International Clinical and Medical Case Reports Journal
Research Article (ISSN: 2832-5788)

Daily Variation of Planning Target Volume Position in Prostate Cancer Patients Treated With Helical Radiotherapy

Victor Eliseo Caceros Figueroa*
Oncologist-Radiation Therapist, Salvador

Citation: *Victor Eliseo Caceros Figueroa. Daily Variation of Planning Target Volume Position in Prostate Cancer Patients Treated With Helical Radiotherapy. Int Clinc Med Case Rep Jour. 2022;1(3):1-8.*
Doi: https://doi.org/10.5281/zenodo.6859440
Received Date: 07 July, 2022; **Accepted Date:** 14 July, 2022; **Published Date:** 16 July, 2022
***Corresponding author:** Victor Eliseo Caceros Figueroa. Oncologist-Radiation Therapist, Salvador

ABSTRACT

Background and Purpose

Prescribing an accurate dose of radiation when treating prostate cancer using skin marks alone is very challenging due to the mobility of the prostate from a variety of factors. This study measured the daily variation of the Planning Target Volume (PTV) position in patients with prostate cancer treated with Image-Guided Radiotherapy (IGRT).

Materials and Methods

From May 2011 to June 2011, 38 IGRT sessions from four patients diagnosed with localized prostate cancer were registered. IGRT was performed using a helical tomotherapy machine with a megavoltage computed tomography system. PTV variation was measured daily by comparing tomography coordinates to the corresponding skin marks on patients.

Results

Differences in displacement were found between X (left-right), Y (anterior-posterior), and Z (up-down) axes. Displacements were greater in X with a range of 33 mm (range, -20 to 13 mm), followed by Z with 18.6 mm (range, -6.1 to 12.5 mm), Y with 11.2mm (range, -5.8 to 5.4 mm), and roll (clockwise-counterclockwise) with 0.7° (-1.6 to 3.1°). Large prostate shifts were found between 18.4% to 52.6% in X, 2.6 to 7.9% in Y, and 21.1% to 94.7% in Z.

Conclusion

Large displacements and large prostate shifts were detected in all patients. IGRT contributed to reduced exposure of excessive radiation to OAR, which would not have been possible with skin mark guides alone. Adequate IGRT should be employed to make daily adjustments to the PTV location.

Keywords: Prostate cancer; Image-guided radiotherapy; Intensity-modulated radiotherapy

INTRODUCTION

Radiotherapy for prostate cancer has overcome many challenges over the last decade. The relationship between radiation dose and response to treatment,[1] optimal radiation doses above 66 Gy,[2] the use of newer technologies such as three-dimensional conformal radiotherapy, multi-energy linear accelerators,[3] intensity-modulated radiotherapy (IMRT),[1,3,4] and Image-Guided Radiotherapy (IGRT) have contributed to the improvement of radiotherapy in its safety and efficacy. Standard treatment definitions and calculation of maximum radiation dose to organs at risk (OAR) by the Radiation Therapy Oncology Group (RTOG) and the American Society of Radiation Oncology have also contributed to safer treatment planning.[5]

Skin marks were initially used as a guide for radiation treatment. However, such guidance did account for important factors such as the prostate's mobility, the fullness of the bladder and rectum and human error in daily positioning. Therefore, the prostate could be easily left outside the planning area. Numerous studies have demonstrated that the prostate's range of movement can be very pronounced and random, hence the importance of considering such factors during treatment planning.[6-11] X-rays were then used to locate the bladder, rectum, and pelvic bones allow physicians to determine the prostate's position easily.[12]

Currently, IGRT allows for direct visualization of the prostate, allowing for better conformality and decreases exposure of the bladder, seminal vesicles, and rectum to excessive radiation, reducing potential side effects. IGRT is independent of external skin marks and bone structures; the exact location of the prostate can be determined using ultrasound, Computed Tomography (CT), magnetic resonance imaging, and positron emission tomography scans before each treatment session.[6-12] New advances such as the combination of IGRT, conformal radiotherapy, and IMRT have permitted higher treatment doses up to 86 Gy and fewer side effects.[1,2,4]

This study aimed to measure the daily variations of the Planning Target Volume (PTV) position and the percentage of large prostate shifts (>5 mm) in X (left-right), Y (anterior-posterior), Z (up-down), and roll (clockwise-counterclockwise) axes using IGRT to standardize clinical target volume margins in the region and decrease the amount of radiation to OAR.

MATERIALS AND METHODS

Participants

Between May and June 2011, four patients diagnosed with localized prostatic adenocarcinoma by histology were randomly selected during treatment planning; only four patients were selected because of heavy patient flow and the limited time required to collect data at the facility manually. The mean age of four patients included was 74.5 years (range, 69 to 80 years). We measured Gleason score, prostate-specific antigen value, and tumor-node-metastasis scores for each patient (Table 1). Skin tattoos were marked during the planning phase to guide the placement of the treatment field. Subjects were later treated with IMRT using TomoTherapy Hi-Art (TomoTherapy Incorporated, Madison WI, USA) in 38 fractions using radiation doses between 2 Gy and 2.3 Gy each time. Before each session, the isocenter was aligned with the skin marks, and then a CT was made to verify the exact location of the prostate.

Table 1: Patient demographic and clinical characteristics.

Patient	Age	Gleason Score	PSA (ng/mL)	Tumor staging		
				T	N	M
1	69	9	100	3	0	0
2	77	6	6	1	0	0
3	72	6	8.4	3	0	0
4	80	8	14	2	0	0

Abbreviations: PSA- Prostate-Specific Antigen; T, Tumor; N- Lymph nodes; M- Metastasis.

Materials

We used a linear accelerator with a multilayer collimator for 6 MV IMRT and a mega-voltage 3.1 MV CT scan, which allowed daily scans for patients before each treatment session. All patients had a simulation CT scan before treatment planning using a six-slice CT scanner (Somatom Sensation 6, Siemens Incorporated, Erlangen, Germany). Images were exported to the MIM Vista Planning Software to outline the targets (MIM Software Incorporated, Cleveland OH, USA) and then exported to TomoTherapy Planning system, V4.1 (Accuray Incorporated, Madison WI, USA). Once the treatment was optimized, the prescription dose was approved, and OAR was protected, the plan was sent to the TomoTherapy Hi-Art Treatment System.

Procedure

Before each session, all patients had a megavoltage CT (MVCT) scan (3.1 MV, 20 rpm, 3-mm resolution) to determine the prostate's exact position and OAR. During each session, images were fused with the simulation CT, using fusion algorithms based on bone and soft tissue landmarks (Figure 1). To achieve greater precision, a manual adjustment to the images was also made (Figure 2). The prostate's variance during each session was registered and checked for validity.

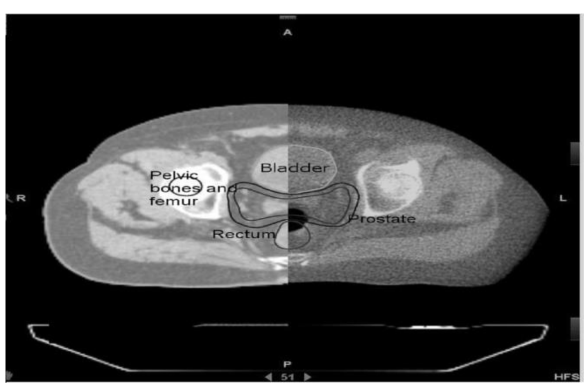

Figure 1: Fusion image of a simulation CT (left) and daily CT (right) based on a bone and soft tissue landmark algorithm. The skin and bladder are aligned, but the prostate and rectum are not. Two contours are observed on the prostate: the inner one marks the prostate's margins, and the outer one the treatment margins. Abbreviation: CT, computed tomography.

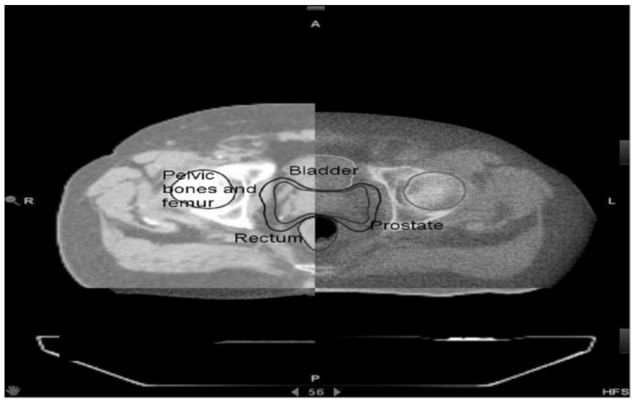

Figure 2: Fusion image of a simulation CT (left) and daily CT (right) obtained after aligning the prostate and organs at risk. Two contours are observed on the prostate, the inner one marks the prostate's margins and the outer one the treatment margins. Abbreviation: CT, computed tomography.

Statistical analysis

The obtained data were analyzed using SPSS IBM SPSS Statistics for Windows Version 19.0 (IBM Corp., Armonk, NY). Since data had a nonparametric distribution, a Kruskal Wallis analysis of variance was used to test a difference in the X, Y, and Z positions among the pooled values of the 38 sessions considered in the study.

RESULTS

The sample consisted of 608 individual measurements obtained from 38 sessions from the four selected patients. The median, minimum, maximum, range, and interquartile range of the measurements are summarized in Table 2. Daily displacements were greater in the X position with a range of 33 mm (-20 to 13 mm), followed by Z with 18.6 mm (-6.1 to 12.5 mm), Y with 11.2 mm (-5.8 to 5.4 mm), and roll with 0.7° (-1.6 to 3.1°). We found a statistically significant difference between the medians of the distances of displacement in these positions ($H = 187$, $p < 0.001$).

A comparison of the percentage of large prostate shifts in the X, Y, and Z positions for each patient is shown in Figure 3. Patient 4 had the greatest amount of large prostate shifts, 94.7% in the Z position and 52.6% in the X position. Overall, the ranges of large prostate shifts found were 18.4% to 52.6% in the X position, 2.6% to 7.9% in Y and 21.1% to 94.7% in Z.

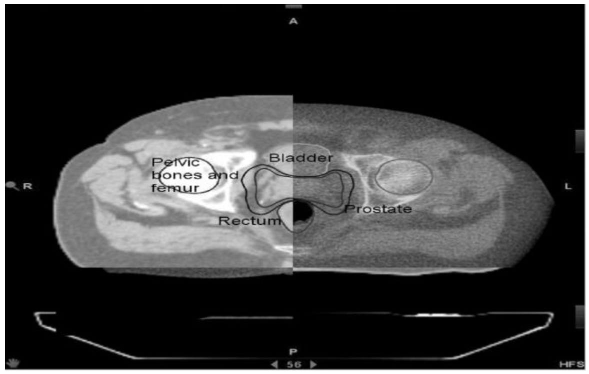

Figure 3: Percentage of large shifts in the prostate movement for each of the study patients.

Table 2: Summary statistics of daily planning target volume variation during the 38 radiotherapy sessions.

Position	Median (mm)	Minimum (mm)	Maximum (mm)	Range (mm)	Interquartile range	P value
X (LR translation)	-2.6	-20	13	33	7	p=<0.001[a]
Y (AP translation)	0.8	-5.8	5.4	11.2	3.9	
Z (IS translation)	4.4	-6.1	12.5	18.6	5.1	

[a]Kruskal Wallis Test.

Abbreviations: LR- Left-Right Translation; AP- Anterior-Posterior Translation; IS- Inferior-Superior Translation.

DISCUSSION

This study examined the daily displacement of the PTV position and the percentage of large prostate shifts in patients diagnosed with prostate cancer and treated with helical radiotherapy in our center. IGRT allows for the adjustment of daily patient setup and the positional correction of the radiation beams during radiation delivery and decreases target delineation errors. Additionally, the use of IGRT allows for the reduction of planning margins.[13] Higher gradients of dose distribution require a precise determination of target position; this is particularly relevant for prostate cancer radiotherapy because the prostate gland's position within the pelvis is likely to change between treatment fractions.[3] Aubry et al. found MVCT IMRT to be safe and reliable in reducing treatment planning errors compared to other commonly used methods without image guidance.[8] Failure to account for variations of the prostate gland position due to the deformability and mobility of the surrounding gastrointestinal and genitourinary organs during RT may compromise its normal function and increase toxicity in surrounding tissues.[14] Rectal and bladder fullness and exclusive reliance on external fiducial markers or skin tattoos are not as reliable as the patient's anatomy. The limiting factor for dose escalation in radical radiotherapy is the increased acute or late treatment-related toxicity rate. The use of radiotherapy techniques with high radiation doses like IMRT, radiosurgery, or hypofractionation requires adequate image guidance to improve therapeutic indexes and correct any set-up discrepancies.[14-16]

Our results showed a wide range of displacements, predominantly in the X position, representing an important percentage of large prostate shifts and very little change in rotation. Patients had scores of 0 to 1 in the Acute Radiation Morbidity Scoring Criteria for the genitourinary and lower gastrointestinal areas at the end of the sessions.[17] Drozdz et al. concluded that high-precision IGRT for prostate cancer should be based on implanting intraprostatic fiducial markers that help detect prostate variability and avoiding high radiation levels to the bladder neck.[15]

In our study, the greatest range of displacement was found to be in X, followed by Z and Y. We found a statistical association between the median distance of displacement between X, Y, and Z; our data are consistent with random prostate movements. Alasti et al. and Antlak et al. reported ranges of prostate movement in the Y and X directions, which differ from our findings.[6,7] Patient 4 had the greatest amount of displacement, mainly in the Z position.
The Z-axis is of particular interest because of the placement of the bladder and rectum in relation to the prostate. The margin of error should be minimal in this direction; such displacements could result in greater toxicity. This is especially true when dose scaling is used; the anterior wall of the rectum could receive significantly high doses of radiation if this zone is not controlled.

We evaluated roll in our study, which accounts for rotational movements. Rotational movement had a range of 4.7°. Rotational movement is not established as a value to be corrected in the international literature because most treatment systems cannot detect rotation.

Finally, at least 18.4% of sessions had large prostate shifts in X (left-right), 21.1% in Z (up-down), and 2.6% in Y (anterior-posterior). These patients could have received excessive radiation to OAR, but the treatment was provided via IGRT.[17,18] Wong et al., in a much larger series, studied 540 consecutive CT scans of 108 patients. They found larger prostate shifts in Y (anterior-posterior) at 54%, followed by X (left-right) at 34%, and Z (up-down) at 27%.[19] Their results are consistent with similar studies but differ from our results.

Despite our small patient sample (due to the number of patients received by the center and the availability of the radiotherapy team), the units of analysis were the 608 individual measurements across 38 sessions. This number was considered suitable for the analysis. Regardless, the study was limited by the small population of patients, although the results were significant. Results may have been different if more patients would have been included and if the time difference between the treatment date and the publication date had been reduced.

CONCLUSION

Large displacements and large prostate shifts were detected in all patients. IGRT contributed to reduced exposure of excessive radiation to OAR, which would not have been possible with skin mark guides alone. Adequate IGRT should be employed to make daily adjustments to the PTV location.

REFERENCES

1. Pollack A, Zagars GK, Starkschall G, Antolak, JA, Lee JJ, Huang E, et al. Prostate Cancer Radiation Dose Response: Results of the M. D. Anderson phase III Randomized Trial. Int J Radiat Oncol Biol Phys. 2002;53(5):1097-1105.
2. Roach M 3rd, Hanks G, Thames H Jr, Schellhammer P, Shipley WU, Sokol GK, et al. Defining Biochemical Failure following Radiotherapy with or without Hormonal Therapy in Men with Clinically Localized Prostate Cancer: Recommendations of the RTOG-ASTRO Phoenix Consensus Conference. Int J Radiat Oncol Biol Phys. 2006;65:965-974.
3. Kupelian PA, Reddy CA, Carlson TP, Altsman KA, Willoughby TR. Preliminary Observations on Biochemical Relapse-Free Survival Rates after Short-Course Intensity-Modulated Radiotherapy (70 Gy at 2.5 Gy/fraction) for Localized Prostate Cancer. Int J Radiat Oncol Biol Phys. 2002;53:904-912.
4. Zelefsky MJ, Fuks Z, Hunt M, H J Lee, D Lombardi, C C Ling, et al.: High Dose Radiation Delivered by Intensity Modulated Conformal Radiotherapy Improves the Outcome of Localized Prostate Cancer. J Urol. 2001;166:876-81.
5. Michalski JM, Lawton C, El Naqa I, Mark Ritter, Elizabeth O'Meara, Michael J Seider, et al. Development of RTOG Consensus Guidelines for the Definition of the Clinical Target Volume for Postoperative Conformal Radiation Therapy for Prostate Cancer. Int J Radiat Oncol Biol Phys. 2010;76:361-368.
6. Alasti H, Petric MP, Catton CN, Warde PR. Portal Imaging for Evaluation of Daily On-Line Setup Errors and Off-Line Organ Motion During Conformal Irradiation of Carcinoma of The Prostate. Int J Radiat Oncol Biol Phys. 2001;49:869-884.
7. Antolak JA, Rosen II, Childress CH, Zagars GK, Pollack A. Prostate Target Volume Variations During a Course of Radiotherapy. Int J Radiat Oncol Biol Phys. 1998;42:661-672.
8. Aubry JF, Beaulieu L, Girouard LM, Aubin S, Tremblay D, Laverdière J, et al. Measurements of Intrafraction Motion and Interfraction and Intrafraction Rotation of Prostate by Three-Dimensional Analysis of Daily Portal Imaging with Radiopaque Markers. Int J Radiat Oncol Biol Phys. 2004;60:30-39.
9. Balter JM, Sandler HM, Lam K, Bree RL, Lichter AS, ten Haken RK. Measurement of Prostate Movement over the Course of Routine Radiotherapy Using Implanted Markers. Int J Radiat Oncol Biol Phys. 1995; 31:113-118.
10. C J Beard 1 , P Kijewski, M Bussière, R Gelman, D Gladstone, K Shaffer, et al. Analysis of Prostate and Seminal Vesicle Motion: Implications for Treatment Planning. Int J Radiat Oncol Biol Phys. 1996;34:451-458.

11. Peter W M Chung , Tara Haycocks, Tanya Brown, Zoe Cambridge, Valerie Kelly, Hamideh Alasti,, et al. On-line aSi Portal Imaging of Implanted Fiducial Markers for the Reduction of Interfraction Error During Conformal Radiotherapy of Prostate Carcinoma. Int J Radiat Oncol Biol Phys. 2004;60:329-334.
12. M J Zelefsky, D Crean, G S Mageras, O Lyass, L Happersett, C C Ling,, et al. Quantification and Predictors of Prostate Position Variability in 50 Patients Evaluated with Multiple CT Scans During Conformal Radiotherapy. Radiother Oncol. 1999;50:225-234.
13. Dang A, Kupelian PA, Cao M, Agazaryan N, Kishan AU. Image-Guided Radiotherapy for Prostate Cancer. Transl Androl Urol. 2018;7:308-320.
14. Radiation Therapy Oncology Group: Acute Radiation Morbidity Scoring Criteria. (2015). Accessed: April 28, 2021.
15. Drozdz S, Schwedas M, Salz H, Foller S, Wendt TG. Prostate Cancer Treated with Image-Guided Helical TomoTherapy® and Image-Guided LINAC-IMRT: Correlation between High-Dose Bladder Volume, Margin Reduction, and Genitourinary Toxicity. Strahlenther Onkol. 2016;192:223-231.
16. Kupelian PA, Willoughby TR, Reddy CA, Klein EA, Mahadevan A. Hypofractionated Intensity-Modulated Radiotherapy (70 Gy at 2.5 Gy per fraction) for Localized Prostate Cancer: Cleveland Clinic Experience. Int J Radiat Oncol Biol Phys. 2007;68:1424-1430.
17. Zhou J, Uhl B, Dewit K, Young M, Taylor B, Fei DY, et al. Analysis of Daily Setup Variation with Tomotherapy Megavoltage Computed Tomography. Med Dosim. 2010; 35:31-37.
18. Ghilezan M, Yan D, Liang J, Jaffray D, Wong J, Martinez A. Online Image-Guided Intensity-Modulated Radiotherapy for Prostate Cancer: How Much Improvement Can We Expect? A Theoretical Assessment of Clinical Benefits and Potential Dose Escalation by Improving Precision and Accuracy of Radiation Delivery. Int J Radiat Oncol Biol Phys. 2004;60:1602-1610.
19. Wong JR, Grimm L, Uematsu M, Oren R, Cheng CW, Merrick S, et al. Image-Guided Radiotherapy for Prostate Cancer by CT-Linear Accelerator Combination: Prostate Movements and Dosimetric Considerations. Int J Radiat Oncol Biol Phys. 2005;61:561-569.