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Role of Imrt in Reducing Penile, Rectal and Bladder Doses in Dose Escalation for Prostate Cancer.

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ABSTRACT: PURPOSE: In three- dimensional conformal radiotherapy (3D-CRT), penile tissue adjacent to the prostate, rectum and bladder are exposed to significant doses of radiation. This is likely to be a factor in development of posttreatment erectile dysfunction as well as rectal and bladder toxicity.in this study , we investigate whether intensity modulated radiation therapy (IMRT) leads to lower radiation exposure to proximal penile tissues, rectum, bladder when compared with 3D-CRT.

Methods and Materials: Twenty patients with localized prostate cancer were selected for this study. Using identical structure sets, 3D-CRT and IMRT plans were designed for each patient. 3D-CRT was planned using CMS FOCUS treatment planning system (TPS). A 4 field arrangement using 6 MV photons was selected for all patients. For IMRT planning, static step and shoot treatment plans were generated using 7 beam and 7 intensity levels of 6 MV photons. Treatment plans were optimized in KONRAD inverse planning system using weighted quadratic difference of prescribed and calculated dose distribution method. The PPT upto the beginning of the penile shaft (usually 2-3cm), bladder and rectum was outlined by radiation oncologists. PPT was subdivided into 3 segments (P1,P2,P3) and radiation dose to each segment was calculated. In addition PPT was subdivided into corporal cavernosa (cc) and corpus spongiosum (bulb CS). The prostate dose was escalated from 50 to 74 Gy. Target 95% (dose to 95% volume) and D mean (mean dose) were used in comparison among treatment plans.

RESULTS : D_{95} for PTV was 4.6% lower in IMRT plans than 3D-CRT planes in our study. For all critical structures, IMRT plans demonstrated markedly lower doses compared with 3D-CRT plans. In IMRT planes P1 dose was reduced by 20 Gy (36%) , P2,3 doses were reduced by 14 Gy(45%), CC dose was reduced by 12 Gy(44%), CS dose was reduced by 11 Gy (42%) as compared to 3D-CRT plan. Bladder dose was reduced by 9 Gy (16% less) in IMRT plan as compared to 3D-CRT plan while rectal dose was reduced by 8 Gy(13% less). Doses to rt femur was 15 Gy (45% less) lower in IMRT plan compared to 3D-CRT plan while it was 16 Gy (47% less) lower for left femur.

I. INTRODUCTION PROSTATE

Prostate cancer remains one of the most prevalent and least understood of all human malignancies. Pathological evidence suggest that neoplastic changes of the prostate epithelium begin early in man's adult life, but do not become clinically evident or relevant until decades later.[1]

The incidence of prostate cancer and its mortality rates are highest in America and the lowest in Asia. The rates in India are less than one tenth of the rates seen in USA, but are increasing rapidly particularly in Delhi, Mumbai and Bangalore.[2,1]

Radiotherapy plays an important role in treating early and medium stage prostate cancer. Sufficient radiation dose to the target tumour has often been limited by the associated toxicities due to the target proximity to normal structures such as rectum and bladder near the irradiated region.[3] Other treatment option is radical prostatectomy. With treatment outcomes being comparable between modalities, toxicity and quality of life issues have become increasingly important in patients treatment decisions. A significant issue in determining quality of life after prostate cancer treatment is that of erectile dysfunction (ED). Rates of ED after radical prostatectomy have been reported in the literature ranging from 29-91%.[4-21] The rates of ED after conventional radiotherapy range from 40-65% [22-27] and the rates of ED after brachytherapy range from 16-50%.[28]

Post radiation ED has been postulated to involve damage to the proximal penile structures.[29,30] Using 3D-CRT , previous date have shown that high doses of radiation are delivered to erectile tissue in the proximal penis.[31] Data

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indicates that volume and dose exposure of penile tissues are related to post treatment ED. [32] We have done this investigation to document the ability of IMRT to reduce PPT dose and doses to rectum, bladder and femur as compared with 3D-CRT.

II. METHODS AND MATERIALS

Twenty patients with localized prostate cancer were selected for this study. All patients underwent X ray simulation. Patients were immobilized in pelvic thermoplast mould. Rectal catheter was used to identify rectum. Patients were then transferred to CT scan and 2.5mm thick slice CT were taken. Contouring of targets and normal structures (bladder, rectum, penile structures, and femoral heads) was performed on ONCOR workstation. The following penile structures were identified: the proximal portion of the corporal bodies up to the beginning of the penile shaft (corporal cavernosa {CC} and the proximal corpus spongiosum {bulb}). The bulb and CC together constituted the combined proximal penile tissues (PPT). The PPT were divided into three segments: proximal (P1), middle (P2), and distal (P3). The radiation dose to each segment and to the entire PPT was calculated.

The initial planning target volume (PTV1) included both prostate and seminal vesicles with a 1 cm margin in all directions, whereas the boost planning target volume (PTV2) consisted of prostate only with a 1 cm margin. PTV1 dose was 50 Gy and the PTV2 dose was escalated to 74 Gy. The planning goal was to cover 95% of the PTV with the prescription dose.

3D-CRT was planned using CMS FOCUS treatment planning system (TPS). A 4 field arrangement using 6 MV photons was selected for all patients. For IMRT planning, static step and shoot treatment plans were generated using 7 beam and 7 intensity levels of 6 MV photons. Treatment plans were optimized in KONRAD inverse planning system using weighted quadratic difference of prescribed and calculated dose distribution method.

Dose parameters used for treatment plan evaluation were: D95 (Dose to 95% of target volume) for PTV and Dmean(mean dose) for normal structures. For IMRT plans, PTV2 coverage was compared with that achieved in 3D-CRT plans.

III. RESULTS:

In 3D-CRT dose priscription is 95% of isodose line should cover 100% of PTV volume and in IMRT 95% of the PTV volume should receive at least 95% of priscribed dose. D95 for PTV was 4.6% lower in IMRT plans than 3D-CRT planes in our study.

Table 1: mean dose, percentage dose and p value of two groups.

ORGAN AT RISK	3DCRT (MEAN DOSE)	IMRT (MEAN DOSE)	DOSE %	P value
P1	56	36	36	<0.05
P2+P3	31	17	45	<0.05
CC	27	15	44	<0.05
CS	26	15	42	<0.05
BLADDER	57	48	16	<0.05
RECTUM	61	53	13	<0.05
RT FEMUR	33	18	45	<0.05
LF FEMUR	34	18	47	<0.05

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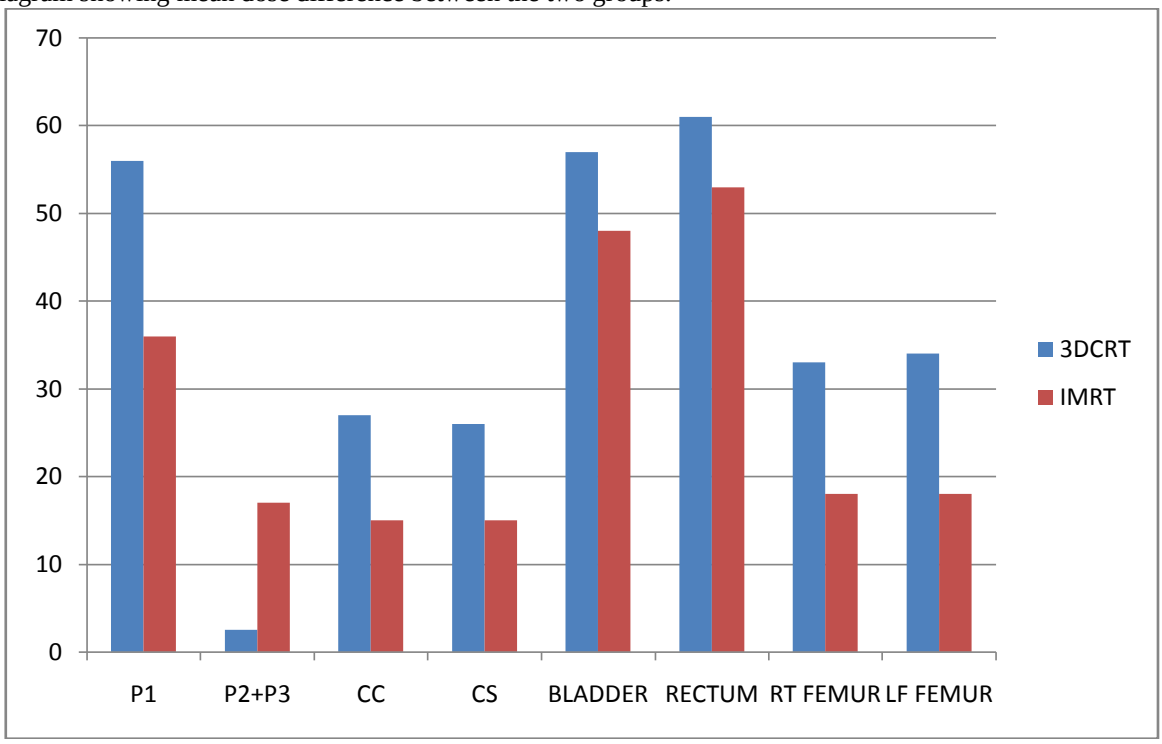
Diagram showing mean dose difference between the two groups.



For all critical structures, IMRT plans demonstrated markedly lower doses compared with 3D-CRT plans. In IMRT planes P1 dose was reduced by 20 Gy (36%) , P2,3 doses were reduced by 14 Gy(45%), CC dose was reduced by 12 Gy(44%), CS dose was reduced by 11 Gy (42%) as compared to 3D-CRT plan. Bladder dose was reduced by 9 Gy (16% less) in IMRT plan as compared to 3D-CRT plan while rectal dose was reduced by 8 Gy(13% less). Doses to rt femur was 15 Gy (45% less) lower in IMRT plan compared to 3D-CRT plan while it was 16 Gy (47% less) lower for left femur.

IV. DISCUSSION

At present treatment outcome for prostate cancer patients are comparable between radiation therapy and radical prostatectomy, so patients decision mainly depends upon the treatment toxicity and quality of life. One of the major concerns for the patients of carcinoma prostate after either treatment is that of sexual potency after treatment. [33] Numerous reports have been published regarding the incidence and impact of, as well as the possible mechanism for, post radiation erectile dysfunction. [5,6,10,15-17,22,30]

Zelefsky et al. [27] reported a 5-year actuarial risk of post radiation erectile dysfunction of 60% following 3DCRT. The authors identified both radiation dose > 75.6 Gy and neoadjuvant hormone therapy as independent predictors of erectile dysfunction after radiation therapy. Fisch et al. [30] also reported a dose dependent relationship with post radiation erectile dysfunction. In their report, the authors found that if 70% of the penile bulb exceeded 70 Gy, the likelihood of developing erectile dysfunction increased significantly, whereas at doses less than 40 Gy, the risk was significantly lower.

Compared with 3DCRT, IMRT plans show a remarkable reduction in dose to some penile structures with p value of less than 0.05. This may be attributed to a high degree of dose conformity achieved in IMRT plans compared with 3DCRT. As the P1 segment is nearest to the apex of prostate, a portion of it is included in PTV1. However, when IMRT is used, the dose to the lateral section is significantly reduced, although dose to the central portion of P1 remains high. Similarly because CC surrounds the central bulb, the reduction of dose to the CC in IMRT plans is greater compared with the bulb.

V. CONCLUSION

The use of sophisticated IMRT planning techniques can reduce the volume of the proximal corporal bodies receiving high doses of radiation. It also reduces doses to bladder and rectum. IMRT allows for dose escalation in prostate cancer while keeping organ at risk doses significantly lower

compared to 3DCRT. This may help preserve sexual function and prevent bowel, bladder toxicity after high dose radiation therapy.

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