TO ASSESS THE DOSIMETRIC IMPACT ON PROSTATE, BLADDER AND RECTUM IN CARCINOMA PROSTATE DUE TO INTERFRACTIONAL ANATOMICAL VARIATION IN IMAGE GUIDED RADIATION THERAPY.

Oncology

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ABSTRACT

Prostate cancer is second most frequent cancer in men and fifth leading cause of death worldwide. Most radiotherapy patients with prostate cancer are treated with intensity modulated radiotherapy. IMRT requires high spatial accuracy in localizing the target volume and high precision in treatment delivery, because even a small geographic miss can have a large dosimetric effect. However, the patient setup position and anatomy changes daily, particularly in the prostate region, due to rectum and bladder filling. Materials Methods: We analyzed 30 patients with prostate cancer patient treated with IMRT kV CBCT was performed for each patient twice per week during the entire course of treatment. The bladder, rectum, prostate and PTV were contoured on each CBCT scan. Results: Delivered dose of prostate D95% and prostate D100% was 99.15% and 93.66% respectively and mean value of V70 for bladder was 16% and delivered value was 16.45%. Whereas the mean value of V70 of plan for rectum was 18.12% and delivered value was 27.58%. Conclusion: Interfractional variation during prostate radiotherapy can results in substantial difference between planned and delivered doses, particularly in critical structure. IG-IMRT is useful tool in assessing dosimetric changes in critical structure due to interfractional anatomical interfractional anatomical variation in prostate radiotherapy.

KEYWORDS

Prostatic neoplasms, Image-guided radiotherapy(IGRT), Intensity-modulated radiotherapy (IMRT).

INTRODUCTION

Prostate cancer is the second most frequent cancer diagnosis made in male and fifth leading cause of death worldwide. Based on GLOBOCAN 2018 estimates, 1,276,106 new cases of prostate cancer were reported worldwide in 2018, with higher prevalence in the developed countries.^{1,2} Most radiotherapy patients with prostate cancer are treated with intensity modulated radiotherapy (IMRT). Especially Volumetric Modulated Arc therapy (VMAT) helps to get highly conformal dose distributions for the planning target volume (PTV) while minimizing the dose given to the organs at risk and with short delivery time^(3,4,5). Intensity Modulated Radiotherapy (IMRT) requires high spatial accuracy in localizing the target volume and high precision in treatment delivery, because even a small geographic miss can have a large dosimetric effect⁽⁶⁾. However, the patient setup position and anatomy changes daily, particularly in the prostate region, due to rectum and bladder filling. Intensity-modulated radiotherapy (IMRT) for prostate cancer has facilitated the delivery of high radiation doses to the prostate and is associated with excellent biochemical tumor control outcomes for patients with localized disease⁽⁷⁾. It has been well reported that interfraction prostate deformation is common during the course of prostate RT owing to daily bladder and/or rectal filling. The high mobility of the bladder and the rectum causes uncertainty in radiation doses prescribed to patients with prostate cancer who undergo radiotherapy (RT) multifraction treatments⁽⁸⁾.

MATERIAL AND METHODS

This study was conducted at Bhagwan Mahaveer Cancer Hospital and Research Centre and Institute, Jaipur from October 2015 to June 2017. Total 30 histologically proven cases of prostate cancer in whom radical radiation therapy to pelvis indicated and IGRT was delivered were included. Patients of carcinoma prostate who could not complete the planned radiation therapy, already received RT to pelvis, required urinary catheterization, undergone any surgery in the past upon bladder, prostate or rectum were excluded.

Patients were simulated with bladder and rectal protocol. Patients were immobilised comfortably in supine position. Planning NCCT and CECT scan images were taken using Philips Big Bore CT (64 slice) scanner from the level of L2-L3 to mid thigh with 3 mm cuts in the axial plane. CTV includes whole prostate and any possible extra capsular extension, with either the base of, or the entire seminal vesicles (SV). The risk of involvement of the seminal vesicles is defined using the Roach formulae.

Low risk of seminal vesicle involvement- $PSA + [(GS - 6) \times 10] < 15\%$
Moderate high risk of seminal vesicle involvement- $T3$ or $(PSA + [(GS$

$- 6) \times 10] > 15\%$

Prostate outlining starts on the mid gland slice along the fat plane between the prostate and pelvic floor muscles and along Denovilliers' fascia posteriorly. Selected patients with a risk of lymph node involvement 15–35 per cent, according to the Roach formula, may benefit from pelvic lymph node irradiation.

Roach formula

Risk of lymph node involvement = $2/3 PSA + [(GS - 6) \times 10]$

Clinical target volume for these patients includes prostate, seminal vesicles and the common, internal and external iliac, presacral, hypogastric and obturator lymph nodes.

The standard margin is 5 mm grown isotropically around the CTV. To limit the dose to the rectum, the posterior margin is reduced to 3 mm. The OARs (organ at risk) were delineated using standard guidelines⁽⁹⁾. Maximum and minimum allowable dose to PTV dose constraints for the organ at risk used was as per RTOG 0924 guidelines⁽¹⁰⁾.

DOSE PRESCRIPTION TO PTV:-70-80 Gy @1.8-2.0 Gy per fraction.

6-10 MV energy photon beam was used for treatment by external beam radiotherapy (EBRT). During treatment the kilo Voltage Cone Beam CT (kV CBCT) images were taken with Varian On Board Imagers (OBI™) in Clinac® iX Linear accelerator machine during image guided Intensity Modulated Radiation therapy (IG-IMRT). kV CBCT was performed for each patient twice per week during the entire course of treatment. The CBCT images for each fraction were registered to the planning CT by 3D/3D match algorithm with respect to bony anatomy, using an Eclipse Treatment Planning System. The average number of scan obtained during 7-7.5 week course of IG-IMRT was 14. Total number of scan obtained was 420. All scans encompassed the entire treatment field using 3 mm slices. The bladder, rectum, prostate and PTV were contoured on each CBCT scan.

Dose calculation on CBCT

Daily fraction doses were recalculated on the corresponding daily images, and resulting dose distributions were transferred onto the planning scans. Voxel-wise dose accumulation was carried out in RayStation using the software's deformable image registration module and compared to the planned dose distribution¹¹. In order to use CBCT images for dose calculation, the image pixel values were converted from CBCT numbers to physical density using the ROI CT number

mapping method as reported¹². After that, the original plan was rigidly copied to the CBCT image data set for dose recalculation.

RESULTS:

Mean dose of PTV D95 (%) of plan was 99.65 % and delivered dose was 96.53%. The delivered dose is less by an average of 3.12% as compared to the planned dose which was statistically significant ($p < 0.001$).

Table 1: Dosimetric changes in PTV D95%, prostate D95% and prostate D100%

Parameters	Planning Dose	Delivered Dose	P' Value	% Difference
PTV D95%	99.65±1.584	96.53±4.452	<0.001	3.12
Prostate D95%	99.99±0.0385	99.15±2.524	0.074	0.839
Prostate D100%	95.85±6.77	93.66±7.404	0.237	2.19

Figure 1 : Dosimetric Changes In Ptv D95%, Prostate D95% And Prostate D100%

Figure 2 : Dosimetric Changes In Bladder V70% And Rectum V70%.

Mean dose of prostate D_{95%} of plan was 99.99% and mean dose of prostate D_{100%} of plan was 95.85%. Delivered dose of prostate D_{95%} and prostate D_{100%} was 99.15% and 93.66% respectively. Delivered dose prostate D_{95%} is less by an average of 0.839% as compared to the planned dose which was not statistically significant ($p = 0.074$). The delivered dose prostate D_{100%} is less by an average of 2.19 % as compared to the planned which was not statistically significant ($p = 0.237$).

Table 2 : Dosimetric Changes In Bladder V70% And Rectum V70%.

Parameter	Planning Volume	Delivered Volume	P' Value	% Difference
Bladder V70	16±9.951	16.45±11.27	0.868	0.4577
Rectum V70	18.12±6.568	27.58±8.233	<0.001	9.457

In present study for rectum and bladder, the V₇₀ was compared with the original plan. Mean value of V₇₀ of plan for bladder was 16±9.951% and delivered value was 16.45±11.27%. The delivered value is more by an average of 0.4577% as compared to the planned value which was not statistically significant ($p=0.868$). Value of V₇₀ of plan for rectum was 18.12±6.568% and delivered value was 27.58±8.233%. The delivered value is more by an average of 9.457% as compared to the planned value which was statistically significant ($p<0.001$).

DISCUSSION:

In our study, recorded dosimetric changes during the course of treatment and compared them with planning CT. Cumulative delivered doses were calculated for 30 patients with rigid registration of the kV-CBCT to the planning CT. Image guided -IMRT has been accepted as the standard treatment technique in prostate malignancy as it has ability to target the CTV while sparing surrounding normal tissue. This presumes accurate target definition at the time of planning and accurate target localization throughout the treatment.

Mean age of study population was 65.70 years (range: 49-81). Mean dose of prostate D_{95%} was 99.99% and mean dose of prostate D_{100%} was 95.85%. The delivered dose prostate D_{95%} and prostate D_{100%} were 99.15% and 93.66% respectively. The delivered dose prostate D_{95%} is less by an average of 0.839 % as compared to the planned dose which was not statistically significant ($p=0.074$). The delivered dose prostate D_{100%} is less by an average of 2.19 % as compared to the planned which was not statistically significant ($p=0.237$).

Results of present study correspond with Godley A et al., showed prostate D_{100%} dose was less by an average of 2.9% as compared to the planned dose. They concluded that less than 3% difference between delivered and planned prostate coverage indicates that the PTV margin of 5mm was sufficient. Further reduction in PTV margin requires

adaptive approach, such as online replanning, to address the large interfractional anatomic variation. This difference in prostate was in close agreement with our finding as we have also noted less than 3% difference in prostate D_{100%}⁽¹³⁾.

Another study conducted in 20 patients by Peng C et al., prostate D_{100%} was less by an average of 1.9± 1.6% for the daily dose distribution compared with that for the original plan. For 62% of all the fractions, the prostate D_{100%} was comparable to the planned value. For 32% of all the fractions, the decrease in the prostate D_{100%} was 1-3%. For 6% of the fractions, the prostate D_{100%} decreased by 3-15 %⁽¹⁴⁾. Mean decrease in the PTV D_{95%} was 7.0 % ± 10.6 % (SD). In 8.4% of fractions, the PTV D_{95%} was lower than that for the original plan by 5-15%. In 23.7% of fractions, the PTV D_{95%} less by was 2-5%. It was almost the same as that for the original plan by 67.9% of all fractions. In maximum number of fractions PTV D_{95%} decrease was less than 5%, this is in close agreement with our finding⁽¹⁴⁾.

In our study Mean dose PTV D_{95%} was 99.65% and delivered dose was 96.53%. The delivered dose is less by an average of 3.12% as compared to the planned dose which was statistically significant ($p < 0.001$). In present study D_{95%} is well covered with 95% of absorbed dose, which in accordance with recommendations of ICRU 83⁽¹⁵⁾.

In the present study for rectum and bladder, the V₇₀ was compared with the original plan. Mean value of V₇₀ for bladder was 16% and delivered value was 16.45%. The delivered value was more by an average of 0.46% as compared to the planned dose which was not statistically significant ($p=0.868$) and was also less than the QUANTEC recommended value of 35% of the bladder volume⁽¹⁷⁾.

Whereas the mean value of V₇₀ of plan for rectum was 18.12% and delivered value was 27.58%. The delivered value was more by an average of 9.46% as compared to the planned dose which was statistically significant ($p<0.001$) and this was more than the QUANTEC recommended value of 20% of the rectum volume⁽¹⁸⁾.

Huang et al. used CBCT to analyze the changes of bladder and rectum during fractionated radiotherapy of prostate. The difference in the volume and radiation dose were 44% and 18% (± 17%) respectively for the bladder and 36% (± 29%) and 22% (± 15%) respectively for the rectum¹.

Akin et al. assessed the variation in dose volume parameter (V40%, V50%, V60%, V65%) for the bladder and rectum, and found that the delivered dose was higher than the planned dose. V40%, V50%, V60%, and V65% of bladder were 20% or higher than calculated in the planning CT. While for rectum V40% was 8.7% higher, V50% was 0.725% higher, V60% was 6.81% higher and V65% was 37.49% higher as compared to the planned value⁽¹⁰⁾.

Though we are prescribing charcoal tablet and laxative to all our patients, not all are being treated in the early morning hours. By treating them early in the morning, there is a chance that gaseous distension avoided thereby reducing the dose.

CONCLUSION

Interfractional variation during prostate radiotherapy can result in substantial difference between planned and delivered doses, particularly in critical structure. IG-IMRT is useful tool in assessing dosimetric changes in critical structure due to interfractional anatomical interfractional anatomical variation in prostate radiotherapy. Bladder and bowel protocol should be used during treatment planning and daily treatment.

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