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Dosimetric comparison of prostate radiotherapy between pelvic node-positive and node-negative patients

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► ***Original article***

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ABSTRACT

Background: The importance of dose in prostate radiotherapy is well known, and the dosimetric effects of radiotherapy in node-positive or node-negative patients with prostate cancer have become an important issue. ***Materials and Methods:*** Helical tomotherapy (TH) plans of 19 pelvic node-positive [THpn(+) plan] or node-negative [THpn(-) plan] patients with prostate cancer were retrospectively created in our clinic. In these plans, the beam angle was set to cover the planning target volume (PTV) of prostate cancer and minimize the dose to the organs at risk, including the bladder, rectum, femoral head, and bowel. ***Results:*** There were no differences in the conformity index, D_{max}, D_{mean}, and homogeneity index of PTV between the THpn (+) and THpn (-) plans ($p>0.05$). However, V95 in the THpn (+) plan was lower than that in the THpn (-) plan ($p=0.017$). Moreover, D_{max}, V75, V70, V65, V60, V50, V40, V30, and V20 for the rectum were not significantly different between the two plans ($p>0.05$), whereas D_{mean} was significantly different ($p=0.025$). D_{max}, V70, V65, and V60 for the bladder were not significantly different between the two plans ($p>0.05$), whereas V55, V50, V40, and V30 were significantly different ($p<0.05$). Finally, D_{max} and V50 for the femoral head and bowel were significantly different between the two plans ($p<0.05$). ***Conclusion:*** The THpn (+)] and [THpn(-) plans achieved acceptable target dose coverage in prostate radiotherapy.

Keywords: *Prostate cancer, TomoHelical, irradiation.*

INTRODUCTION

Novel radiotherapeutic techniques achieve a highly improved dose distribution during the management of prostate cancer [1]. Previously, the coplanar beam arrangement was considered the gold standard; currently, however, various radiation techniques that can deliver relatively high doses to the prostate are available [2], including image-guided intensity-modulated radiotherapy (IG-IMRT) [3], helical tomotherapy (TH) with multileaf collimators [4], modulated volumetric arc therapy (VMAT), CyberKnife (CK; an advanced robotic system) [5], and salvage radiotherapy (SRT) [6]. Recent advances in radiotherapeutic techniques have enabled the delivery of highly conformal and homogeneous doses to the target volume while sparing the organs at risk (OARs) [7, 8].

The advantage of IMRT in decreasing acute bowel toxicity during whole-pelvis radiotherapy [WPRT node (+)] in high-risk patients with prostate cancer has been demonstrated in several recent studies in both primary and postoperative settings [9, 10]. Postprostatectomy radiotherapy improved the outcomes of patients with positive surgical margins [11] and a subset of patients with pelvic lymphatic involvement [12]; however, the 10-year progression-free survival rate of these patients remained between 56% and 61% [13, 14]. Diverse maximum safe doses to the rectum and bladder have been recommended, with the doses at 65% of the rectal and bladder volumes,

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or below 70 Gy, being the most preferred ones (15, 16). Meanwhile, the doses of V50<2% and Dmax<50Gy have been recommended for the femoral head [17].

In the present study, we aimed to decrease the OAR volume using two TH plans (pelvic node positive or node negative) and compared the developed plans with those of patients with prostate cancer in whom the planning target volume (PTV) coverage had been achieved. Such planning can ensure acceptable toxicity to the OARs. The novelty of these plans is that they minimize radiation exposure of the OARs during prostate radiotherapy.

MATERIALS AND METHODS

Patients

In the present planning study, we included 11 pelvic node-positive patients and 8 pelvic node-negative patients with primary prostate cancer, who had undergone prostate-conserving therapy. The median patient age was 48 (24–80) years, and all patients underwent radiotherapy according to the TH plans between March 2016 and August 2017 at the Department of Radiation Oncology of our university hospital. All procedures were approved by the Dicle University Medical Faculty Ethics Committee for Noninterventional Studies (#06.06.2018/197). The TH plans for the included patients were retrospectively created after receiving their informed consent. The eligibility criterion was the presence of histopathologically proven early stage or pelvic node-positive disease. We compared the pelvic node-positive [THpn (+)] and node-negative [THpn(-)] plans for prostate-conserving radiotherapy.

Simulation, contouring, planning, and plan assessment

Computed tomography (CT) images (Toshiba) were obtained for each patient and reconstructed at a slice interval of 3 mm. In the supine position, the patients were screened with a fix-knee (Civco Inc., Orange City, Iowa, USA) immobilization tool. At 30 minutes before CT, the patients were requested to evacuate the bladder and then drink 0.5 L of water. Pharmacological and mechanical preparations or endorectal balloon (e.g., enema) were not used. The volume contours and CT images were input in a TH system (Accuray Inc., Sunnyvale, CA, USA) to create the treatment plans. The TH plans were created to cover the PTV and minimize the dose to the OARs. The OARs included the bladder, rectum, femoral head, and bowel in each patient, and the prostate was included in the irradiation volume. The pitch, field width, and modulator factor of the TH plans were 0.287, 2.5 cm, and 3.0 (0.5–4.0), respectively.

The dose required to cover the PTV was prescribed as 80 Gy across 40 fractions of 2.0 Gy per day. As a dose restriction for the PTV, D95 was defined as the minimum dose delivered to 95% of the PTV, and D95 was ≥95% of the prescribed dose. V95 (76 Gy) was defined as the percentage of the PTV receiving at least 95% of the prescribed dose, and V95% was ≥95% of the PTV. Conformity index (CI) was used to evaluate the target dose conformity, and homogeneity index (HI) was used to analyze the uniformity of dose distribution in the target volume. The dosimetric effects on the target and OARs and the treatment time for each TH plan were assessed by a radiation oncologist.

Statistical analysis

Data were analyzed using SPSS 16.0 (SPSS, Chicago, IL, USA). All data are presented as mean and/or median and standard deviation. Differences in the dosimetric end-points between the THpn (+) and THpn(-) plans were analyzed using the Wilcoxon signed-rank test. Differences were considered significant at $p<0.05$.

RESULTS

We analyzed the differences in dosimetric values between the THpn (+) and THpn(-) plans. Table 1 summarizes the dose parameters of PTV in the two TH plans and the results of dosimetric comparison of these TH plans in patients with prostate cancer. Figure 1 present the dose

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distribution in the THpn (+) and THpn (-) plans, respectively. In the present study, the CI values in the THpn (+) and THpn (-) plans were 0.93 and 0.96, respectively (p>0.05). Similarly, the HI values did not significantly differ between the THpn (+) (0.21) and THpn (-) plans (0.23) (p>0.05). Both TH plans achieved clinically acceptable target dose coverage for prostate radiotherapy in this study. However, the D_{max} of PTV (p=0.674) and mean V95 (the volume receiving 74.1 Gy) (p=0.017) were significantly different between the two plans.

Among the OARs, D_{mean}, V75, V40, V30, and V20 for the rectum; D_{mean}, V60, V55, V50, V40, and V30 for the bladder; D_{max} and V50 for the femoral head; and D_{max} and V50 for the bowel were significantly lower in the THpn (-) plan than in the THpn(+) plan (p<0.05).

Table 1. Comparision of dosimetric parameters for the PTV and OARs between in TH plan.

Parameter	Pelvic Node (+)		Pelvic Node (-)		P value
	Median	Range	Median	Range	
PTV					
Dmax	83.25	75.84-88.16	81.46	78.70-86.81	0.674
Dmean	79.1	71.86-86.1	78.5	76.38-82.82	0.779
V95%	98.25	97.4-99.8	99.71	98.1-99.98	0.017
Rectum					
Dmax	80.3	74.47-88.16	79.9	76.4-86.8	0.327
Dmean	42.22	36.76-50.24	38.32	21.3-39.39	0.025
V75	3.74	0-19.74	5.85	0.2-11.57	0.05
V70	8.48	1.62-28.43	9.83	2.6-18.86	0.093
V65	13.37	5.45-34.6	14.17	6.41-25.69	0.123
V60	24.76	8.75-40.2	19.25	10.11-31.43	0.575
V50	33.13	16.12-49.84	28.95	17.10-39.9	0.123
V40	57.81	40.40-66.8	40.25	21.6-46.6	0.012
V30	71.19	57.17-92.2	53.4	25.9-62.6	0.012
V20	83.8	79.4-97.7	75.7	31.4-81.9	0.012
Bladder					
Dmax	82.5	75.84-86.73	80.85	78.4-85.99	0.779
Dmean	45.66	31.17-50.65	30.63	17.8-40.1	0.012
V70	14.1	7.02-24.32	9.32	5.32-16.2	0.161
V65	18.51	11.32-33.40	13.1	7.29-19.40	0.263
V60	24.63	16.03-42.1	16.95	8.99-23.3	0.036
V55	33.3	20.1-48.3	20.15	11.1-27.8	0.017
V50	40.75	28.88-53.2	23.5	13.1-34.2	0.012
V40	57.7	31.14-74.6	30.65	17.6-45.7	0.012
V30	72.5	41.7-86.5	39.9	22.9-59.6	0.012
Femur Heads					
Dmax	54.1	36-60.5	33.25	20.42-40.72	0.012
V50	0.55	0-3.49	0	0-0	0.028
Bowel					
Dmax	50.2	25.7-62.34	4.15	2.6-8.1	0.012
V50	0	0-6.54	0	0-0	0.31
PTV					
HI	0.1	0.07-0,16	0.12	0.08-0.29	0.21
CI	0.95	0.87-0.97	0.94	0.88-0.96	0.077

Vx, volume (%) receiving x dose (Gy) or higher; Dmax, maximum dose; Dmean, mean dose.

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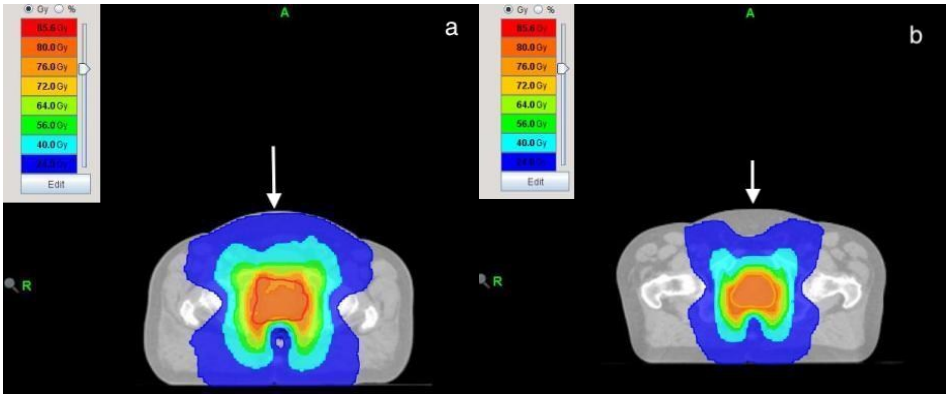

Figure 1. Dose distributions of PTV at prostate (arrow-head) for **(a)** THpn (+) patients and **(b)** THpn (-) patients. Different color regions in plans demonstrating exposed radiation doses.

DISCUSSION

Modern radiotherapeutic techniques aim to provide a more homogenous dose that is compatible to the target volume and, at the same time, spares the OARs [18]. VMAT has been considered a reliable option to protect the OARs from radiation during prostate radiotherapy. Thanks to the modern tools of radiation delivery, prostate radiotherapy can be administered both effectively and safely. IMRT, VMAT, CK, and TH are commonly selected for the management of low-risk prostate tumors. Comparisons and calculations of dose distribution among different radiotherapeutic techniques have been reported in the literature [19]; however, integral dose for the radiotherapy of localized prostate cancer remains controversial [20]. Setup correction strategies determine the PTV margins, and the PTV depends on the setup correction. Due to the misalignment between the prostate and pelvic lymph nodes and the broad margins around the pelvic lymph node, the prostate bed constitutes the smallest part of the prostate PTV. This forms a large intersection zone between the pelvic node-positive part of the PTV and the bladder, rectum, and femoral head. According to a previous study, no correction strategy is optimal, and a comprehensive evaluation of dosimetric effects is imperative [21]. Considering that different doses are delivered to the prostate and pelvic lymph node, it is not easy to translate the differences in the intersection zone to their effects on doses delivered to the OARs. In a previous study including pelvic node-positive or node-negative patients, V95 was 95% and D_{max} was <107% of the PTV [22]. In the present study, V95 was 98.25% in the THpn(+) plan and 98.1% in the THpn(-) plan, while D_{max} was 83.25 Gy in the THpn(+) plan and 81.46 Gy in the THpn(-) plan. In a previous study, the CI of the prostate PTV was 0.98 [22]. In the present study, the CI was 0.93 in the THpn (+) plan and 0.96 in the THpn (-) plan ($p>0.05$). Similarly, the HI value did not significantly differ between the THpn (+) (0.21) and THpn(-) plans (0.23) ($p>0.05$).

TH decreases acute gastrointestinal (GI) toxicity but increases acute genitourinal (GU) toxicity [23]. In a previous study, the rate and prevalence of GI toxicity improved with improved dose compatibility and tumor targeting [24]. Meanwhile, acute GU toxicity was not significantly reduced with these *so-called* improvements [25]. IMRT, VMAT, and RapidARC combined with arc-modulated cone beam therapy and TH may achieve the desirable dose distribution while effectively sparing the OARs, specifically the bowel [26]. During the pre-IMRT period, most part of the pelvic bowel is inevitably exposed to the prescribed radiation dose; consequently, acute UGI toxicity remains a major concern related to this treatment, particularly in light of the relatively weak evidence of the clinical benefits of WPRT [27]. The recommended clinical dose limits for the bowel are a D_{max} of 56 Gy and V50 of 15%. In the present study, the D_{max} was 50.2 Gy in the THpn (+) plan and 4.15 Gy in the THpn (-) plan, while V50 was 0% in both plans ($p<0.05$).

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Advances in external beam radiotherapeutic techniques have enabled the delivery of the desired dose while reducing toxicity in patients with prostate cancer [28, 29]. A previous study showed that clinician differences in goal setting did not change acute toxicity, often due to the negligible distinction between the bladder–prostate and rectal–prostate interfaces [30]. If the bladder dose induces GU toxicity, the difference in prostate volume is unlikely to be prone to consequences. However, if the actual prostate dose itself induces GU toxicity, the differences in target volume may lead to changes in toxicity. As expected, the volumes for both groups are typically larger than those in ultrasound-based studies [31]. The recommended maximum safe dose to the bladder and rectum is >65% of the respective volume, or <70 Gy [32]. In the present study, V70 was 14.1% in the THpn (+) plan and 9.32% in the THpn(-) plan (p>0.05).

A previous study sought to establish an optimized TH plan for localized dose-escalated prostate radiotherapy [33] based on the recommended dose limits of V65<15% and V70<1% for the rectum [34, 35]. In our study, V70 and V65 were respectively 8.48% and 13.37% in the THpn (+) plan and respectively 9.83% and 14.17% in the THpn (-) plan (p>0.05). The dose limits are D_{max}<55Gy and V50<2% for the femoral head. In this study, D_{max} and V50 were respectively 50.2 Gy and 0% in the THpn (+) plan and respectively 4.15 Gy and 0% in the THpn(-) plan (p<0.05).

Overall, we demonstrated that modern radiotherapeutic techniques indeed achieve desirable outcomes in terms of minimizing the radiation dose delivered to the OARs in pelvic node-negative patients with prostate cancer. Further comprehensive studies are warranted to elucidate the effects of node positivity or negativity in patients undergoing prostate radiotherapy.

CONCLUSION

The dosimetric values in both THpn(+) and THpn(-) plans were lower than the recommended limits. Based on all parameters, the THpn(-) plan may be superior to the THpn(+) plan, as it minimizes the radiation dose to the rectum, bladder, bowel, and femoral head while achieving adequate PTV coverage, with fewer hot-spots.

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