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Hypofractionation in Prostate Cancer: Possible in Indian Scenario

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Objective:

A Retrospective analysis of carcinoma prostate patients treated with androgen deprivation therapy and hypofractionated radiotherapy at HCG Cancer Centre, Vadodara from February 2018 to September 2019.

Materials and Methods:

14 patients with carcinoma prostate were treated at HCG Cancer Centre, Vadodara between February 2018 to September 2019. The patients were investigated with prostatic biopsy, MRI Pelvis, Bone scan / PSMA PET CT, Serum PSA, Serum creatinine, CBC.

After the initial workup, the patients were risk-stratified according to the risk categories. The treatment was decided as per the risk categories **(**5**)**. The patients were explained all the treatment options available for their respective categories (Listed below) after proper discussion at the MDT.

Very Low Risk: ACTIVE SURVEILLANCE/RADICAL RT/RADICAL PROSTATECTOMY

Low Risk: ACTIVE SURVEILLANCE/RADICAL RT/RADICAL PROSTATECTOMY

Favourable Intermediate Risk: ACTIVE SURVEILLANCE/RADICAL RT/RADICAL PROSTATECTOMY

Unfavourable Intermediate-Risk Group: RADICAL RT+ADT(6MONTHS)/RADICAL PROSTATECTOMY

High-Risk Group: RADICAL RT+ ADT (2 YEARS).

UNFAVOURABLE HIGH-RISK GROUP and HIGH-RISK GROUP patients were subjected to neoadjuvant hormonal therapy before starting radiation. Radiation was delivered by IGRT as per the CHHIP PROTOCOL to a dose of 60 Gy in 20 fractions at 3 Gy per fraction 5 days a week over 4 weeks. Strict bladder and rectal protocols were followed with daily imaging with Cone Beam CT to verify the position of the target rectum and bladder.

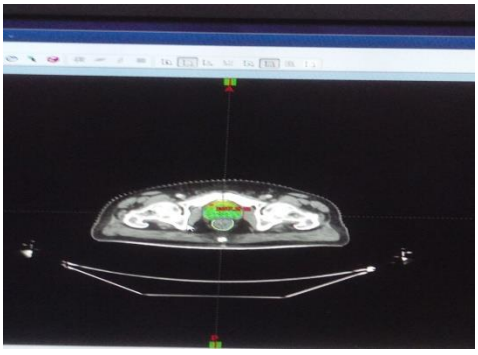

Figure 1

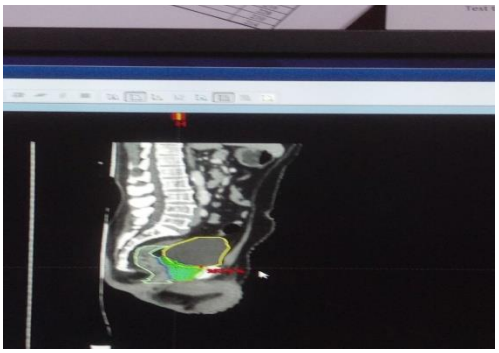

Figure 2

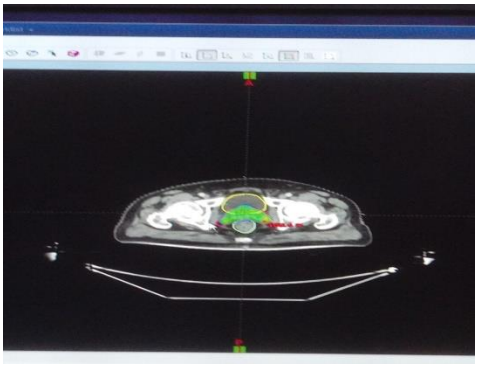

Figure 3

Figure 1,2,3: IMAGES OF TREATMENT PLAN OF HYPOFRACTIONATION OF PROSTATE CANCER

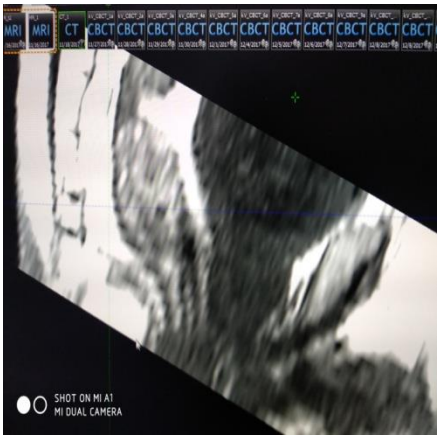

Figure 4

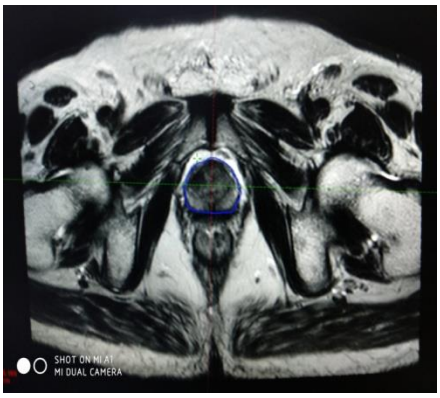

Figure 5

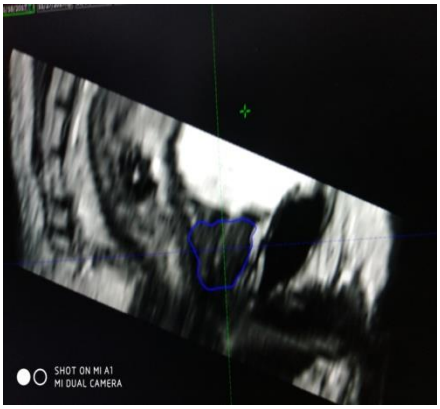

Figure 6

Figure 4,5,6: USE OF MRI IMAGES FOR TREATMENT PLANNING AND CONTOURING

Results:

RESPONSE

COMPLETE RESPONSE	13
PARTIAL RESPONSE	1
TOTAL	14

Table 1

LONG TERM GI TOXICITY

GRADE	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
NUMBER OF PATIENTS	8	6	0	0	0

Table 2

LONG TERM BLADDER TOXICITY

GRADE	GRADE 0	GRADE 1	GRADE 2	GRADE 3	GRADE 4
NUMBER OF PATIENTS	4	8	2	0	0

Table 3

All patients tolerated the treatment well with no major acute toxicities. The patients had a good response rate. The patients were followed up for late toxicities as well and most of them have not developed any major complications so far with the most severe toxicity being grade 2 bladder toxicity in 2/14 patients. The major advantage was compliance as the patients were able to complete treatment in 4 weeks and had almost completed treatment by the time, they started developing acute toxicities.

Discussion

Prostate is a slow-growing tumor with an alpha/beta ratio of 1.8 Gy **(**1**)**. A lot of work has been done on dose escalation carcinoma prostate. However, there are very few trials regarding hypofractionation in prostate cancer even though radiobiologically prostate should be susceptible to high dose per fraction given its low alpha-beta ratio. The probable reason for that may have been the concern of late bladder and rectal toxicities. However, now with modern treatment delivery techniques and daily onboard CBCT available in most of the machines hypofractionation can be delivered safely and effectively. The biggest evidence for the same came with THE CHIPP TRIAL **(**1**)** which proved non-inferiority of hypofractionation (60gy/30#) over the conventional fractionation with no major increase in long-term toxicities. The same protocol has been followed in our study where the tumor has been treated to a dose of 60GY in 20 fractions @ 3Gy per fraction over 4 weeks. The patients tolerated the treatment well with no major acute or long-term toxicities with good response rates. The protocol used here is similar to the one used at Tata Medical Centre, Kolkata **(**3**)**. The major learning point from this study was the strict execution of rectal and bladder protocols with daily CBCT on the treatment couch. This small intervention along with strict adherence to dose constraints makes hypofractionation safe and effective in prostate cancer.

Also, another major factor to be taken into account is the difference in the radiation delivery techniques. While in earlier days radiation was mostly delivered by conventional techniques based on X-Ray based techniques, most modern centers now use conformal techniques such as IMRT, Rapid Arc with CT-based planning. Also, another major advancement is the improvement in the planning software which now allows easy fusion of CT with MRI which allows easy delineation of the prostate and rectum. Prostate offers a unique example where the use of modern technology has helped in the precise delivery of radiation doses with minimum toxicity and hypofractionation is a classic example.

Hypofractionation also offers advantages to the patients. The overall treatment duration is reduced from 2 months to 1 month. It is not only logistically important but it is also important to note that most of the cases of carcinoma prostate belong to the geriatric population and hence the compliance rates also increase. Also as the treatment duration in hypofractionation is almost half that of conventional fractionation it is easier to convince the patients to complete the treatment as by the time the toxicities develop the treatment is almost about to get over. This also reduces the overall treatment rates. One important point to be noted is that while supporters of dose escalation **(**2,6**)** talk about the delivery of higher doses to the prostate what is not talked about is the percentage of patients who can complete their treatment. On the contrary, the compliance rates are much higher in the hypofractionation regimens.

The concern regarding long-term toxicities in hypofractionation may be real but they were much more common when using conventional treatment techniques. These can be prevented if all the precautions are followed viz. use of MRI fusion for delineation of the prostate, strict adherence to dose constraints in treatment plans, strict adherence to the daily bladder and rectal protocols, daily imaging with CBCT to verify smooth execution of bladder and rectal protocols.

Conclusion

These results help us conclude that hypofractionation is a safe, effective, and practical treatment option for carcinoma prostate patients. However strict bladder rectal and imaging protocols need to be followed for safe delivery of treatment.

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