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Comparison of Dose Decrement from Intrafraction Motion for Prone and Supine Prostate Radiotherapy

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Abstract

Background and Purpose—Dose effects of intrafraction motion during prone prostate radiotherapy are unknown. We compared prone and supine treatment using real-time tracking data to model dose coverage.

Material and Methods—Electromagnetic tracking data was analyzed for 10 patients treated prone, and 15 treated supine, with IMRT for localized prostate cancer. Plans were generated using 0, 3, and 5 mm PTV expansions. Manual beam-hold interventions were applied to reposition the patient when translations exceeded a predetermined threshold. A custom software application (SWIFTER) used intrafraction tracking data acquired during beam-on to model delivered prostate dose, by applying rigid body transformations to the prostate structure contoured at simulation within the planned dose cloud. The delivered minimum prostate dose as a percentage of planned dose (Dmin%), and prostate volume covered by the prescription dose as a percentage of the planned volume (VRx%) were compared for prone and supine treatment.

Results—Dmin% was reduced for prone treatment for 0 ($p=0.02$) and 3 mm ($p=0.03$) PTV margins. VRx% was reduced for prone treatment only for 0 mm margins ($p=0.002$). No significant differences were found using 5 mm margins.

Conclusions—Intrafraction motion has a greater impact on target coverage for prone compared to supine prostate radiotherapy. PTV margins of 3 mm or less correlate with a significant decrease in delivered dose for prone treatment.

Keywords

Prostate; Radiotherapy; Prone; Tracking; Calypso

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INTRODUCTION

Prostate radiotherapy may be administered using either prone or supine patient setup. Although supine treatment is often preferred due to concern for respiratory motion in the prone position[4, 8, 22] and improved patient comfort[1, 27], prone treatment has been advocated to improve setup reproducibility and reduce the dose to the rectum and bladder[12, 16, 26].

The application of real-time fiducial tracking during radiotherapy allows for comparative study of intrafraction prostate motion for both prone and supine treatment. While intrafraction prostate motion during supine treatment is well characterized[10, 11, 13, 17, 28], there are conflicting data regarding the extent of prostate translation during prone treatment. Some studies have reported greater translation of the prostate in the prone compared to supine position [4, 8], and others have found the motion to be equivalent[2, 27]. Additionally, rotational motion of the prostate during prone positioning has never been investigated and may have significant dosimetric consequences, as has been demonstrated in supine prostate treatments [17].

We have previously developed a model to compare the actual delivered prostate dose with the planned dose[15], using real-time tracking data to account for translational and rotational organ motion. For supine treatment we observed patient-specific reductions in target coverage due to intrafraction motion, with the greatest effect observed for reduced PTV margins[17]. This prior study has highlighted that a considerable degree of dosimetric variance can be observed across many patients treated to the prostate due to differences in target geometry and motion. We suspected that differences in the prone setup position would introduce an additional source of variance that may further impact target coverage and thus should be investigated. The purpose of this study was to compare the impact of organ motion on delivered dose for prone and supine prostate radiotherapy, and to evaluate if PTV margins could be reduced for prone treatment.

METHODS

Medical records and fiducial tracking data were reviewed for 10 patients treated prone, and 15 treated supine, with definitive intensity modulated radiation therapy (IMRT) for prostate cancer utilizing the Calypso® 4D Localization System (Calypso Medical, Seattle WA) between November 2007 and February 2010. Tumor stage included men with T1c (n=20), T2 (n=3), and T3 (n=2) disease, and risk stratifications[3] included low (n=12), medium (n=7), and high risk (n=6) disease. Patient characteristics were generally balanced between the prone and supine groups, although body mass index was greater for prone (median 35) compared to the supine (median 28) treatment ($p<0.001$, Student's unpaired two tailed t-test). Detailed patient characteristics are shown in Table 1.

Our institutional protocol for prostate fiducial marker placement and radiotherapy treatment planning has been previously described[17, 19] and is summarized in the supplemental materials. The clinical target volume (CTV) was formed by contouring the prostate on the CT and MR fusion images. Since we did not analyze motion of the lymph nodes or seminal vesicles in this study, a new volume containing the prostate only was contoured for higher risk patients whose clinically treated volumes included either the seminal vesicles or pelvic lymph nodes.

For each patient, 0 mm, 3 mm, and 5 mm uniform expansions were applied about the prostate to create PTV volumes. Five or seven field IMRT plans using a step-and-shoot multi-leaf collimation (SMLC) technique were generated with a planning goal of 100% CTV and 98% PTV coverage by the prescription dose. The prescription dose ranged from 70

Gy in 2.5 Gy fractions to 79.2 Gy in 1.8 Gy fractions. Rectum constraints were applied such that the volumes of rectum receiving greater than 65 Gy (V65) and 40 Gy (V40) were no more than 17% and 35%, respectively. Bladder constraints were applied such that the V65 and V40 were no more than 25% and 50%, respectively.

Real-time electromagnetic tracking was obtained at 0.1 second intervals for all patients. Our method of modeling the delivered radiotherapy dose using a custom Matlab program called SWIFTER (Semi-Automatic Workflow using Intra-fraction Fiducial-based Tracking for Evaluation of Radiotherapy) has been previously described[18], and is summarized in the supplemental materials. For the patients in this study, manual beam hold was performed by therapists for instances when the target isocenter moved a certain distance from machine isocenter. Therapists were given discretion to use either a 3 mm or 5 mm intervention threshold based on the degree of intrafraction motion observed at the first fraction. For supine setup the intervention threshold was set at 3 mm displacement for all fractions. For prone setup the intervention threshold was set at 3 mm displacement for 152/381 fractions (40%), and 5 mm displacement for 229/381 (60%) fractions. Example motion traces for prone and supine treatment are shown in Figure 1.

Dosimetric coverage accounting for intrafraction motion was assessed for each PTV margin by calculating the minimum delivered prostate dose as a percentage of plan (Dmin%), and the prostate volume covered by the prescription dose as a percentage of the planned volume at prescription (VRx%). Student's unpaired two tailed t-test was then used to compare Dmin% and VRx% between the prone and supine treatment groups. To assess for any bias introduced from variability in the tracking limit range among prone patients, Dmin% was compared between patients treated in the prone position using either a 3 mm or 5 mm tracking limit range.

To evaluate deformation during prone and supine treatment, inter-transponder distances sampled at 0.1 second intervals throughout treatment were analyzed and the distributions were compared between prone and supine setup using a two-sample Kolmogorov-Smirnov (KS) test. Histogram plots of inter-transponder distances were generated for prone and supine setup, and variability of the measured inter-transponder distances was compared to the known positional accuracy of the tracking system (<0.5 mm)[21].

Student's unpaired two tailed t-test was used to compare PTV coverage, dose to the rectum and bladder, mean intrafraction isocenter displacement, prostate rotation, Dmin, and VRx% between the prone and supine treatment groups. The two-sample Kolmogorov-Smirnov (KS) test was used to compare the variability of intertransponder distance between the prone and supine groups. Differences between groups were considered statistically significant for p-values < 0.05.

RESULTS

Treatment plan parameters are illustrated in Table 2 (Supplemental Materials). There was no significant difference in the percentage of PTV covered by prescription dose between the 0 mm, 3 mm, and 5 mm margin plans (p=NS, Student's paired two tailed t-test) or between the prone and supine groups (p=NS, Student's unpaired two tailed t-test). Reduced PTV margins correlated with a reduction in the rectum and bladder V65 and V40 parameters for both prone and supine treatment (Table 2 – Supplemental Materials).

Table 3 (Supplemental Materials) illustrates the mean translational and rotational motion for both prone and supine treatment compared with the position at simulation. Increased translational and rotational intra-fraction motion was observed for prone compared to supine setup (p<0.001 for each motion component, Student's unpaired two tailed t-test).

Figure 2 shows planned (black) and delivered (red) DVH curves, and Table 4 shows the effect of patient motion on delivered dose for 0, 3, and 5 mm PTV margins both for the prone and supine treatment groups. Dmin% was significantly reduced for prone compared to supine treatment for 0 ($p=0.02$) and 3 mm ($p=0.03$) PTV margins. VRx% was reduced for prone compared to supine treatment only for 0 mm margins ($p=0.002$). No significant differences were found for 5 mm PTV margin plans.

The variability in displacement thresholds (3 versus 5 mm) used by the Calypso System to signal therapists to intervene treatment during tracking showed no impact on dosimetric coverage. There was no difference in Dmin% among patients treated in the prone position for treatment using 3 mm ($n=4$) compared to 5 mm ($n=6$) therapist intervention thresholds during treatment delivery ($p=NS$). Figure 3 (Supplemental Materials) illustrates similar Dmin% at each PTV margin for treatment with 3 mm compared to 5 mm therapist intervention thresholds for the prone cohort. Figure 4 (Supplemental Materials) displays histograms of inter-transponder distance deviation from the mean for the entire prone and supine patient cohorts across all fractions. There was greater variability in inter-transponder distance for supine compared to prone setup ($p<0.0001$, two-sample KS test).

DISCUSSION

Both prone and supine setup positions are frequently used for prostate radiotherapy. We applied real-time tracking data to compare the effect of intrafraction motion on delivered prostate dose between prone and supine setup for various PTV margins. While equivalent dose coverage between prone and supine setup was observed for 5 mm PTV margins, coverage was compromised when PTV margins were reduced.

Increased intrafraction displacement measured for patients treated prone is consistent with previously reported studies[1, 9]. Bittner et al studied prostate motion in the prone position using real-time electromagnetic tracking and found prostate displacement $>2\text{mm}$ during 38% of treatment[2]. This degree of translational motion for prone setup is similar to that observed in our series (mean composite displacement $2.3 \pm 1\text{ mm}$). Studying the motion trends of patients treated in a prone position can provide a comparison of patient movement, although no conclusions about the dosimetric impact of prone positioning can be made. By incorporating dosimetric assessment using the SWIFTER application, we provide an evaluation of the dose effect of this motion.

Notably, for most patients treated with 5 mm margins, the effect on delivered dose for prone compared to supine motion was relatively small, but increased as margins were reduced to 3 mm and 0 mm. A reduced Dmin%, but not VRx% was observed using 3 mm PTV margins for prone compared to supine treatment. The observation of a reduced minimum prostate dose, but only minor change in the percent volume at prescription dose, suggests that prostate deviations from the PTV primarily occurred for small peripheral prostate volumes. Although no change in VRx% between prone and supine treatment was observed for the population as a whole, reductions in VRx% were noted for select patients in the prone group. For 2/10 patients treated prone using 3 mm PTV margins with the greatest dose reduction, Dmin% was reduced to 84 and 89 percent of the planned dose, illustrated by the degree of difference between the black planned and red delivered dose curves (Figure 2a, middle). Significant individual variability in patient motion has been previously reported[11, 13, 28], in particular for treatment without use of a rectal balloon. Due to the implication of patient-specific motion on individualized target coverage, we caution against use of PTV margins less than 5 mm for prone treatment without use of a rectal balloon. The impact of adding a rectal balloon to reduce variability in intrafraction motion is of interest for further study. Given variability in the therapist intervention threshold used for our prone patients,

we compared Dmin% for treatment with either a 3 mm or 5 mm intervention threshold and found similar Dmin% values for both intervention thresholds. This similarity in Dmin% suggests that variability in the intervention threshold did not bias our comparison with supine treatment, although a larger cohort would be necessary to rigorously study the dosimetric effect of threshold differences. Our data should not be extrapolated for patients treated without real-time tracking, since intrafraction tracking allows for therapist intervention if prostate translations exceed the displacement threshold value. Although counterintuitive that a dose decrement is observed for 3 mm and 5 mm PTV margins with an intervention threshold of 3 mm, two factors contribute to this occurrence. First, the 3 mm action threshold was applied along each axis (superior-inferior, left-right, anterior-posterior). If a patient were to deviate 3 mm from the planned position in each direction, it would result in a total composite displacement of $\sqrt{3^2+3^2+3^2} = 5.2$ mm. Second and perhaps of greater importance is the effect of rotation on the dose decrement. Greater prostate rotations were observed for the prone cohort, and although checked prior to each treatment, no intervention threshold for prostate rotations was used.

Although our study has some limitations, it also has significant strengths. Ideally, prone and supine setup would have been compared in a paired fashion, with each patient undergoing one prone and one supine simulation. The patient characteristics of our cohort were generally balanced between prone and supine setup (Table 1), although body mass index was greater for the prone treatment group. Prone treatment was chosen for several patients when obese body habitus prevented supine tracking, since operation of the Calypso System requires that the implanted transponders are within a certain proximity to the electromagnetic array. We cannot discount the possibility that obese body habitus may have altered the pattern of motion in the prone position, although a similar pattern of motion (Figure 1) was observed throughout the prone cohort, regardless of body mass index.

Our model used real-time tracking data to individually calculate the delivered prostate dose for each patient, based on rigid body transformations of the prostate within the planned dose cloud. Individualized dose calculation is an advance over prior models of prostate motion that were limited to analysis of translational motion without modeling of delivered dose[2, 4, 8, 27]. Although we believe our model to be an accurate calculation of prostate dose delivery, some approximation was necessary for calculation of delivered dose. We modeled the prostate as a rigid body, and neglected any possible organ deformation. Prior studies have characterized deformation as measuring 2 mm or less[14, 24]. One MRI study of prostate deformation in 25 patients by Nichol et al measured random prostate surface deformation of 1.5 mm, with surface contouring uncertainty of 0.8 mm[14]. To evaluate if deformation may have altered prostate anatomy, we measured intrafraction variability in intertransponder distance (Figure 4 – Supplemental Materials). Deformation as measured by intertransponder distance variability was statistically increased for supine compared to prone treatment, although most intertransponder distance variability was generally small, and within the 0.5 mm positional accuracy of the tracking system (Figure 4 – Supplemental Materials). Real-time integration of imaging and dose-calculation is required to more definitively study the effect of intrafraction deformation, to account for all anatomic changes, in particular along the prostate edge. Though limited by current technology, several groups are working towards development of magnetic resonance guided radiotherapy, which would potentially solve this problem by integration of real-time imaging with dose recalculation[5, 7, 20].

It is of interest to model the impact of intrafraction motion on rectum dose, since volumetric imaging studies suggest variability in rectum position during radiotherapy may alter rectum dose by up to 15%[6]. Since the implanted transponders can only provide direct motion data for the target alone, our primary objective for the current study was to model the delivered

prostate rather than rectal dose. A more thorough analysis of dose to the rectum would ideally involve periodic imaging, which could provide full volumetric data. It would be of interest for future study to model rectal motion relative to prostate fiducial position by incorporating data from daily imaging such as cone beam CT, which was not available for the current cohort. Although not a direct aim of our study, it is notable that dose to rectum and bladder was reduced for patients planned in the prone compared to supine position (Table 2 – Supplemental Materials). Similar findings were reported in prospective trials where patients were simulated and planned both prone and supine[16, 26], although this difference has been proposed to be an artifact of increased rectal volume due to air filling in the prone position[26].

In comparing prone and supine treatment, we reported the dose impact of intrafraction motion for varying PTV margins, but refrained from defining what constitutes “adequate” or “inadequate” treatment. Although we demonstrated a greater impact of intrafraction motion on prostate dose for prone positioning, the decision to treat prone or supine rests on many factors including patient tolerance and rectum or bladder dose considerations. Interventions not utilized in the current study, such as placement of a rectal balloon during treatment, may also help to reduce prostate motion in either the prone or supine treatment position[23, 25], and are of interest for future study.

CONCLUSION

Intrafraction motion during prostate radiotherapy has a greater impact on target coverage for prone compared to supine treatment. PTV margins of 3 mm or less correlate with a significant decrease in delivered dose for prone compared to supine treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Real-time tracking data for prone (A) and supine (B) treatment, including right/left (top), superior/inferior (middle), and anterior/posterior (bottom) tracking data. The shaded regions illustrate when the treatment beam was turned on for each of the planned fields. A unique pattern of superior/inferior and anterior/posterior motion is evident for prone treatment, consistent with greater influence of respiration on intrafraction movement.

Figure 2. Prostate Dose Volume Histogram (DVH) curves for the entire prone (A) and supine (B) cohorts, illustrating the planned (black) and delivered (red) prostate dose for each PTV margin. A greater decrement between the planned and delivered dose is evident for prone treatment, with a greater effect as PTV margins are decreased.

Table 1

Patient Characteristics

Treatment Position	Prone	Supine
Number of patients	10	15
Median Age	68 yrs.	71 yrs.
(Range)	(50–83 yrs)	(58–83 yrs.)
Tumor Stage (%)		
T1c	8 (80)	12 (80)
T2a	1 (10)	1 (7)
T2c	1 (10)	-
T3a	-	1 (7)
T3b	-	1 (7)
Risk Stratification (%)		
Low	3 (30)	9 (60)
Medium	3 (30)	4 (27)
High	4 (30)	2 (13)
Median Body Mass Index (Range)	35 (23–42)	28 (18–41)
Median Prescribed	7740 cGy	7380 cGy
Dose (Range)	(7000 – 7740 cGy)	(7000 – 7920 cGy)

Table 4

Effect of patient motion on dose for each treatment position and PTV margin

PTV margin	0 mm			3 mm			5 mm		
	Treatment Position	Prone	Supine	<i>p</i> ¹	Prone	Supine	<i>p</i> ¹	Prone	Supine
Delivered Dmin as % of planned Dmin		86.7 ± 7	92.8 ± 6	0.02	95.7 ± 6	99.2 ± 2	0.03	97.6 ± 5	100.1 ± 0.4
Delivered VRx% as % of planned VRx%		94.8 ± 3	98.2 ± 1	0.002	99.6 ± 1	100.0 ± 0.2	NS	99.8 ± 0.4	100.0 ± 0

Abbreviations:

¹ *p* = statistical *p*-value denoting level of significance;

² NS = not statistically significant at level *p*<0.05