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ORIGINAL ARTICLE

Dosimetric Evaluation of Intensity Modulated Radiotherapy and Three-Dimensional Conformal Radiotherapy Treatment Plans for Prostate Cancer

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OBJECTIVE

We evaluated the homogeneity index and conformity index using intensity modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3D-CRT) treatment plans in prostate cancer.

METHODS

Twenty treatment plans for ten patients were created using 3D-CRT of four-fields with gantry angles of 0^0, 90^0, 180^0, and 270^0; and IMRT of five-fields with gantry angles of 0^0, 72^0, 144^0, 216^0, and 288^0 on an Eclipse Treatment Planning System (version 15.6). The volume of reference isodose, target volume, maximum isodose in the target, reference isodose, dose at 95% of planning target volume (PTV), dose at 2%, 5%, and 98% of PTV, and prescribed dose were collected from the dose volume histogram of each plan. The conformity index and homogeneity index (HI) were then calculated. The doses of the organs at risk were also collected and evaluated.

RESULTS

The HI of the twenty patients who underwent the treatment plan with 3D-CRT was 1.088±0.03, which shows good homogeneity, but less homogeneity when compared with plans done with IMRT (1.072±0.02).

CONCLUSION

The use of IMRT treatment plan for prostate cancer proved to be superior over 3D-CRT in terms of conformity and homogeneity, as well as sparring dose to organ at risk.

Keywords: Conformity index; homogeneity index; intensity modulated radiotherapy; prostate cancer; 3D-conformal radiotherapy.

Introduction

Till date, cancer is among the most feared diseases with high mortality rate. Consistence with this, an estimated number of new cancers were diagnosed in 2019 in the United State as 1.762.450, with a total of 606.880 deaths recorded.[1] In Nigeria, according to the International Agency on Research on Cancer, as of 2018, the total number of new cases was 115.950, with 70.327 deaths recorded.[2] Prostate cancer is the second leading cause of cancer in men. In 2019, a total of 174.650 men were diagnosed with prostate cancer in the United

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States (cancer.net) and, in Nigeria, an estimated hospital prevalence of between 127 and 185.5 per 100.000 males admitted in hospitals were diagnosed of prostate cancer.[3] Prostate cancer can be treated by surgery, radiation therapy, chemotherapy, cryotherapy, hormone therapy and immunotherapy, and newer technological development.[4] Radiation therapy has a dynamic role in the treatment of prostate cancer. It involves the use of various treatment plans (TPs) such as 2D- technique, 3D-Conformal Radiation Therapy (3D-CRT), and intensity modulated radiotherapy (IMRT). 2D- technique involves manual calculations and does not spare organs at risk (OAR). 3D-Conformal Radiation Therapy (3D-CRT) is a conformal TP that conforms the radiation doses to the target and, in history, was the best TP for prostate cancer, but results to little sparing of OAR. With intensity modulated radiotherapy (IMRT), the reduction of radiation effect on normal tissues has improved. Research has shown that IMRT has more advantages compared to 3D-CRT in the treatment of prostate cancer. In this study, we investigated the use of homogeneity index (HI) and conformity index (CI) in the evaluation of 3D-CRT and IMRT plans for optimal treatment delivery.

Materials and Methods

Patients Selection

Ten patients with malignant neoplasm of prostate that received radiotherapy with IMRT on a clinical linear accelerator (LINAC), Vitalbeam model (Varian Medical System, Palo Alto, CA, USA) in our department from June 2019 to January 2020 were analyzed, retrospectively.

Simulation and Contouring

Each patient was asked to stay on a supine position on a whole-body board (Radon Medical Equipment, Yenimahalle/ANKARA) without immobilization and was simulated with a 16-slice computed tomography (CT) simulator (Optima 580; GE Healthcare, Waukesha, WI, USA). The plans were sequentially done in three phases. The clinical treatment volume (CTV) for one of the cases was contoured in two phases and nine cases were contoured in three phases. Each planning target volume (PTV) was contoured with 0.5 cm margin from each CTV. Phase 1 (PH 1) contains the prostate, seminal vesicle, and lymph node. Phase 2 (PH 2) contains the prostate and seminal vesicle only, while phase 3 (PH 3) contains the prostate only. However, the case with two phases had phase 1 (the prostate+seminal vesicle+lymph node) and phase 2 (the prostate only) (Table 1). The OARs, which are rectum, bladder, and femoral heads (left and right), were also contoured according to the Radiation Therapy Oncology Group (RTOG) atlas for contouring of normal tissue [5] using the Eclipse TP system version 15.6.

TPs

Two plans were generated for each patient using the Eclipse TP system version 15.6, with energy of 6 MV photons. The prescribed dose was as follows: 76 Gy for three cases; 79 Gy for six cases; and 69 Gy for the patient planned in two phases as shown in Table 1. The different prescription was due to the different non-use of uniform prescription model in our center. The oncologist's prescription type depended on the cancer stage. Each 3D-CRT plan was produced using four beams (box technique) at the gantry angles of 0°, 90°, 180°, and 270°. Multi-leaf collimators (MLC 120 model) were used at 0.5 cm away from PTV to reduce dose to OAR and for more conformity of the 3D-CRT plans. The IMRT plans were done using five beams at the gantry angles of 0°, 72°, 144°, 216°, and 288°. The intensity optimization for each of the beam portals for all IMRT plans was achieved by setting dose constraints and priorities for PTV and OAR until the constraints were met, following the International Commission on Radiation Units and Measurement (ICRU) protocol for dose prescription, with a minimum coverage dose of 95% and maximum accepted dose of 107%.[6] The doses were calculated using Anisotropic Analyses Algorithm in the Eclipse TP system, with the treatment table or couch not included in the calculation volume.

When creating the IMRT plan for a LINAC equipped with an MLC, there were two delivery options: step-and-shoot and sliding window. For this study, the sliding window was adopted for all the IMRT plans.

The Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) analysis and Radiation Therapy Oncology Group (RTOG) Report 62 (a review of Report 50) guideline were adopted for the dose constraint reaching the OAR. The guideline stipulates that

Table 1 Showing the prescribed doses for the ten patients for both 3D-CRT and IMRT

Phases	69 Gy	76 Gy	79 Gy
PH 1	45Gy/25fr	46Gy/23fr	45Gy/25fr
PH 2	24Gy/12fr	10Gy/5fr	9Gy/5fr
PH 3		20Gy/10fr	25Gy/14fr

3D-CRT: Three-dimensional conformal radiotherapy; IMRT: Intensity modulated radiotherapy.

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not more than 35% of the rectum should receive 60 Gy (V60 Gy <35%) and not more than 20% of the rectum should receive 70 Gy (V70 Gy <20%). Also, for the bladder, not more than 15% of the bladder should receive 80 Gy (V80 Gy <15%), not more than 25% should receive 75 Gy (V75 Gy <25%), not more than 35% should receive 70 Gy (V70 Gy <35%), and not more than 50% should receive 60 Gy (V60 Gy <50%). For the femoral heads, not more than 5% of the femoral heads should receive 50 Gy (V50 Gy <5%).[5,7-9]

Dose Volume Analysis

The plan sums for the different plans were generated and data were collected from their dose volume histogram (DVH). From the DVH, the value of dose in Gy reaching the following volume of PTV was recorded: V2%, V5%, V50%, V95%, and V98%. Also, the maximum isodose in the target (Imax) and the reference isodose reaching V95% of PTV were also recorded.

CI and HI

CI and HI were calculated and recorded for each TP using the following equations:[10,11]

$$\mathbf{CI} = \frac{V_{RI}}{TV} \quad (1)$$

Where $\boldsymbol{V_{RI}}$ **is** volume of the target receiving 95% of the prescribed dose and $\boldsymbol{TV}$ is the total volume of the target.

$$\mathbf{HI\ (H_1)} = \frac{I_{max}}{RI} \quad (2)$$

Where I_{max} is maximum dose in the target RI is reference isodose and

$$\mathbf{H_2} = \frac{D_{\geq 5\%}}{D_{\geq 95\%}} \quad (3)$$

Where:
$D_{\geq 95\%}$ is dose at 95% of planning target volume
$D_{\geq 5\%}$ is dose at 5% of PTV
Using the calculated conformity and homogeneity indices according the RTOG protocol, we evaluated the TP that conforms more to PTV and is more homogeneous. The RTOG protocol defines the range of conformity and homogeneity as follows:

- If CI value is between 1 and 2; then, the treatment is in accordance with the protocol.
- If CI value is between 2 to 2.5 and 0.9 to 1; then, there is a minor deviation of the protocol.
- If the CI value is >2.5 and <0.9, it is considered as a severe deviation from the protocol.

For homogeneity, the ideal value for HI is 1 and it increases as the plan becomes less homogeneous. Values closer to 1 are more homogeneous than values away from 1. The mean doses reaching the rectum, bladder, Right, and left femoral heads were also analyzed for each plan.

Statistical Analysis

A two-tailed pair t-test was used to compare the mean of the different TPs at critical significant value of 5%.

Results

In this study, the dose distribution for IMRT plan is more aligned to PTV than that of 3D CRT plan (as shown in Figure 1), which, in turn, reduces the dose to OAR. The dose coverage for both 3D-CRT and the IMRT TPs met the required criteria of at least 95% of the prescribed dose of PTV. The dose maximum was in the range of 105.5%–108% for 3D-CRT plans,

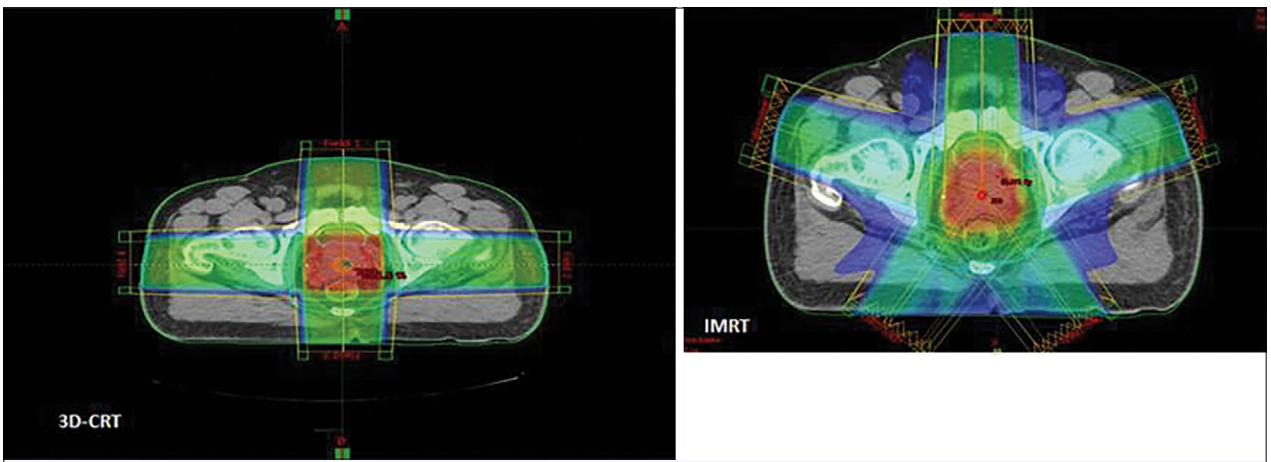


Fig. 1. Showing the dose distribution of a 3D-CRT and IMRT plans for a selected patient.

although it was one of the plans that had up to 108%, which was due to the large size of the PTV. However, the dose maximum for IMRT was in the range of 104.5%–106.7%.

Figure 2 shows the DVH of patients planned with 3D-CRT (left) and IMRT (right) treatment techniques, comparing their PTVs. The square box shows the PTV coverage of the TP done using IMRT technique, while the triangular shape is the PTV coverage of the TP done using 3D-CRT TP technique.

HI

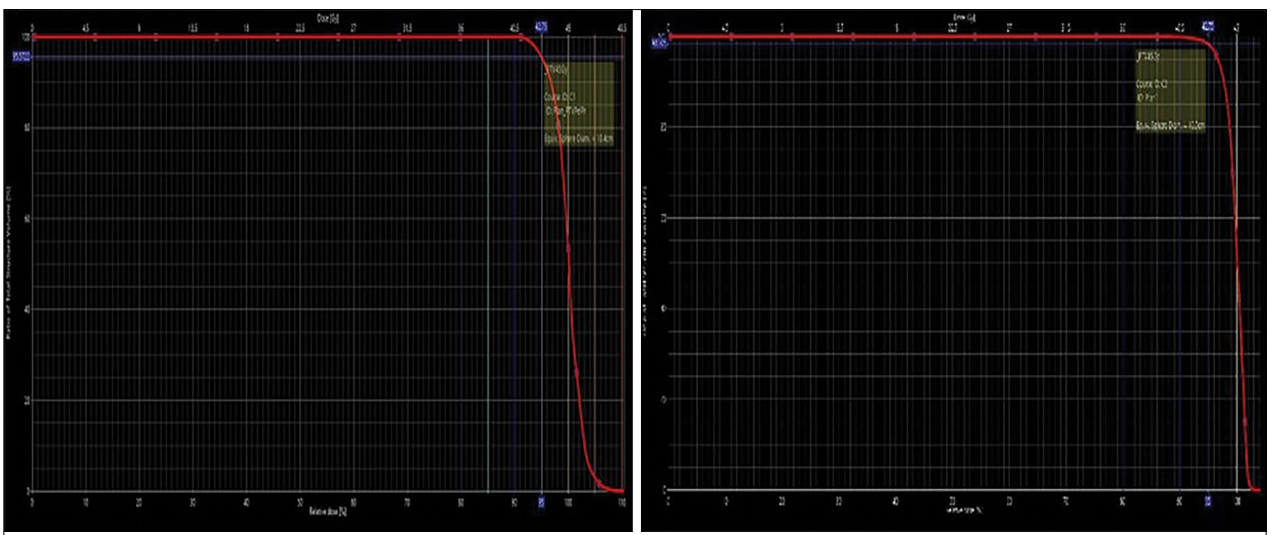
Results from the HI, H1, for the ten patients planned with 3D-CRT were in the range of 1.069–1.170, with an average of 1.088±0.03. For IMRT, HI were in the range of 1.056–1.102, with an average of 1.072±0.002. Also, HI (H_2) for 3D-CRT were in the range of 1.029–1.128, with an average of 1.062±0.04. However, for IMRT, HI (H_2) were in the range of 1.021–1.069, with an average of 1.044±0.02.

CI

The CI for each TP was calculated using equation 1. Figure 2 shows the dose coverage from the DVH. Table 2 shows the comparison between the CI of 3D-CRT and IMRT.

OAR

The dose to OAR of each patient planned using 3D-CRT was compared to that of IMRT, as shown in the DVH in Figure 3. The DVH shows the dose to the rectum (brown), bladder (purple), left femoral head (blue), and right femoral head (sky-blue) for both TP. Tables 2 shows the mean results of dose to OAR for 3D-CRT and IMRT.



3D-CRT plan IMRT plan

Fig. 2. Comprasion between the PTV coverage of the plan sum of 3D-CRT and IMRT plan.

Table 2 Comparison between the Organ at Risk for 3D-CRT and IMRT plans. V20 (Gy) and V50 (Gy) represents the dose to 20% volume and 50 % volume of the OAR respectively. (QUANTEC)

Organs At Risk	3D-CRT		IMRT	
	V20 (Gy)	V50 (Gy)	V20 (Gy)	V50 (Gy)
Rectum	66.48±4.30Gy	53.76±4.00Gy	54.68±6.70Gy	42.25±4.90Gy
Bladder	61.21±8.20Gy	52.39±5.10Gy	49.12±8.90Gy	31.44±9.40Gy
Femoral-Head L	43.12±3.40Gy	35.85±5.80Gy	33.53±4.50Gy	22.00±12.40Gy
Femoral-Head R	36.02±8.50Gy	38.10±3.60Gy	33.42±4.10Gy	21.97±12.60Gy

3D-CRT: Three-dimensional conformal radiotherapy ; IMRT: Intensity modulated radiotherapy; OAR: Organs at risk; QUANTEC: The Quantitative Analysis of Normal Tissue Effects in the Clinic.

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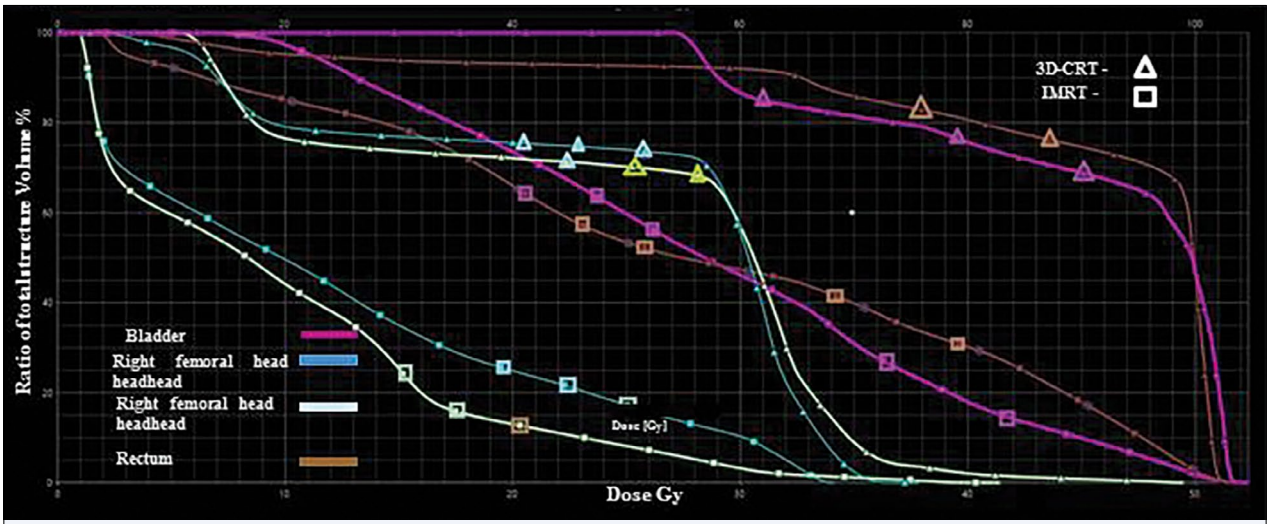

Fig. 3. DVH of OAR for 3D-CRT and IMRT treatment planning tecniques for one patient.

Discussion

In the treatment of cancer, sparing of OAR is one of the goals of radiotherapy. This was considered in this study. Both techniques were evaluated for sparing of OAR using the plan sum of the three phases. This study was aimed at comparing 3D-CRT and IMRT TPs in the treatment of neoplasm of prostate by comparing their HI, CI, and dose to OAR. The results from this study (Tables 2) show that IMRT is much better than 3D-CRT in terms of sparing of OAR. For 3D-CRT, it was observed that it was difficult to meet the RTOG dose constraint protocol for rectum, since the dose reaching 50% volume of the rectum was more than 50 Gy in most cases (Table 2); however, most of the plans met the QUANTEC protocol of 20% of the volume receiving 70 Gy (Table 2). For IMRT, the dose to OAR was within the tolerance set by RTOG and QUANTEC (Tables 2).

Table 2 shows the comparison between the OAR of 3D-CRT and that of IMRT. V20 (Gy) and V50 (Gy) represents the dose to 20% and 50% volume of OAR, respectively (QUANTEC). There was 21% reduction in dose to 20% volume of the rectum in IMRT and 27% reduction in dose to the 50% volume of the rectum in IMRT relative to the 3D-CRT plans. 20% reduction in dose to 20% volume of the bladder and 40% reduction in 50% volume of the bladder in IMRT was also observed. More also, in the 20% volume of the right femoral head, there was 7.2% reduction and 42% reduction in the 50% volume of the right femoral head in the IMRT plans. The 20% of the left femoral head experienced a 27% reduction in dose and 39% reduction in 50% volume of the dose received in the left femoral. These results were not comparable with other works because other studies evaluated different parameters.

Although several studies evaluated 3D-CRT and IMRT plans for single phase, this study paid more attention to plans of three phases and evaluation was done using their plan sum. More also, studies evaluating one and two phases were compared with our results. These studies adopted the HI defined by Wu et al.[12] In this study, the HI adopted was defined by RTOG protocol (defined as H_1) and Yoon et al., (defined as H_2), as stated in the materials and methods, and were compared using similar standard. From the result of this study (Table 3), HI ($\mathbf{H_1}$) for IMRT showed a better homogeneity when compared to that of 3D-CRT (p-value=0.03). This result was close to that of $\mathbf{H_2}$ (Table 3); however, there was no statistically significant difference between the two techniques (p-value=0.16). By relating the two results got from both protocols, it was discovered that the HI formula defined by Yoon et al., was closer to 1 than the RTOG protocol, since HI closer to 1 is the baseline for good homogeneity according to both protocols. Also, in this study, the result of CI (Table 3) shows that the conformity of IMRT (0.99) was better than that of 3D-CRT plans (0.91), such that it had a conformity closer to 1 than that of 3D-CRT. There was a statistically significant difference between the mean of both plans (p-value=0.23). Compared to the study of Crowe et al.,[13] this CI of this study was closer to 1 when using the RTOG protocol. This was consistent with the study by Cristofaro et

Table 3 Summary of results from this study

TECHNIQUE	3D-CRT	IMRT	p
Number of patients	10	10	
Max Total Volume of PTV	1488 cm^3	1488 cm^3	
Mean Total Volume of PTV	645.8 cm^3	645.8 cm^3	
Min Total volume of PTV	96.2 cm^3	96.2 cm^3	
Mean Homogeneity index (H_1)±mean deviation	1.088±0.03	1.07±0.002	0.03
Mean Homogeneity index (H_2)±mean deviation	1.062±0.04	1.044±0.02	0.16
Conformity index (CI)±mean deviation	0.91±0.39	0.99±0	0.23
Rectum (mean values±mean deviation)			
D_{max} (Gy)	77.64±29.09 Gy	76.75±23.11 Gy	0.60
D_{mean} (Gy)	60.83±441.74 Gy	44.22±180.50 Gy	0.18
V35 (%)	92.47±434.03	73.92±785.17	0.45
V40 (%)	90.29±725.42	60.77±757.50	0.09
V50 (%)	57.48±3366.9	29.97±646.8	0.09
Bladder (mean values±mean deviation)			
D_{max} (Gy)	78.02±22.44	78.28±22.54	0.86
D_{mean} (Gy)	56.79±281.54	42.14±88.73	0.009
V35 (%)	91.94±267.23	62.31±337.60	0.00065
V40 (%)	93.56±379.11	46.82±495.98	0.0001
V50 (%)	59.17±3469.7	24.86±626.22	0.043
Right Femoral head (mean values±mean deviation)			
D_{max} (Gy)	51.24±250.6 Gy	47.85±250.56 Gy	0.52
D_{mean} (Gy)	33.18±330.4 Gy	20.76±497.34 Gy	0.89
V35 (%)	31.16±2857.7	13.36±1390.0	0.157
V40 (%)	34.40±6104.6	10.28±730.92	0.308
V50 (%)	5.39±251.40	0.35±2.45	0.25
Left Femoral head (mean values±mean deviation)			
D_{max} (Gy)	52.65±204.89 Gy	37.63±1262.5 Gy	0.117
D_{mean} (Gy)	35.23±304.04 Gy	21.08±422.4 Gy	0.468
V35 (%)	69.63±1627.5	30.52±2196.7	0.022
V40 (%)	36.86±5510.2	13.91±1363.0	0.25
V50 (%)	6.61±24.82	1.11±24.82	0.39

3D-CRT: Three-dimensional conformal radiotherapy; IMRT: Intensity modulated radiotherapy PTV: Planning target volume.

al.[14] and Jamal, et al.[15] The result from this study contradicts that of Kinhkikar, et al.,[16] since their CIs were 0.97±0.02 and 0.98±0.02 for IMRT and 3D-CRT, respectively, thus resulting in a better conformity in 3D-CRT than in IMRT. This may be due to the level of experience of the IMRT planner.

In this study, the mean dose to the left femoral head was reduced by 40.2% in IMRT. This was consistent with the study by Uysal et al.,[17] who reported a mean dose of 18.79±18.79 and 31.5±4.11 Gy for IMRT and 3D-CRT, respectively, thus resulting in 40.3% reduction. This was also consistent with the study by Cristofaro, et al., and Crowe et al. In Table 3, the volume of the bladder receiving 35 Gy (V35) had 20.1% reduction in IMRT and this result was close to the result of Kinhikar et al., with 23.7% reduction in IMRT for V35. The volume of the bladder receiving 40 Gy had a reduction of 49.9% reduction in IMRT relative to 3D-CRT. This was higher than the 41%, 37.61%, 24.7%, and 26.8% reported by Cristofaro, et al., Ashman et al.,[18] Uysal et al., and Kinhikar et al., respectively. For the rectum, the volume receiving 40 Gy had a 32.7% reduction in IMRT relative to 3D-CRT. Crowe et al., had a reduction of 49% in the volume receiving 40 Gy in IMRT, while 50% reduction was reported by Kinhikar et al. However, Cristofaro, et al., had 34% reduction, which is closer to our result. Other studies by Wortel et al.[19] and Panayiotis et al.[20] also had reduction in IMRT.

Generally, the results from this study were comparable to that of other studies; however, homogeneity and conformity indices were better and had lesser dose to OAR.

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Conclusion

Twenty TPs of 3D-CRT and IMRT were created and their CI and HI were evaluated for ten prostate patients. Also, the dose to OAR was evaluated. The use of IMRT TP technique for prostate cancer proved to be superior over 3D-CRT and in sparring dose to OAR. More also, the control of normal tissue complication probability is better with plans done in more than one phases compared to those done in a single phase.

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