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Comparison of various common whole pelvic radiotherapy (WPRT) and local radiotherapy (LRT) procedures to treat prostate cancer based on dosimetric parameters and radiobiological models

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► ***Original article***

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ABSTRACT

Background: Comparing three whole pelvic radiotherapy (WPRT) procedures as well as two local radiotherapy (LRT) procedures with each other for the treatment of prostate cancer patients using dosimetric parameters and radiobiological models: tumor control probability (TCP), normal tissue complication probability (NTCP), and equivalent uniform dose (EUD). ***Materials and Methods:*** Two groups of prostate cancer patients underwent WPRT (n=16) and LRT (n=16) procedures. In the WPRT group, the patients treated with two intensity modulated radiation therapy (IMRT+IMRT) procedures at two consecutive phases. Then, two other techniques including a three dimensional (3D) conformal radiation therapy (3DCRT) phase followed by an IMRT phase (3DCRT+IMRT) and also two consecutive 3DCRT procedures (3DCRT+3DCRT) were carried out on the patients' data. In the LRT group, the patients treated with just an IMRT technique. Then a 3DCRT technique was also performed on the patients' data. All the WPRT and LRT procedures compared with each other based on the dosimetric parameters and radiobiological models. ***Results:*** The mean of dosimetric parameters did not exceed the specified dose constraints for the bladder and femoral heads in the 3DCRT+ IMRT, and for the bladder in the 3DCRT technique. In the WPRT and LRT procedures, the TCP values for the prostate did not reveal any significant differences (P>0.05). The NTCP results in accordance with the dosimetric results for the organs at risk (OARs) showed a significant decrease in the IMRT+IMRT (WPRT) and the IMRT (LRT) techniques (P<0.05). However, the EUD results were dependent on the type of the procedure and OARs. ***Conclusion:*** For selecting the appropriate treatment technique for each prostate cancer patient, a compromise between the dosimetric and radiobiological evaluation of the WPRT and LRT procedures should be considered.

Keywords: *Prostate cancer, whole pelvic radiotherapy (WPRT), local radiotherapy (LRT), dosimetric parameters, radiobiological models.*

INTRODUCTION

Prostate cancer is a serious health problem and the second leading cause of cancer death in men [1]. Surgery, proton beam therapy, and external beam radiation therapy (EBRT) are the current treatment options [2, 3]. EBRT could be carried out either with the intensity-modulated radiation therapy (IMRT) or 3D conformal radiation therapy (3DCRT) techniques [4-7]. In IMRT and 3DCRT techniques, the prescribed dose is delivered by either the whole pelvic radiotherapy (WPRT) or local radiotherapy (LRT) procedures.

The choice of the WPRT and LRT procedures for treating patients depends on the lymph node (LN) involvement, and where only the WPRT procedure, is used. The WPRT procedures are commonly performed in two phases by combining different radiotherapy techniques. The treatment planning technique, margins, and delivered dose used in both phases are different. Nevertheless, the LRT procedure is done in one phase by delivering just a single dose [8-11]. The appropriate radiation field size is especially challenging for the patients with prostate cancer wherein the LNs are part of the treatment field [12]. Therefore, in WPRT procedures where a large area of the pelvic LNs is irradiated, a technique with the best results should be considered for implementation. The organs at risk (OARs) may receive noticeably different dose distributions from the IMRT and 3DCRT procedures [13].

The IMRT tends to irradiate large volumes of OARs with low radiation doses, whereas the 3DCRT tends to irradiate a small volume of OARs with moderate to high doses [14]. Additionally, the IMRT is claimed to show better dosimetric results in sparing the OARs than the 3DCRT [15, 16]. Although the use of IMRT has become quite familiar and prominent for prostate cancer treatment, the dose limits to OARs have not been standardized yet. However, for the techniques with better clinical outcomes by the IMRT compared with 3DCRT, the resulting effects remain ambiguous [13].

Preferring a specific therapeutic approach requires assuring a significant benefit over the other ones for tumor control. Evaluating EBRT procedures by a quantitative criterion for selecting an optimum irradiation technique plays an important role on the outcome of radiation treatments. Dose distributions and dose-volume histograms (DVHs) are two standard and well-established indicators helping to differentiate available treatment procedures for obtaining the most desirable clinical outcome [17]. Several studies have noted that the radiobiological ranking of treatment plans assists clinicians to find optimum treatment procedures when the relevant dose distributions and DVH results are very close to each other and hard to differentiate [18, 19].

Therefore, using radiobiological modeling is recommended for creating a radiobiological index to evaluate dose distributions [20]. Biological modeling uses the DVH of a given plan and biological parameters of OARs and tumor type for calculating the normal tissue complication probability (NTCP) and tumor control probability (TCP). Conclusively, it would be desirable to use both the dosimetric parameters and radiobiological models in optimization process of various available treatment planning protocols.

While some studies have been conducted to assess the outcomes of IMRT techniques in patients with prostate cancer, there are still some concerns about the overall superiority of such techniques over the 3DCRT. Some limitations of IMRT techniques are related to their increased risk of secondary malignancies as well as the increased time and cost compared to 3DCRT. The overall superiority of each radiotherapy procedure must be expressed based on evaluating both of the dosimetric and radiobiological outcomes of all the OARs in the tumor region, since similar dosimetric parameters in various procedures may have significantly different radiobiological outcomes.

Therefore, it seems that a comprehensive comparison of common WPRT and LRT procedures based on the dosimetric as well as radiobiological evaluations could be more indicative. To the best of our knowledge, no specific study has been conducted to compare WPRT procedures and LRT procedures with

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each other for treating prostate cancer patients. Hence, in this study we aimed to compare three different WPRT procedures and two LRT procedures with each other based on the familiar dosimetric parameters as well as radiobiological models including the TCP, NTCP, and EUD on prostate cancer patients.

MATERIALS AND METHODS

Patient selection

The study was carried out from September 2019 up to June 2020 on two groups of prostate cancer patients including 16 men treated with the WPRT procedure (mean age: 73 years; range: 55–91) and another 16 men with the LRT procedure (mean age: 71 years; range 55–87) at Roshana Radiation Oncology Center (Tehran, Iran). The intermediate-risk was defined when the patients had one of the factors including stage T2b-c, or Gleason score=7, or prostate-specific antigen (PSA)=10-20 ng/mL. The patients having more than one of these factors or stage T3, or Gleason score >7, or PSA > 20 ng/mL were defined as the high-risk. The patients with low-risk tumors were not included in the study.

The ethics committee of Tarbiat Modares University (TMU) approved the study (IR.MODARES.REC.1397.163). All the procedures performed in the study involving human participants were in accordance with the Helsinki Declaration (1964) and its' amendments.

Imaging and contouring

For each patient, three gold fiducial markers were placed in appropriate locations of the prostate. All the patients underwent computed tomography (CT) and magnetic resonance imaging (MRI) examination. Before performing the CT and MRI, all the patients were instructed to have their bowels empty and drink 300 ml of water 20 min before examination and treatment sessions. CT images were performed using a 16-slice CT scanner (Siemens Medical Solutions, Forchheim, Germany). The CT parameters were 120 KVp, 230 mAs, 1 mm slice thickness, 512×512 matrix size; 0.976×0.976×1 mm^3 voxel size, and 50 cm field of view (FOV). The MR images were acquired on a 1.5 T MR system (Ingenia, Siemens Medical Solutions, Germany) with an endorectal coil for acquiring high spatial resolution images. The T2-weighted MRI parameters were as follows: 7920 ms TR/, 93 ms TE, 3 mm slice thickness, 320×320 matrix size, 0.062×0.062×3 mm^3 voxel size, and 20 cm FOV. These CT and MR images were rigidly registered and all the images of every patient were effectively placed at the same spatial reference frame [21]. The images were imported into the Varian Eclipse v.13.6 (Varian Medical System Inc, Palo Alto, CA, USA) treatment planning software (TPS) for WPRT and LRT planning. The planning target volumes (PTVs) and OARs including: seminal vesicles (SVs), LNs, bladder, rectum, and femoral heads were delineated on the patients' images by a radiation oncologist.

WPRT planning

In the WPRT procedure, the patients were treated with two consecutive IMRT techniques (IMRT+IMRT) performed at two phases. Then, two other WPRT procedures including: a 3DCRT phase followed by an IMRT phase (3DCRT+IMRT), and two consecutive 3DCRT phases (3DCRT+3DCRT) were studied on the patients' data. Both of the IMRT+IMRT and 3DCRT+IMRT procedures were planned by 6 MV photon beams delivering a total dose of 50 Gy in 2-Gy fractions to the patients' prostate, SVs, and LNs followed by 30 Gy in 2-Gy fractions to the prostate alone. At both of the phases, the seven fields' technique was used at various gantry rotation angles including 0°,65°,95°,135°,225°,265°, and 295°. The relevant margins chosen for the prostate were 6 and 7 mm along the "posterior" and "cranial-caudal, transverse, and anterior" directions, respectively. A margin of 10 and 7 mm was also used for the SVs and LNs, respectively. For the 3DCRT+3DCRT procedure, the dose was delivered at two phases by using 6 and 18 MV photon beams. At the first phase, a dose of 50 Gy with 2Gy/fraction was delivered by a four-field (AP, PA, and lateral) box

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technique with an 18 MV photon beam and at the second phase, a dose of 30 Gy with 2Gy/fraction was delivered with a 6 MV photon beam.

LRT planning

In the LRT procedure, the patients were treated with an IMRT technique. Then, a 3DCRT technique was studied on the patients' data. For both of the IMRT and 3DCRT techniques, a total dose of 80 Gy with 2Gy/fraction was delivered with 6 MV photon beams. All the patients were treated by a seven-fields technique at various gantry rotation angles including 0°,65°,95°,135°,225°,265°, and 295°. For these techniques, the relevant margins chosen for the prostate were 6 and 7 mm along the "posterior" and "cranial-caudal, transverse, and anterior" directions, respectively. A 10 mm margin was also used for the SVs.

Treatment planning evaluation

The WPRT as well as LRT treatment plans were compared with each other based on the dosimetric parameters as well as the TCP, NTCP, and EUD parameters derived from radiobiological models.

Dosimetric parameters

Based on isodose distributions and DVHs for the target and OARs, three WPRT planning procedures including IMRT+IMRT, 3DCRT+IMRT, and 3DCRT+3DCRT were compared with each other. A comparison was also made between two LRT planning procedures including an IMRT and 3DCRT. In the WPRT and LRT planning, the PTV encompassed 95-107% of the prescribed dose. Based on the DVHs and according to the dose constraint mentioned in table 1, doses were reported for the PTVs and OARs volumes.

Radiobiological models

For radiobiological evaluation of the treatment plans, the Bio Suite (Clatterbridge Cancer Centre, Bebington, UK; Version: 10-01-2018) software was used [22]. The TCP was calculated for both of the WPRT and LRT plans by using the LQ-based Poisson TCP model [23] in which the TCP is formulated over a structure's voxels weighted probability function as seen in equation 1.

$$TCP = \prod_{i=1}^{M} P(D_i)^{v_i} \quad (1)$$

where M is the number of voxels and $v_i = V_i / V_{ref}$ is the relative volume of the voxel.

The NTCP was estimated using the Lyman-Kutcher-Burman (LKB) model [24]. This model parameters are given by Burman *et al.* [25] and compiled by Emami *et al.* [26]. The LKB model is designed to describe complication probabilities for a uniformly irradiated whole or partial organ volume. According to the LKB model, the NTCP is calculated using equations 2 and 3:

$$NTCP = 1/\sqrt{(2\pi)} \cdot \int_{-\infty}^{t} e^{-u^2/2}\, du \quad (2)$$

in which:

$$t = \frac{D_{eff} - TD_{50}}{mTD_{50}} \quad (3)$$

where D_{eff} is the dose that if given uniformly to the entire volume will lead to the same NTCP as an actual non-uniform dose distribution, TD_{50} is the uniform dose given to the entire organ that results in 50% complication risk, and m is a measure of the slope of the sigmoid curve.

The EUD parameter was calculated using equation 4:

$$EUD = \left[\sum \frac{(V_i D_i)^a}{1}\right]^{1/a} \quad (4)$$

where v_i is the fractional organ volume receiving a dose D_i and a is a tissue-specific parameter that describes the volume effect.

Statistical analysis

Data were analyzed using the GraphPad Prism software (GraphPad Software, Inc., San Diego, CA, USA). The D'Agostino–Pearson test was applied for assessing the normality of data [27]. To compare the mean of dosimetric and radiobiologic variables in the WPRT procedures, one way ANOVA or Kruskal–Wallis test was used when the data followed a normal or non-normal

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distribution, respectively. To compare the mean of variables in the LRT procedures, t-test or Mann–Whitney test was used when the data followed the normal or non-normal distribution, respectively. P-values less than 0.05 were considered as statistically significant.

Table 1. Dose constraints used for the WPRT and LRT procedures.

Organs at Risk	Dose-Volume Parameter
Bladder[a]	V80 < 15% V75 < 25% V70 < 35% V65 < 50%
Rectum[a]	V75 < 15% V70 < 20% V65 < 25% V60 < 35% V50 < 50%
Femoral Heads[b]	[c] V40 < 40% V50 < 10%

[a]QUANTEC recommendations. [b]RTOG recommendations. [c]V40: structure volume receiving at least 40 Gy.

RESULTS

Dosimetric and radiobiological analysis of WPRT procedures

The dosimetric comparison of OARs between the WPRT procedures is presented in table 2. According to the table, significant differences are noted between the IMRT+IMRT and 3DCRT+3DCRT techniques, and also between 3DCRT+IMRT and 3DCRT+3DCRT techniques (P<0.05) for the bladder based on all the dosimetric parameters. The results of the 3DCRT+IMRT technique show an increase in all the dosimetric parameters for the bladder compared to the IMRT+IMRT technique, but these differences were not statistically significant for the V80, V75, and V70 percentages (P>0.05). For the rectum, significant differences are noted in all the dosimetric parameters for the IMRT+IMRT vs. 3DCRT+IMRT, IMRT+IMRT vs. 3DCRT+3DCRT, and also 3DCRT+IMRT vs. 3DCRT+3DCRT (P<0.05). The differences reported for the femoral heads in all the dosimetric parameters between the IMRT+IMRT and 3DCRT+IMRT and IMRT+IMRT and 3DCRT+3DCRT techniques were significant (P<0.05).

However, no significant difference was noted between the 3DCRT+IMRT and 3DCRT+3DCRT techniques for the mean dose (Gy) parameter (P>0.05). In general, for the bladder and femoral heads in the two techniques of IMRT+IMRT and 3DCRT+IMRT, the mean of dosimetric parameters is not exceeded the given dose constraints presented in table 1. Nevertheless, the mean of dosimetric parameters for the rectum in the 3DCRT+IMRT and 3DCRT+3DCRT techniques exceed the dose constraints.

The radiobiological comparison of the prostate and OARs between the WPRT procedures is presented in table 3. The TCP results for the prostate did not reveal any significant differences between all the WPRT procedures (P>0.05). Evaluation of the NTCP results in OARs showed significant differences between the WPRT procedures (P<0.05). The results of EUD evaluation showed a statically significant difference (1.7%) for the prostate between the IMRT+IMRT and 3DCRT+3DCRT techniques (P=0.004). However, no significant difference was reported between the IMRT+IMRT and 3DCRT+IMRT techniques, as well as the 3DCRT+IMRT and 3DCRT+3DCRT for the EUD (P>0.05).

Evaluation of the EUD results in organs such as the bladder and femoral heads indicated significant differences between all the WPRT procedures (P<0.05). The EUD results showed a significant difference for the rectum between the IMRT+IMRT and 3DCRT+3DCRT techniques (9.01%), and 3DCRT+IMRT and 3DCRT+3DCRT (5.40%) (P<0.05). Nevertheless, the difference reported between the IMRT+IMRT and 3DCRT+IMRT techniques was not statistically significant (P=0.058).

Dosimetric and radiobiological analysis of LRT procedures

The dosimetric comparison of OARs between the LRT procedures is presented in table 4. According to the table, for the bladder, significant differences are noted between the IMRT and 3DCRT techniques for all the dosimetric parameters (P<0.05) except the percentage of V65 (P=0.0594). Moreover,

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significant differences are noted for the rectum and femoral heads for all the dosimetric parameters between the IMRT and 3DCRT techniques (P<0.05). The IMRT plans delivered a smaller mean dose to the bladder (8.56 Gy), rectum (15.87 Gy), right femur head (16.35 Gy) and left femur head (14.39 Gy). In general, for the rectum and the femoral heads in the 3DCRT technique, the mean of dosimetric parameters exceeds the given dose constraints presented in table 1.

The radiobiological comparison of the prostate and OARs between the LRT procedures is presented in table 5. As could be seen, the TCP results in the prostate does not reveal any significant differences between the IMRT and 3DCRT techniques (P=0.8308). Evaluation of the NTCP results for all the OARs showed a significant increase in the 3DCRT compared to the IMRT technique (P<0.05). Results of the EUD evaluation for the prostate and bladder did not reveal any significant differences between the IMRT and 3DCRT techniques (P>0.05). Nonetheless, a significant increase was noted when the 3DCRT technique was compared to the IMRT technique for the rectum and femoral heads (P<0.05).

Table 2. Comparison of the dosimetric parameters among all the investigated WPRT procedures.

Structure	Dosimetric Parameters	IMRT+IMRT	3DCRT+IMRT	3DCRT+3DCRT	P-value		
		mean±SD	mean±SD	mean±SD	IMRT+IMRT vs. 3DCRT+IMRT	IMRT+IMRT vs. 3DCRT+3DCRT	3DCRT+IMRT vs. 3DCRT+3DCRT
Bladder	V80 (%) [a]	5.52±3.43	6.45±4.39	13.16±3.62	0.758	<0.0001	0.0005
	V75 (%)	13.62±5.07	16.51±9.29	27.72±8.99	0.568	<0.0001	0.0008
	V70 (%)	18.91±6.67	22.67±9.28	34.25±12.52	0.527	0.0002	0.0046
	V65 (%)	25.45±8.02	36.09±8.94	48.34±8.67	0.0029	<0.0001	0.0006
	Mean dose (Gy)	50.33±4.51	58.58±5.03	65.83±4.82	< 0.0001	<0.0001	0.0003
Rectum	V75 (%)	12.52±3.83	18.9±5.97	27.21±6.44	0.0059	<0.0001	0.0003
	V70 (%)	17.67±2.73	26.45±5.99	35.52±10.86	0.0042	<0.0001	0.003
	V65 (%)	23.49±3.23	34.76±8.9	46.06±5.27	<0.0001	<0.0001	0.0001
	V60 (%)	31.65±5.97	46.43±10.74	57.72±10.53	0.0002	<0.0001	0.0038
	V50 (%)	44.86±6.98	61.9±10.12	71.57±11.2	<0.0001	<0.0001	0.017
	Mean dose (Gy)	47.17±4.5	54.08±4.84	63±6.4	0.0018	<0.0001	<0.0001
Left Femur Head	V40 (%)	20.45±6.97	34.82±6.73	52.66±5.47	<0.0001	<0.0001	<0.0001
	V50 (%)	4.08±2.36	8.29±3.79	13.15±2.39	0.0005	<0.0001	<0.0001
	Mean dose (Gy)	29.19±3.95	38.71±3.07	39.54±4.64	<0.0001	<0.0001	0.832
Right Femur Head	V40 (%)	20.24±8.88	34.39±8.56	52.29±5.42	<0.0001	<0.0001	<0.0001
	V50 (%)	4.46±3.79	8.15±2.81	12.49±2.99	0.0064	<0.0001	0.0012
	Mean dose (Gy)	29.2±3.73	38.68±2.73	40.21±3.94	<0.0001	<0.0001	0.443

Table 3. Comparison of the radiobiologic parameters among all the investigated WPRT procedures.

Structure	Radiobiologic Parameters	IMRT+IMRT	3DCRT+IMRT	3DCRT+3DCRT	P-value		
		mean±SD	mean±SD	mean±SD	IMRT+IMRT vs. 3DCRT+IMRT	IMRT+IMRT vs. 3DCRT+3DCRT	3DCRT+IMRT vs. 3DCRT+3DCRT
Prostate	TCP (%)	69.85±3.1	68.74±2.04	68.13±1.5	0.261	0.063	0.752
	EUD (Gy)	85.82±1.8	84.93±1.3	84.35±1.26	0.113	0.004	0.404
Bladder	NTCP (%)	0.07±0.10	1.89±1.03	3.41±2.75	0.002	<0.0001	0.048
	EUD (Gy)	49.13±4.75	57.42±4.48	61.35±3.55	<0.0001	<0.0001	0.049
Rectum	NTCP (%)	9.53±2	13.41±2.1	23.3±3.25	<0.0001	<0.0001	<0.0001
	EUD (Gy)	65±2.33	67.58±2.3	71.44±4.08	0.058	<0.0001	0.0002
Left Femur Head	NTCP (%)	0.0006±0.0025	0.045±0.079	0.14±0.12	0.01	<0.0001	0.0051
	EUD (Gy)	29.06±3.68	36.86±2.15	40.9±4.11	< 0.0001	< 0.0001	<0.0001
Right Femur Head	NTCP (%)	0.0006±0.0025	0.044±0.07	0.126±0.13	0.01	<0.0001	0.0054
	EUD (Gy)	28.75±3.85	36.08±2.58	40.31±4.46	<0.0001	<0.0001	<0.0001

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Table 4. Comparison of dosimetric parameters between the investigated LRT procedures.

Structure	Dosimetric Parameters	IMRT mean±SD	3DCRT mean±SD	P-value
Bladder	V80 (%)	3.06±1.87	11.78±4.85	<0.0001
	V75 (%)	11.9±3.98	21.66±4.53	<0.0001
	V70 (%)	16.39±5.1	24.88±7.25	0.0006
	V65 (%)	22.3±6.41	29.57±13.37	0.0594
	Mean dose (Gy)	38.68±5.11	47.24±8.69	0.0020
Rectum	V75 (%)	12.62±5.28	32.52±4.73	<0.0001
	V70 (%)	15.71±2.96	37.74±4.51	<0.0001
	V65 (%)	20.55±2.63	44.39±3.94	<0.0001
	V60 (%)	25.29±4.35	57.64±6.63	<0.0001
	V50 (%)	36.26±3.78	70.11±6.72	<0.0001
	Mean dose (Gy)	41.67±1.96	57.54±3.86	<0.0001
Left Femur Head	V40 (%)	11.73±3.75	41.53±8.49	<0.0001
	V50 (%)	1.79±1.04	15±3.53	<0.0001
	Mean dose (Gy)	25.8±3.36	40.19±4.87	<0.0001
Right Femur Head	V40 (%)	11.87±5.15	42.77±7.6	<0.0001
	V50 (%)	1.9±0.8	11.64±2.33	<0.0001
	Mean dose (Gy)	23.5±5.15	39.85±5.23	<0.0001

Table 5. Comparison of radiobiologic parameters between the investigated LRT procedures.

Structure	Radiobiologic Parameters	IMRT mean±SD	3DCRT mean±SD	P-value
Prostate	TCP (%)	70.57±1.49	70.46±1.59	0.8308
	EUD (Gy)	85.83±2.01	85.81±1.91	0.9668
Bladder	NTCP (%)	0.048±0.02	1.06±0.44	<0.0001
	EUD (Gy)	45.94±6.47	47.95±6.08	0.3714
Rectum	NTCP (%)	9.52±1.8	25.3±4.66	<0.0001
	EUD (Gy)	64.47±3.93	72 ±1.45	<0.0001
Left Femur Head	NTCP (%)	0.0005± 0.0004	0.12±0.07	<0.0001
	EUD (Gy)	26.74±1.47	41.12±6.5	<0.0001
Right Femur Head	NTCP (%)	0.0006± 0.002	0.115±0.09	<0.0001
	EUD (Gy)	26.48±1.96	40.95±6.79	<0.0001

DISCUSSION

More adaptation to the tumor volume and less damage to the OARs are the most important factors for choosing a radiation therapy procedure. The overall superiority of each procedure must be expressed based on evaluating both of the dosimetric and radiobiological outcomes of all the OARs in the tumor region because some procedures having similar dosimetric parameters may have significantly different radiobiological outcomes. To the best of our knowledge, no specific study has been carried out to compare WPRT procedures with each other, as well as, LRT procedures with one another in prostate cancer patients. Therefore, in this study a comprehensive comparison was made between three WPRT procedures (IMRT+IMRT, 3DCRT+IMRT, and 3DCRT+3DCRT) as well as two LRT procedures (IMRT and 3DCRT) based on not only common dosimetric parameters but also radiobiological outcomes including TCP, NTCP, and EUD for treating prostate cancer patients.

Comparing the dosimetric evaluation of the OARs showed that the IMRT+IMRT procedure results in a remarkable decrease in the doses received by the OARs compared to the 3DCRT+3DCRT. Ashman *et al.* [8] examined the correlation between clinical morbidity and dosimetric parameters for WPRT in prostate cancer using either two consecutive IMRT (IMRT+IMRT) or two consecutive 3DCRT (3DCRT+3DCRT) techniques. They reported that IMRT+IMRT was superior to 3DCRT+3DCRT in limiting the volume of OARs within high-dose regions. In our study, the bladder mean dose was in close agreement with that of Ashman *et al*., while the rectum mean dose was considerably higher because of differences in treatment planning procedures and prescribed doses. Nevertheless, in addition to the dosimetric parameters we assessed radiobiological outcomes to compare various extra radiation treatment procedures. Luxton *et al.* [16] compared local-field irradiation (LFI) and extended-field irradiation (EFI) procedures for prostate cancer treatment. In their LFI procedures, a dose of 70 and 74 Gy were used for IMRT and 3DCRT techniques, respectively. Furthermore, in their EFI, a dose of 70 Gy was delivered for both the two consecutive IMRT (IMRT+IMRT) and two consecutive 3DCRT

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(3DCRT+3DCRT) techniques. They reported that for all the OARs, the mean NTCP tended to be lower for IMRT+IMRT and IMRT compared with 3DCRT+3DCRT and 3DCRT, respectively. Reported differences were statistically significant for rectum in LFI and EFI procedures and bladder in EFI procedures.

Our NTCP results for the rectum are in accordance with Luxton *et al.*'s data, while for the bladder and femoral heads our results are not in agreement with theirs due to the differences in treatment planning procedure and delivered doses. Similar to our results, Luxton *et al.* reported greater TCP for IMRT+IMRT and IMRT than 3DCRT+3DCRT and 3DCRT. However, in our study, in addition to the mean dose, various dosimetric parameters (the percentage of V80, V75, V70, and V65 for bladder, and V75, V70, V65, V60, and V50 for the rectum, and V40 and V50 for the femoral heads) and besides the TCP and NTCP, the radiobiological EUD parameter was also assessed. Moreover, in addition to the IMRT+IMRT and 3DCRT+3DCRT procedures, we assessed the 3DCRT+IMRT procedure that has not been addresses by Luxton *et al.*.

Yu *et al.* [6] carried out a review study to determine whether the IMRT technique can provide better clinical outcomes in comparison with the 3DCRT technique for patients with prostate cancer. They stated that IMRT should be considered a better choice. The main difference between our study and Yu et al. was the prescribed dose to the whole prostate and LNs, dosimetric and radiobiologic comparison between WPRT procedures and also LRT procedures. Moreover, we observed that despite the high-dose prescribed for the IMRT technique (80 Gy), the doses delivered to the OARs do not exceed the limits.

Cambria *et al.* [28] compared treatment plans of 57 patients to analyze the reliability of the LKB model. They reported that the performance of the LKB model could be as reliable as the performance of DVH constraints. In accordance with Cambria *et al.* study, our results confirmed that, in addition to the dosimetric parameters, using the LKB model can be useful for assessing the outcomes of various treatment procedures.

Mesbahi *et al.* [29] assessed the planning results by the comparison of 3DCRT and IMRT plans in terms of radiobiological metrics including TCP, NTCP, and EUD. In agreement with our study, they concluded that IMRT plans are superior to 3DCRT in terms of NTCP for the OARs. Their data were also in accordance with ours in terms of TCP calculation indicating no significant benefit with IMRT plans compared to 3DCRT plans. Nevertheless, our study was different as we evaluated various dosimetric parameters and additional treatment procedures. Bhardwaj *et al.* [30] analyzed the dosimetric and radiobiologic advantages between IMRT and 3DCRT procedures. In their study, 24 patients with localized prostate carcinoma were planned using 3DCRT and IMRT techniques. They analyzed treatment plans using mean, median, maximum dose, and DVH. They also calculated TCP and NTCP for the prostate and OARs. Similar to the Bhardwaj *et al.*, our mean dose to the bladder and rectum in the 3DCRT was higher than the IMRT technique. However, due to the different treatment planning procedures, our mean delivered dose was higher. Their NTCP results for the rectum were in accordance with ours, while their NTCP results for the bladder were not in agreement with ours.

Moreover, similar to our results, Bhardwaj *et al*. [30] reported greater TCP for IMRT than 3DCRT. Nevertheless, in addition to the LRT procedures, we assessed WPRT procedures based on the radiobiological EUD parameter, besides the TCP and NTCP, as well as different extra dosimetric parameters compared to that reported earlier [30].

CONCLUSION

The results of this study indicated that dosimetric and radiobiologic parameters of OARs improved significantly for the WPRT (IMRT+IMRT) and LRT (IMRT) compared with the other WPRT procedures and 3DCRT technique. Nevertheless, based on some dosimetric and radiobiologic parameters, there was no statistically significant difference between the three WPRT and two LRT

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procedures. Therefore, it can be concluded that the selection of an appropriate treatment technique should be decided via a compromise to be made between the dosimetric and radiobiological outcomes of various WPRT and LRT procedures chosen for every patient.

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