaging frequency at each time.

To determine planning margins to account for intrafraction prostate motion, we calculated the percent of time during each fraction that the prostate displacement was greater than the given magnitudes of 1, 2, 3, 5, and 10 mm. In addition, a principal component analysis (PCA) was performed on each of the uncorrected fractions to characterize the 3-dimensional directions of prostate motion. PCA breaks down the data into 3 orthonormal principal component vectors, with the first in the direction of greatest variance. The second is orthogonal to the first and in the direction of greatest remaining variance, and the third is orthogonal to the other two and in the direction of least variance. The PCA provided the direction and magnitude of prostate motion as described by the variance of the probability distribution of prostate position.