

Observations of Prostate Intrafractional Motion during External Beam Radiation Therapy

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Abstract— Results of real-time monitoring of prostate intrafractional motion during external beam radiation therapy are presented based on the observation using the Calypso 4D localization system with implanted electron-magnetic transponders in the prostate gland. Prostate displacement during treatment was sampled at a frequency of 10Hz and the data for 105 patients was analyzed. The fractional time that the prostate was displaced by more than 3, 5, 7 and 10mm was calculated for each patient. The statistical results of the prostate displacement in each direction and possible reduction from employing intrafractional intervention are discussed. About 29% of the treatment fractions needed intervention at least once if the displacement threshold was 3mm off the base line in all the three directions and the percentage was reduced to 5% after the threshold increased to 5mm. The percentage time of prostate off the base line by 3mm and 5mm in any direction is 13.4% and 1.8%, respectively, for the 105 patients investigated, and 41% and 15% respectively for 7 patients who exhibited the largest prostate motion, if no intervention was performed during the treatment. The mean and standard deviation of the prostate displacement were less than 1mm in any direction for all the patients. In contrast, the mean values for the 7 patients were significantly higher, 1.4mm in S-I direction and 2.3mm in A-P direction. Comparing with other geometrical uncertainties, the prostate intrafractional motion is not a major contributor for the general patient population and prostate motion tracking during the treatment plays a small role in the treatment margin reduction. However, a small fraction of patients who have large intrafractional motion can benefit significantly from real-time motion tracking and threshold-based intervention based on our current margin setting.

Keywords— Prostate Cancer, Intrafractional Motion, Treatment Margin

I. INTRODUCTION

There are several different geometrical uncertainties during radiotherapy that may affect treatment outcome. Great attention has been paid to some of them, such as setup error or interfractional motion with some new localization techniques used in clinical practice and the delineation error when the target volume is delineated with guidance of multiple image modalities. Knowledge about prostate intrafractional

motion and its effects for radiotherapy is still less clear though it has been investigated by some investigators [1-3] using different techniques. These studies have provided a general understanding of the frequency and magnitude of the prostate intrafractional motion. However, they have been limited either in patient population and fraction number or in that the prostate was not continuously monitored, was monitored for a relatively short time, or was not actually monitored during radiation therapy. Continuous observation during the entire fraction of radiation therapy is necessary to fully understand the nature of prostate intrafractional motion.

4D localization systems, such as the fluoroscopic X-ray imaging system with/without implanted fiducial markers and the Calypso 4D localization system (Calypso Med. Tech. Inc., Seattle, WA) with implanted Beacon transponders [4-6] are clinically available and observations on real-time prostate motion have been reported [5-7]. With intrafractional intervention, 4D localization systems can track tumor motion and reduce its effects. However, it is well known that intrafractional motion of the pelvic anatomy has relatively less effect on the treatment than other sources of geometrical uncertainty and 4D prostate motion tracking is costly and challenging. Therefore, it is important to know how much we can gain from prostate motion tracking and the feasibility of treatment margin reduction with intrafractional interventions and 4D treatments.

In this work, results of continuous observation of prostate intrafractional motion are reported. Some examples of prostate intrafractional motion behaviors and the displacement distribution are shown for some patients. Prostate motion in each direction and 3D, the fraction time of certain displacement range and statistical results of the prostate displacement during the radiation therapy are presented. Statistical distributions of the prostate intrafractional displacement were calculated for general patient population and specifically for patients who exhibited the largest intrafractional motion. They were also calculated for treatments with different threshold-based intervention and 4D treatments for the entire patient population and the small group of patients. The gains of using the 4D localization system for prostate treatment were evaluated based on the uncertainty reduction.

II. MATERIAL AND METHODS

A. Calypso 4D localization system

The Calypso 4D Localization System with implanted electromagnetic transponders (Calypso Beacons) can continuously monitor the location of the tumour and it is commercially available for prostate treatments. The implanted Beacon transponders can be detected by the system at a frequency of 10Hz and the three-dimensional positions of the transponders and the target isocenter or the geometric centre of the implanted Beacons can then be tracked. The system can be used to objectively guide the initial patient setup by localizing the transponders. It can also provide continuous, real-time localization and monitoring of the prostate. One concern of using planted Beacons and fiducials in radiation therapy is their migration. In order to limit the effects of migration, the planning CT scan is usually taken a week after the implant. Necessary corrections to the Beacons' positions can be made if Beacons migrate during the treatment course.

Prostate intrafractional motion was observed and recorded using two Calypso 4D localization systems in our center. The prostate displacement from the base line was recorded separately in three directions at a frequency of 10Hz and there were 6000×3 to 12000×3 data points for every treatment fraction because the treatment time was 10 to 20 minutes for most of the patients. Each of the treatment fractions was analyzed to determine the fraction of time the prostate was displaced by a certain distance. The fraction of time for prostate displacements >3 , >5 , >7 , and >10 mm was scored for each directions and 3D displacement for individual patient and a patient population. Prostate displacements distribution in a 2D plane was also reported for some patients.

Statistical analysis of prostate displacement in three directions was performed based on the prostate intrafractional motion data for the randomly selected 775 treatment fractions from 105 patients treated in our center. The means and standard deviations for the prostate displacement were calculated in three directions. These values were also calculated after intrafractional interventions with different threshold were performed and the gain on reducing the motion effect from using this technique was evaluated. Threshold-based intrafractional intervention can be performed by stopping the beam delivery (gated treatment) and/or moving the prostate back to the base line by moving the couch whenever the prostate displacement in any direction is more than the predetermined threshold. Same analysis was also performed for some individual patients who have exhibited the biggest intrafractional motion.

III. RESULTS

We have evaluated the continuous motion tracking data for about 4000 fractions of 100 prostate patients. The motion behaviors of prostate varied from stable target at baseline, continuous drift, transient excursion, frequent excursions and some combined behavior. Figure 1 shows some examples. These have been observed by other investigators [6, 7] as well. Some motion patterns were simply irregular and difficult to categorize. The motion behaviors varied from patient to patient, day to day and often unpredictable. Some motion behaviors only happened occasionally for some patients. But we do see more motions for some patients than others.

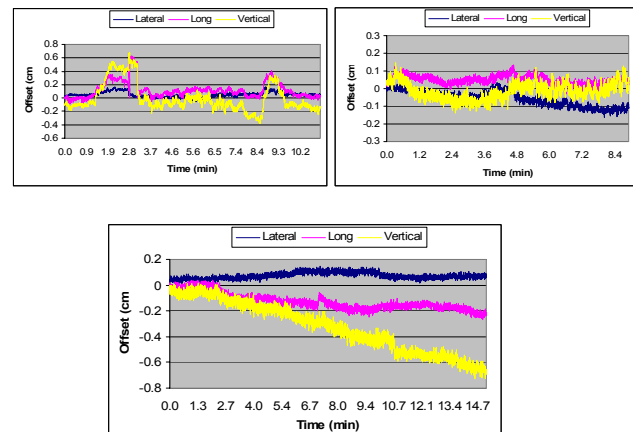


Figure 1 Examples of prostate intrafractional motion behaviors observed with continuous tracking.

The percentage tracking time of 3D displacement beyond a distance was presented for twenty patients in Table 1. The magnitude and duration of the prostate displacements varied widely among the 20 patients. The least displacement was observed in Patient 2 and 16 with only 1.7% and 1.5% tracking time with displacement >3 mm. The most displacement was observed in patient 17. The percentage time for displacement in 3D >10 , >7 , >5 , and >3 mm was 0, 0.5, 21.6 and 45.7%. The average 3D displacements for the population of 20 patients were 19.2% for displacement >3 mm, 3.9% for displacements >5 mm, 0.4% for displacements >7 mm and 0.1% for displacements >10 mm. 3D displacement is a quadratic sum of displacements in three directions and the percentage time included motion to all the directions. Because prostate motion in the lateral direction is not as significant as in other two directions, 2D prostate displacements distribution in sagittal view are shown in Figure 2 for patient 16, patient 7, patient 17 and average of the 20 patients. From left to right is the inferior-superior

direction and from top to bottom is the anterior-posterior direction. The lines from inside to outside indicate that the

Table 1. Percentages of the total electromagnetic tracking time during which the prostate was beyond a 3-dimensional distance. Data are from 20 patients and 157 fractions. Average tracking time was 11.4 minutes per fraction.

Patient #	3-D displacement			
	>10mm	>7 mm	>5 mm	>3 mm
1	0.0	0.0	0.2	23.5
2	0.0	0.0	0.0	1.7
3	0.0	0.0	0.0	3.3
4	0.2	1.0	3.3	14.2
5	0.0	0.0	0.1	6.6
6	0.0	0.3	1.1	3.8
7	0.0	0.0	2.1	13.5
8	0.0	0.0	0.0	12.3
9	0.0	0.1	2.6	8.6
10	0.0	0.0	3.4	48.8
11	0.0	0.0	7.0	39.4
12	0.0	0.0	0.3	14.5
13	0.0	0.0	2.0	21.3
14	0.5	1.5	9.5	35.4
15	0.0	0.0	9.0	35.7
16	0.0	0.0	0.5	1.5
17	0.0	0.5	21.6	45.7
18	0.0	0.1	0.2	7.2
19	0.5	4.3	14.6	36.9
20	0.0	0.0	0.3	10.4
Average	0.1	0.4	3.9	19.2
1 SD	0.1	1.0	5.8	15.5
Medium	0.0	0.0	1.5	13.9
Min	0.0	0.0	0.0	1.5
Max	0.5	4.3	21.6	48.8

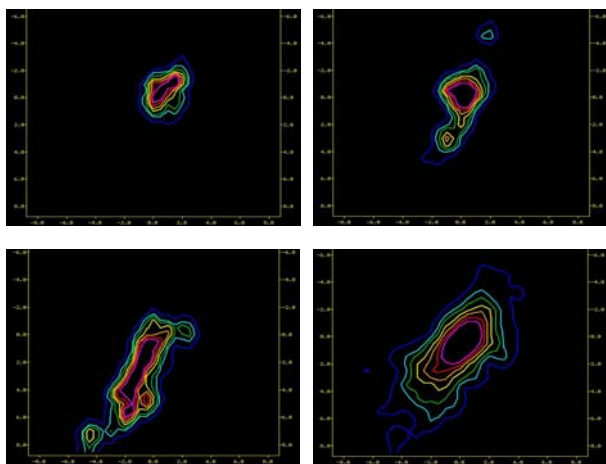


Figure 2. Prostate displacement distribution in sagittal view for patient 16, 7, 17 and average of all 20 patients, From left to right is inferior-superior direction. The lines from inside to outside indicate that prostate displacements have 50, 60, 70, 80, 90, 95 and 99% possibility to be within the areas besieged by the lines.

displacement has 50, 60, 70, 80, 90, 95 and 99% possibility to be within the areas besieged by the lines. We can see from the results that the prostate moves mostly to the inferior-posterior direction. Fraction of time of prostate displacement only in anterior-posterior direction was also analyzed separately in Figure 3 for the 20 patients. Percentage time of prostate displacement in different ranges was presented for these 20 patients and their average (No. 21). Negative value of the range means prostate moves to posterior direction. It is also clear to see that prostate move more frequently to the posterior direction for some patients.

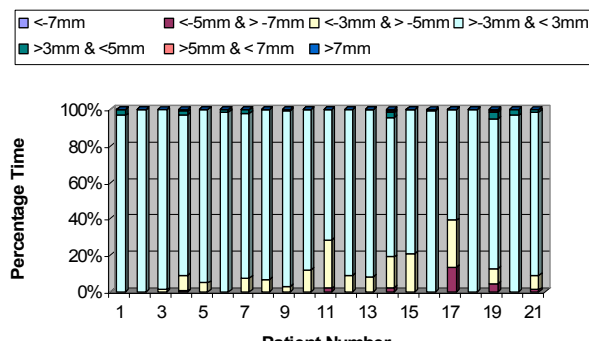


Figure 3. Percentage tracking time of the prostate displacement along posterior-anterior direction within a range for the 20 patients and their average (No. 21).

Among the randomly selected 775 treatment fractions for the 105 prostate patients, 29.3% of them need intervention at least once if the threshold is 3mm from the base line. The rate decreases to 4.8% for a 5mm threshold. The percentage time of the prostate off the base line for 3mm and 5mm in any direction is 13.4% and 1.8% respectively if no intervention is performed during the treatment.

The mean values of the prostate displacement from the base line and the standard deviations of systematic uncertainty and random uncertainty for these 105 prostate patients are shown in Tables 2 for prostate intrafractional motion with no intervention, 5mm and 3mm threshold-based interventions. The positive mean values indicate the prostate moved to the left, the superior and anterior directions respectively and larger margins should be added in these directions. The negative values indicate the prostate moved to the right, inferior and posterior directions and larger margins should be added to those directions. There is no difference is observed in lateral direction after 5mm or 3mm threshold based interventions were performed. This means the intrafractional motion in lateral direction is ignorable. The means and systematic uncertainties of intrafractional motion in superior-inferior and in anterior-posterior directions are all less than 1mm and they become

Table 2. Measured intrafractional displacement with no intervention, 5mm and 3mm threshold-based intervention

	Intervention	Mean(mm)	Σ_{intra} (mm)	δ_{intra} (mm)
L-R	no	0.2	0.34	0.66
	5mm	0.2	0.34	0.66
	3mm	0.19	0.34	0.65
S-I	no	-0.09	0.77	1.38
	5mm	-0.08	0.72	1.32
	3mm	-0.02	0.54	1.07
A-P	no	-0.75	0.80	1.56
	5mm	-0.69	0.70	1.44
	3mm	-0.50	0.50	1.15

smaller after threshold based interventions were performed especially with 3mm threshold. Comparing with other geometry uncertainties whose systematic uncertainties can be more than 2mm, such as setup error and target delineation error, uncertainty caused by the intrafractional motion is not a major contributor to the geometrical uncertainty for the general patient population and therefore prostate motion tracking and threshold-based intervention during the treatment play a small role in treatment margin reduction. However, prostate treatment with motion tracking and setup adjustment during treatment is one kind of adaptive treatment. Therefore, gains from prostate motion tracking for individual patient should be studied as well. Seven of these 105 (6.7%) prostate patients which include patient 17 exhibited significant large intrafractional motion and the percentage time of the prostate off the base line for 3mm and 5mm in any directions was 41% and 15% respectively if no intervention was performed during the treatment. The mean values and the standard deviations of the prostate displacement from the base line for this group of patients are listed in Table 3 for prostate intrafractional motion with no intervention, 5mm and 3mm threshold-based interventions, respectively. The mean value of the error caused by intrafractional motion is significantly bigger than that of general patient population and intrafractional intervention can reduced it to be less than 1mm. The standard deviation in S-I

Table 3. Measured intrafractional displacement with no intervention, 5mm and 3mm threshold-based intervention

	Intervention	Mean(mm)	Σ_{intra} (mm)	δ_{intra} (mm)
L-R	no	0.42	0.50	0.69
	5mm	0.42	0.50	0.69
	3mm	0.42	0.50	0.69
S-I	no	-1.27	0.62	1.74
	5mm	-1.01	0.39	1.4
	3mm	-0.62	0.35	1.05
A-P	no	-2.27	0.76	2.15
	5mm	-1.40	0.46	1.54
	3mm	-0.99	0.31	1.06

and A-P directions can also be reduced by interventions. And thus, treatment margin reduction will be more significant for this group of patient than the general patient population and this group of patient can benefit more from real-time motion monitoring and intrafractional intervention.

IV. CONCLUSIONS

The translational intrafractional motion of prostate was quantified using an electronmagnetic tracking system that can continuously monitor the prostate position during treatment delivery. Prostate motion has more significant effects on a small fraction of patients who have large intrafractional motion but not the general patient population. This group of patients can benefit more from real-time motion tracking and threshold-based intervention with current treatment margin setting. If the treatment margin currently used clinically is suitable for the general patient population, it may not be adequate for this group of patients when the intrafractional motion is not controlled or corrected. Prostate intrafractional motion control may improve the treatment outcome for this group of patients.

REFERENCES

- Langen KM and Jones DT (2001) 'Organ motion and its management', *Int. J. Radiat. Oncol. Biol. Phys.*, 50, pp.265-278
- Mah D, Freedman G, Milestone B et al (2002) 'Measurement of intrafractional prostate motion using magnetic resonance imaging', *Int. J. Radiat. Oncol. Biol. Phys.*, 54, pp.568-575
- Kotte AN, Hofman P, Lagendijk J et al (2007) 'Intrafraction motion of the prostate during external-beam radiation therapy: analysis of 427 patients with implanted fiducial markers', *Int. J. Radiat. Oncol. Biol. Phys.*, 69, pp.419-425
- Balter JM, Wright JN, Newell LJ et al Accuracy of a wireless localization system for radiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2005;61:933-937
- Willoughby T., Kupelian P., Pouliot J. et al. Target localization and real-time tracking using the calypso 4D localization system in patients with localized prostate cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2006;65:528-534
- Kupelian P, Willoughby T., Mahadevan et al. Multi-institutional clinical experience with the Calypso system in localization and continuous, real-time monitoring of the prostate gland during external radiotherapy. *Int. J. Radiat. Oncol. Biol. Phys.* 2007;67:1088-1098
- Langen KM, Willoughby T, Meeks SL et al. Observations on real-time prostate gland motion using electronmagnetic tracking. *Int. J. Radiat. Oncol. Biol. Phys.* 2008;71:1084-1090

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