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RESEARCH ARTICLE

Evolving Prostate Cancer Radiotherapy: Exploring Gonadal Doses in 3DCRT and IMRT with Testicular Shielding

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Abstract

Objective: To compare the dosimetry of IMRT versus 3DCRT in prostate cancer, with a focus on testicular dose using lead testicular shielding. **Materials and Methods:** From January 2021 to January 2022, twenty patients with localized prostate cancer underwent IMRT treatment. Plans for 3DCRT were generated for each patient. Comparison was made between 3D-CRT and IMRT regarding target volume dose uniformity, sparing of critical organs, and testicular doses. **Results:** Significant differences were observed in dose uniformity and sparing of critical organs between the two modalities ($p<0.005$), demonstrating the superiority of IMRT over 3DCRT. However, with lead testicular shielding, comparable testicular doses were achieved with both techniques. **Conclusion:** IMRT offers superior dosimetric advantages compared to 3DCRT. Nevertheless, the testicular dose remains nearly equivalent between the two techniques when utilizing lead testicular shielding.

Keywords: Planned Target Volume (PTV)- Intensity Modulated Radiation Therapy (IMRT)-Testicular Shielding- Dosimetry

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Introduction

Over the past two decades, there has been notable progress in radiation therapy for prostate cancer. The treatment has evolved from simple X-ray fields based on bony structures to more advanced approaches like dose-escalated radiation therapy with image guidance and IMRT. According to the National Comprehensive Cancer Network (NCCN) guidelines, radiotherapy is recommended for patients across all risk groups, either as primary treatment or as part of a multimodal approach [1]. The goal of conformal radiotherapy is to deliver a high dose to the tumor while minimizing radiation exposure to surrounding organs [2].

IMRT, a significant technological advancement in conformal radiotherapy, offers unique capabilities due to its inverse planning feature. This technique involves using intensity-modulated beams with varying intensity levels for each beam direction and source position. Clinical studies have shown the benefits of escalated radiation doses in the radical treatment of localized prostate cancer [3, 4]. However, achieving a high dose to the prostate while minimizing radiation to adjacent organs, and reducing both immediate and long-term gastrointestinal side effects, remains challenging.

With 3DCRT technology, radiation doses of up to 72–74 Gy can be administered. Both historical and prospective data indicate that increased radiation therapy doses improve outcomes in clinically localized prostate cancer [5]. Nonetheless, the dose to the gonads poses a limitation when considering escalated doses for curative intent in locally advanced prostate cancer.

Prostate cancer patients often experience long-term effects of androgen suppression therapy, including various hormone-induced side effects such as an elevated risk of cardiac events, osteoporosis, metabolic syndrome, and diminished sexual function [6, 7]. While the impact of incidental testicular radiation on Leydig cell activity and testosterone production is well-known, the extent and clinical significance of testosterone decline following

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exclusive radiotherapy remain largely uncertain [8, 9].

In this study, we aim to compare testicular doses during 3DCRT and IMRT with lead testicular shielding. Our goal is to gain insight into incidental testicular irradiation and radiation-induced hypogonadism during prostate cancer treatment.

Materials and Methods

The current study is an institutional retrospective cohort review. Twenty prostate tumors with localized illness were included in the investigation. Lead testicular shielding (Figure 1) was used in all the patients at the time of simulation, treatment planning, and treatment execution. Between January 2021 and January 2022, the study was conducted. Prior to treatment, a thorough history and physical examination were performed on every patient. According to the Gleason score, T stage, and initial PSA of the patient, the group was divided into low, middle, and high risk. Patients who had metastases, a history of prostatectomy, chemotherapy, or cancer were disqualified from participating in this study. IMRT was used to treat every patient. Plans for each patient's 3DCRT were created. Regarding target volume dose homogeneity and critical organ doses, the 3D-CRT and IMRT designs were compared. Additionally the testicular doses received by the patients in the two techniques were noted and compared.

Before the simulation, patients were told to drink water, and whenever they felt a need for speed, computed tomography (CT) images with a 3 mm slice thickness were taken. The body's contouring for the neighboring delicate organs was both automatic and manual. The Clinical Target Volume (CTV) included only prostate in low-risk and prostate+seminal vesicle in intermediate-high risk patients. The planned target volume (PTV), with the exception of the posterior edge, which extended for just 5 mm, was represented by an 8 mm expansion of the CTV in all directions. In this work, we compared the critical organ sparing in general and testicular dose in particular, besides the dose homogeneity of the conventional dose (IMRT 70 Gy) with that of the 3D-CRT. For 7-field IMRT, dosimetric planning was done for the following treatment angles: 0, 51, 102, 153, 204, 255, and 306 degrees. For 4-field 3DCRT, dosimetric planning was done at treatment angles of 0, 90, 180, and 270 degrees. Apart from testicular dose, the mean doses of the femoral heads and the values of PTV maximum, PTV minimum, V25 (the volume receiving 25 Gy), V40, and V60 of the rectum and bladder were examined. The goal of this study was to assess the reduction of testicular dose by using the lead testicular shield while treating the malignancy with the best target volume dose uniformity and minimal critical organ irradiation. For this aim, mean values of V25, V40, and V60 of the testes, rectum and bladder as well as mean doses of the femoral heads were computed for 2 different procedures, and the data extracted from DVH's were statistically analyzed.

Figure 1. Lead Testicular Shielding

Statistical Analysis

Statistical analyses were performed in SPSS version 22.0 software (Chicago, ILL, USA) and SAS version 9.4. Significance level was set at P <0.01. As this was an observational study, no ethical clearance was sought.

Results

The IMRT and 3DCRT plans were dosimetrically evaluated. Dose coverage to PTVs in both the techniques achieved the constraint that 95% of the volume is covered by more than 95% of the prescribed dose. Dose homogeneity within the various PTV's was compared. There was a statistically significant difference between both techniques in average dose volume (p<0.001), proving IMRT to be better with respect to 3DCRT as the

Table 1. Average Dose-Volume Statistics for PTV for Both IMRT and 3DCRT Techniques

PTV	IMRT (Gy)	3DCRT (Gy)	p-value
PTV minimum	67	65	0.001
PTV maximum	72.5	74.2	0.001
Mean Dose	70	70.4	0.001

Table 2. Dosimetric Analysis of Parameters for Rectum, Bladder and Femoral heads

Parameters	IMRT (Gy) (mean±SD)	3DCRT (Gy) (mean±SD)	p-value
Rectum V25	74±2.4	78.4±4.27	0.001
Rectum V40	48.2±7.2	52.55±8.4	0.001
Rectum V60	12.55±6.3	27.70±9.3	0.001
Bladder V25	52.4±12.3	65.9±13.4	0.001
Bladder V40	32.6±14.2	51.3±15.2	0.001
Bladder V60	6.45±4.5	29.4±11.8	0.001
Left femoral head	17.7±5.67	28.5±4.3	0.001
Right femoral head	15.7±4.7	33.7±3.3	0.001

Table 3. Testicular Doses Received by the Patients in 3DCRT and IMRT Techniques

Patient	RT Technique	RT Dose (Gy)	Actual Testes Dose (Gy)	Testes Dose with Shield (%)	p-value
1	3DCRT	70	1.26	1.8	<0.01
	IMRT	70	3.43	4.9	<0.01
2	3DCRT	70	1.4	2	<0.01
	IMRT	70	3.36	4.8	<0.01
3	3DCRT	70	1.47	2.1	<0.01
	IMRT	70	0.18	0.25	<0.01
4	3DCRT	70	1.05	1.5	<0.01
	IMRT	70	0.22	0.32	<0.01
5	3DCRT	70	1.33	1.9	<0.01
	IMRT	70	3.29	4.7	<0.01
6	3DCRT	70	1.19	1.7	<0.01
	IMRT	70	3.15	4.5	<0.01
7	3DCRT	70	1.12	1.6	<0.01
	IMRT	70	3.36	4.8	<0.01
8	3DCRT	70	1.33	1.9	<0.01
	IMRT	70	3.22	4.6	<0.01
9	3DCRT	70	1.26	1.8	<0.01
	IMRT	70	3.29	4.7	<0.01
10	3DCRT	70	1.4	2	<0.01
	IMRT	70	3.15	4.5	<0.01
11	3DCRT	70	1.54	2.2	<0.01
	IMRT	70	0.2	0.28	<0.01
12	3DCRT	70	1.12	1.6	<0.01
	IMRT	70	0.2	0.29	<0.01
13	3DCRT	70	1.19	1.7	<0.01
	IMRT	70	3.22	4.6	<0.01
14	3DCRT	70	1.26	1.8	<0.01
	IMRT	70	3.08	4.4	<0.01
15	3DCRT	70	1.05	1.5	<0.01
	IMRT	70	3.29	4.7	<0.01
16	3DCRT	70	1.26	1.8	<0.01
	IMRT	70	3.15	4.5	<0.01
17	3DCRT	70	1.19	1.7	<0.01
	IMRT	70	3.29	4.7	<0.01
18	3DCRT	70	1.33	1.9	<0.01
	IMRT	70	3.22	4.6	<0.01
19	3DCRT	70	1.26	1.8	<0.01
	IMRT	70	3.08	4.4	<0.01
20	3DCRT	70	1.26	1.8	<0.01
	IMRT	70	3.08	4.4	<0.01

doses in IMRT are closer to the mean dose of 70 Gy (Table 1). Significantly lower doses to the entire OAR were achieved using IMRT (Table 2). Moreover, the maximum, minimum and average (mean) doses received by the testes were compared. Testicular doses received by the patients in 3DCRT and IMRT techniques are presented in Table 3. The dose received by the testes was marginally higher in IMRT as compared to 3DCRT.

Discussion

The increased risk of acute and long-term gastrointestinal and genitourinary complications associated with high radiation doses is a significant concern in prostate cancer treatment. Therefore, it is essential to assess dosimetric factors, dose volume guidelines, and constraints for critical structures like the rectum and bladder, which are considered organs at risk. Additionally, individuals with prostate cancer commonly experience enduring adverse

Table 4. A List of the Studies Examining the Testicular Doses and Its Affect on Testosterone Levels and Sexual Function in the Radiotherapy of Prostate Cancer

Study	Number of patients	Age (years)	RT dose (median)	RT technique	ADT	Follow-up (months)	Testicular dose	Hormonal levels	Sexual function
Grigsby et al. [20]	59	NS	65–70 Gy	3D-CRT	NR	24	4.5–6 Gy	Similar testosterone levels. Increased levels of LH and FSH after RT	NR
Tomić et al. [21]	31	65	58–71 Gy	3D-CRT	NR	20	Ranging between 1 Gy to > 10 Gy	Lower testosterone levels at 1 week and 3 months after RT. Testosterone levels returned to baseline 6–12 months after RT	NR
Zagars et al. [5]	85	68	68–76 Gy	3D-CRT	No ADT	3	1.8–2.4 Gy	Lower testosterone levels at 3 months after RT (9%)	NR
Pickles et al. [9]	666	72	65 Gy	3D-CRT	3 months ADT (neoadjuvant or adjuvant)	6	2.2 Gy	Lower testosterone levels at 3 months after RT (83% of the baseline level). Recovery to baseline levels for 60% of the patients, within 18 months after RT.	NR
Ishiyama et al. [6]	39	64	76 Gy	IMRT	No ADT	36	5.3 Gy	Lower testosterone levels at 12, 24, 30, 36 months	NR
Markovina et al. [8]	51 (prostate gland: 41; prostate bed: 10)	64	Prostate gland: 73.8 Gy Prostate bed: 64.8 Gy	IMRT	No ADT	24	0.31–2.4 Gy	Lower testosterone levels at 6 months after RT (–33 ng/dL) Testosterone levels returned to baseline 12 months after RT	NR
Pompe et al. [7]	248	71	70 Gy	IMRT	No ADT	72	NR	Lower testosterone levels for 75% of the patients after RT (median decrease: 30%)	NR
Oermann et al. [19]	26	69	36.25 Gy/5 fx	SBRT (CyberKnife)	No ADT	15	2.1 Gy	Lower testosterone levels for69% of the patients after RT (median decrease: 3.3 nmol/L) No difference in proportion of patients experiencing hypogonadism (before RT/ after RT)	Non-significant decrease in EPIC sexual score: Baseline: 66.7 1-year after RT: 60.1 (p = 0.34)
Yuan et al. [10]	636	69	35–40 Gy/5 fx 38 Gy/4 fx	SBRT	No ADT	24	NR	Lower testosterone levels after RT (median decrease: 3–6 months: −13.4%, 7–12 months: −12.2%, 13–18 months: −11.2% 19–24 months: - 5.0%)	No significant decrease in EPIC sexual score on the whole period Significant decrease in EPIC sexual score between 19 and 24 months (10.9 points decline)

effects of androgen suppression therapy, including a heightened risk of cardiovascular events, osteoporosis, metabolic syndrome, and reduced sexual function.

In this study, we compared IMRT and 3D-CRT plans in terms of dose distribution and critical structure doses in patients with low- and intermediate-high risk prostate cancer, with a focus on gonadal doses. Our findings revealed that IMRT outperformed 3D-CRT in terms of dose uniformity and lower critical organ doses. However, IMRT showed a slightly higher gonadal dose compared to 3D-CRT. IMRT has long been established as the standard of care for prostate cancer treatment, serving as a viable alternative to surgery. In a similar comparison study by Zelefsky et al., IMRT was found to be more effective than 3D-CRT in prostate cancer treatment, with lower doses to critical structures contributing to the improved uniformity of radiation delivery [10].

Consistent with our results, other studies by Lee et al. and Zhu et al. also demonstrated the advantages of IMRT in terms of dose homogeneity and critical organ doses [11, 12]. Additionally, Wolff et al. found that IMRT resulted in lower rectal V40 compared to 3D-CRT, with further support from Vaarkamp et al. who reported decreased rectal V60 with IMRT [13, 14]. Moreover, increasing beam numbers in IMRT positively impacted dose homogeneity and reduced critical organ doses, as observed in the study by Vaarkamp et al., where patients received successful IMRT treatment without increased acute toxicity [14].

In the RTOG 0126 trial, patients receiving high-dose IMRT showed significantly reduced volumes of the bladder and rectum compared to those receiving 3D-CRT, supporting the advantages of IMRT in minimizing critical organ exposure [15, 16]. Similarly, in another study, patients treated with high doses of IMRT experienced less gastrointestinal toxicity compared to those receiving lower doses of 3D-CRT. Notably, the frequency of late toxicities increased with the volume of rectum receiving high radiation doses, as demonstrated in the MD Anderson study [17, 18].

Despite dose escalation, IMRT has been shown to have less late toxicity than 3D-CRT in various institutional datasets. Overall, higher radiation doses are now considered the standard therapy for clinically localized prostate cancer.

Several researchers [20-28] have examined the testicular dose across various techniques, including 3DCRT, IMRT, and SBRT (Table 4). Our investigation uncovered a notable reduction in testicular dose when employing a lead testicular shield. Specifically, we observed a slightly lower testicular dose in 3DCRT compared to IMRT. This discrepancy may be attributed to the higher number of beams in IMRT, leading to increased tissue exposure and integral dose, consequently resulting in greater scatter dose to the testes.

In conclusion, our study highlights the advantages and considerations associated with different radiation therapy techniques in prostate cancer management. Intensity-modulated radiation therapy (IMRT) emerges as a superior choice due to its enhanced dose homogeneity, superior conformity to the target volume, and efficient sparing of organs at risk (OARs). IMRT's capability to optimize dose distribution offers a significant benefit in minimizing radiation-related toxicity while ensuring effective tumor control. Conversely, 3-dimensional conformal radiation therapy (3DCRT) exhibits a noteworthy advantage in terms of lower testicular doses compared to IMRT. This aspect underscores the importance of evaluating not only target coverage and critical organ sparing but also potential impacts on gonadal health, particularly given the long-term concerns associated with androgen suppression in prostate cancer patients.

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Conflict of Interest
Nil

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