



Research Paper

Dosimetric Evaluation between Volumetric Modulated-Arc Therapy (VMAT) and Intensity Modulated Radiotherapy (IMRT) Treatment Techniques for High-risk Prostate Cancer Planned in Three Phases

Adeneye Samuel Olaolu ^{1,2}, Eseoghene John Awhariado ², Joseph Adedayo ², Salako Omolola ¹, Habeebu Muhammad ^{1,2}, Omojola Daniel ³, Adeniji Adeoluwa ², Adebayo Abe ², Rasak Lawal ²

1. Department of Radiation Biology, Radiotherapy and Radiodiagnosis, College of Medicine, University of Lagos, Lagos-Nigeria.
2. Department of Radiotherapy, Nigerian Sovereign Investment Authority–Lagos University Teaching Hospital, Lagos-Nigeria.
3. Department of Radiology, Federal Medical Centre Asaba, Medical Physics Unit, Asaba-Nigeria.

✉ Corresponding author: Dr. Adeneye Samuel Olaolu, Department of Radiation Biology, Radiotherapy and Radiodiagnosis, College of Medicine, University of Lagos, Lagos-Nigeria. Tel: +234 (0)803 538 6915; E-mail: soadeneye@unilag.edu.ng

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Abstract

The primary objective of this study is to evaluate the conformity and homogeneity indices using VMAT and IMRT treatment techniques for prostate cancer planned in three phases. Eighteen participants participated in retrospective research. Using VMAT and IMRT treatment procedures, three Planning Target Volumes (PTVs) of varying dose prescriptions were planned and calculated individually. The dosimetry parameters were all derived from each plan's dose-volume histogram (DVH), to calculate and evaluate the conformity index (CI), homogeneity index (HI), and dose to organs at risk (OARs). There was no statistically significant difference in the means of CIs for all the phases (PH 1, PH 2, and PH 3) between the IMRT (1.02 ± 0.01 , 1.00 ± 0.0 , 1.02 ± 0.05) and VMAT (1.02 ± 0.0 , 1.01 ± 0.0 , and 1.00 ± 0.0), respectively. There was no statistically significant difference between the means of the HI for all the phases (PH 1, PH 2, and PH 3) of IMRT (1.07 ± 0.01 , 1.04 ± 0.0 , 1.05 ± 0.03) and VMAT (1.06 ± 0.01 , 1.04 ± 0.0 , and 1.03 ± 0.0) plans, respectively. A greater percentage reduction in dose to the OARs was recorded for VMAT. VMAT turned out to be superior to IMRT at a lower dose to the OARs for high-risk prostate cases planned in three phases (PTVs).

Keywords: Conformity index; Homogeneity index; Intensity modulated radiotherapy; Prostate cancer; 3D-conformal radiotherapy

Introduction

The use of radiation therapy to treat cancer has progressed rapidly in recent years. Until a more conformed Intensity Modulated Radiotherapy (IMRT) technique with a better sparing dose to organs at risk (OAR) came on board, 3D-conformal radiotherapy was historically the best treatment technique for prostate cancer care, due to its ability to conform to the planning target volume (PTV) and dose sparing to OAR [1-14]. However, a new IMRT treatment approach known as Volumetric Modulated Arc Therapy (VMAT) has

evolved with more promising benefits. Various studies have been conducted to determine the superiority of VMAT over IMRT, with the result that fewer monitor units are needed during treatment, lowering the risk of subsequent malignancy [14-16]. The purpose of this study is to assess the conformity index and homogeneity index of VMAT and IMRT treatment techniques for the treatment of high-risk prostate cancer in three phases (PTVs): prostate, seminal vesicle, and lymph node (phases 1), prostate and seminal vesicle only (phases 2), and prostate only (phase 3).

Materials and Methods

Patients Selection

18 patients with malignant neoplasms of the prostate who had radiation treatment in our department on a clinical linear accelerator (LINAC), Vitalbeam type (Varian Medical System, Palo Alto, CA, USA) from June 2019 to January 2021 were retrospectively investigated. This study only included patients with stage III prostate cancer who had undergone three phases of treatment. The Lagos University Teaching Hospital Health Research Ethics Committee gave the approval for this study with the assigned number ADM/DSCST/HREC/APP/4710.

Simulation

Each patient was simulated in the supine position, on a whole-body board (Radon Medical Equipment, Yenimahalle/ANKARA) with keel and headrest, using a 16-slice computed tomography (CT) (Optima 580; GE Healthcare, Waukesha, WI, USA).

Contouring and Dose Prescription

On an Eclipse TP system version 15.6.05., the plans were performed with three phases. With a prescription dose of 45 Gy in 25 fractions, the prostate, seminal vesicle, and lymph node were included in the first clinical treatment volume (CTV) for phase 1. In the second CTV for phase 2, the prostate and seminal vesicles were selectively treated with a prescribed dose of 9 Gy in 5 fractions. For phase 3, the prostate was treated exclusively in the third CTV, which contains a prescription dose of 25.2 Gy in 14 fractions, resulting in a total prescription dose of 79.2 Gy in 44 fractions and a 1.8 Gy dose per fraction. According to ICRU Report 83 [17], each PTV was given a 0.5 cm margin from each CTV and was labelled Phase 1 (PH 1), Phase 2 (PH 2), and Phase 3 (PH 3). The volume of each PTV is shown in cm³ in Table 1. Each PTV was encircled by NS (normal structure) rings with a thickness of 3 cm and a spacing of 0.03 cm to control the dose reaching the OARs and concentrate it more in the PTV. The

treatment table was shaped away from the body to keep it out of the planning calculations. The rectum, bladder, and femoral heads (left and right) were also identified as OARs using the Radiation Therapy Oncology Group (RTOG) atlas [18].

TPs

Two plans (IMRT and VMAT) were developed for each patient utilising the Eclipse TP system Version 15.6.05, with a 6 MV energy. Five beams were used in the IMRT plans, with gantry angles of 0°, 72°, 144°, 216°, and 288°. (Figure 1). Each phase was planned, optimised, and calculated separately. For each case, the same user origin was used for the three phases. Dose constraints and priorities for the PTVs, NS Ring control, and OARs were established during the intensity optimization for each of the beam portals, as shown in Table 2, using 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) guidelines for the dose constraint reaching the OAR [19]. For each plan, the optimization process was repeated until a minimum coverage dose of 95%, a maximum dose of less than 107 % (according to the International Commission on Radiation Units and Measurement (ICRU) protocol), and the lowest dose possible to the OARs were obtained. Using the sliding window approach, the dosage fluence of each modulated field was supplied with 120-leaf MLCs. The Photon Optimizer (PO) algorithm was used to optimise the IMRT plan (Version 15.6.05). VMAT plans were created separately for each phase for each patient, using two arcs and one isocenter (one 181° clockwise 179° and one 179° counterclockwise 181°). Although the optimization procedure for the VMAT plans took a long time, the dosage constraints and priority were done the same as in the IMRT plan during optimization. The Photon Optimizer (PO) algorithm (Version 15.6.05) was used to optimise the VMAT plan, which included four stages of optimization and 178 control points. The process was repeated until the ICRU protocol's constraints and coverage requirements were met. For both IMRT and VMAT plans, the doses were computed using the Anisotropic Analyses Algorithm (Version 15.6.05) without including the treatment table in the calculation volume.

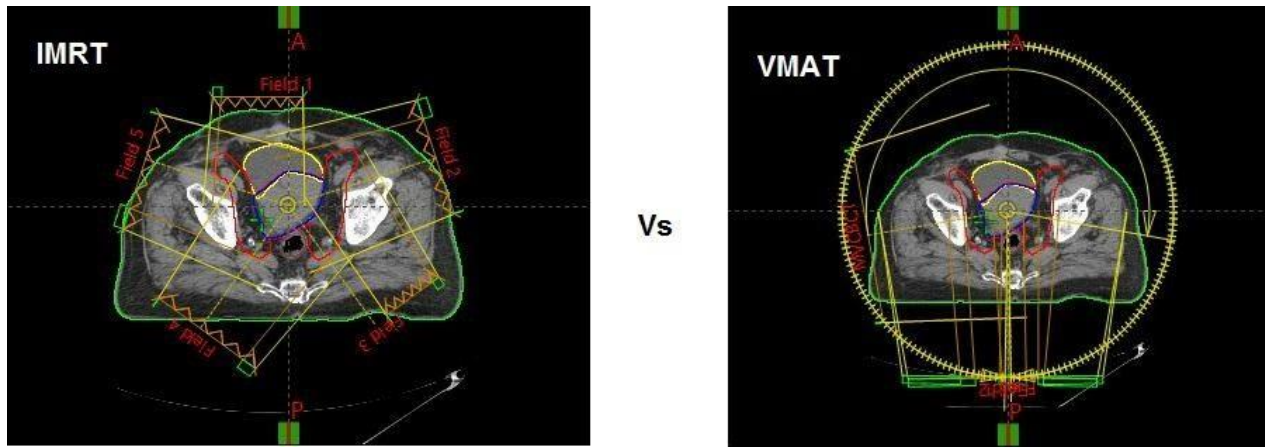


Figure 1. Showing Field placement for IMRT and Arcs orientation for VMAT plans.

Table 1. The volume of the PTVs of the eighteen patients in cm³ contoured for both treatment techniques for prostate cancer

Patients	Volume of PH 1 (cm ³)	Volume of PH 2 (cm ³)	Volume of PH 3 (cm ³)
P1	912.3	125.1	73.8
P2	966.3	179.2	152.1
P3	556.3	149.9	129.4
P4	655.9	214	194.4
P5	684.1	138.3	85.5
P6	613.1	96.1	25.5
P7	575.1	57.3	43.2
P8	628.1	88	61.2
P9	821.2	313.3	276.9
P10	701.7	91.2	82.1
P11	1028.5	191.7	123.3
P12	813	64.9	62
P13	469.4	110.1	80.3
P14	786.2	280.5	274.1
P15	464	100.8	51.5
P16	374.3	39.7	21.4
P17	662.1	210.4	176.2
P18	1330.2	332.5	290.6

Table 2. Dose specification and dose-volume constraints used for the optimization of Intensity Modulated Radiotherapy and Volumetric Modulated-Arc Therapy for prostate cancer

RECTUM	
	V _{75 GY} ≤ 15 %
	V _{70 GY} ≤ 20 %
	V _{65 GY} ≤ 25 %
	V _{60 GY} ≤ 35 %
	V _{50 GY} ≤ 50 %

BLADDER	$V_{75\text{Gy}} \leq 25\%$
	$V_{70\text{Gy}} \leq 35\%$
	$V_{65\text{Gy}} \leq 50\%$
FEMORAL HEADS	$V_{50\text{Gy}} \leq 50\%$

Table 3. Results obtained from the DVH

	VMAT			IMRT					
	PH 1	PH 2	PH3	PH 1	PH 2	PH 3			
Prescribed dose	45.00Gy	9.00 Gy	25.50 Gy	45.00 Gy	9.00 Gy	25.50 Gy			
Max dose	47.96 Gy	9.80 Gy	26.31 Gy	47.95 Gy	9.67 Gy	26.32 Gy			
Min dose	37.73 Gy	7.91 Gy	21.14 Gy	35.16 Gy	8.08 Gy	22.36 Gy			
Mean dose	45.36 Gy	9.44 Gy	25.30 Gy	45.38 Gy	9.37 Gy	25.56 Gy			
Mean HI	1.06 ±0.01	1.04±0.0	1.03±0.0	1.07±0.01	1.04±0.0	1.05±0.03			
P-value	0.467	0.834	0.318	0.467	0.834	0.318			
Mean CI	1.02 ± 0.0	1.01 ± 0.0	1.00 ± 0.0	1.02 ± 0.01	1.00 ± 0.0	1.02 ± 0.05			
P-value	0.285	0.316	0.413	0.285	0.316	0.413	Level of Reduction (%)		
<u>Rectum</u>									
D_{max} (Gy)	46.59	9.43	24.88	46.65	9.20	25.27	0.1	-2.5	1.6
D_{mean} (Gy)	28.32	4.40	9.11	30.17	4.64	10.02	6.5	5.5	10.0
$V_{20\text{Gy}}$ (%)	77.06	0	9.01	79.27	0	13.03	2.9	0	4.5
$V_{35\text{Gy}}$ (%)	37.5	0	0	42.55	0	0	1.3	0	0
<u>Bladder</u>									
D_{max} (Gy)	47.45	9.12	25.84	47.04	14.15	24.93	0.9	33.4	3.7
D_{mean} (Gy)	30.65	3.82	7.61	28.84	3.68	7.78	-5.9	-3.7	2.2
$V_{20\text{Gy}}$ (%)	84.96	0	9.04	78.08	0	6.64	8.1	0	26.5
$V_{35\text{Gy}}$ (%)	30.74	0	0	35.22	0	0	12.7	0	0
<u>Femoral Head-R</u>									
D_{max} (Gy)	34.02	4.51	11.06	38.36	5.06	12.74	11.3	10.9	13.2
D_{mean} (Gy)	16.44	2.49	5.00	16.39	2.38	5.27	0.3	2.49	4.4
$V_{20\text{Gy}}$ (%)	29.16	0	0	40.34	0	0	27.7	0	0
$V_{35\text{Gy}}$ (%)	1.90	0	0	0.89	0	0	-53.2	0	0
<u>Femoral Head-L</u>									
D_{max} (Gy)	33.42	4.47	11.11	35.81	6.24	13.01	6.7	28.4	-43.8
D_{mean} (Gy)	12.95	2.88	5.00	16.34	2.70	5.76	24.8	6.3	13.2
$V_{20\text{Gy}}$ (%)	22.62	0	0	40.29	0.48	0	43.9	100	0
$V_{35\text{Gy}}$ (%)	0.25	0	0	1.37	0	0	81.8	0	0

Dosimetric Analysis and Plan Comparison

The coverage of the three PTVs was measured in this study by comparing the maximum, mean, and minimum doses received by the PTVs, as well as V95 (percentage of the PTV covered by at least 95 % of the recommended dose). The value of dose reaching the following percentage volume of the PTVs was recorded using the Dose Volume Histogram (DVH): D2 %, D5 %, D50 %, D95 %, and D98 %. Also recorded were the maximal isodose in the target (I_{max}) and the reference isodose achieving V95 % of the PTVs. Using the following equation published by Knoos et al. [20], the conformance index was calculated and recorded for each phase and treatment planning technique.

$$\text{Conformity index (CI)} = \frac{V_{RI}}{TV} \quad (1)$$

where V_{RI} is the volume of the target receiving 95% of the prescribed dose and TV is the total volume of the target.

The ideal CI value is 1. The treatment is in accordance with the protocol if the CI value is between 1 and 2. There is a tiny variation from the procedure if the CI value is between 2 and 2.5 and 0.9 to 1. It is deemed a serious deviation from the protocol if the CI value is greater than 2.5 and less than 0.9. The homogeneity measure developed by Yoon *et al.* [21], was used to assess dose uniformity within the PTVs.

$$\text{HI} = \frac{D_{\geq 5\%}}{D_{\geq 95\%}} \quad (2)$$

where $D_{\geq 95\%}$ is the dose at 95% of planning target volume and $D_{\geq 5\%}$ dose at 5% of PTV.

Homogeneity index (HI) has an ideal value of 1 and increases as the plan gets less homogeneous. Those that are closer to 1 are more homogeneous than values that are further away.

The following OAR parameters were estimated from the DVH for each of the phases and composite plans: the maximum dose (D_{max}), mean dose (D_{mean}), and minimum dose (D_{min}) of the rectum, bladder, and both femoral heads; the percentage of the rectal and bladder volumes that received a minimum of 20, 35, 50, 60, and 70 Gy (V20 Gy, V35 Gy, V50 Gy, V60 Gy, V70 Gy); the percentage of the bilateral femoral heads that received a minimum of 20 and 35 Gy (V20 Gy, and V35 Gy). The mean of the different treatment plans was compared using a two-tailed pair t-test, with a p-value of 0.05 being statistically significant.

Results*PTVs' Coverage and Dose Distribution*

For all IMRT and VMAT plans, the ICRU dose prescription protocol was followed, with a minimum coverage dose of 95% and a maximum hot spot dose of 107 % of the prescribed dose to the PTVs. Dose constraints were considered, and the best-optimised plans were chosen. Figure 2 compares the dose coverage from the DVHs for the PH 1, PH 2, and PH 3 PTVs of IMRT and VMAT plans. The IMRT plans cover 95% of the required dose for each PTV, with an average volume of 98.2 % for PH 1 plans, 99.8 % for PH 2 plans, and % volume for PH 3 plans. In the VMAT plans, 95 % of the prescribed dose for each phase averaged 97.8 % volume for PH 1, 99.3 % volume for PH 2, and 99.6 % volume for PH 3. Figure 3 illustrates the dose distribution for both methods of planning. Table 3 shows the average of the research outcomes.

OARs

The DVHs for the OARs for both IMRT and planning approaches are shown in Figure 4. Table 3 shows the D_{max} (Gy), D_{mean} (Gy), V20 Gy (%), V 35 Gy (%) dose to OARs for the various phases, and Table 4 shows the composite D_{max} (Gy), D_{mean} (Gy) doses to OARs, as well as doses to V20 Gy (%), V 35 Gy (%), V50 Gy (%), V60 Gy (%), V 75 Gy (%) of the OARs.

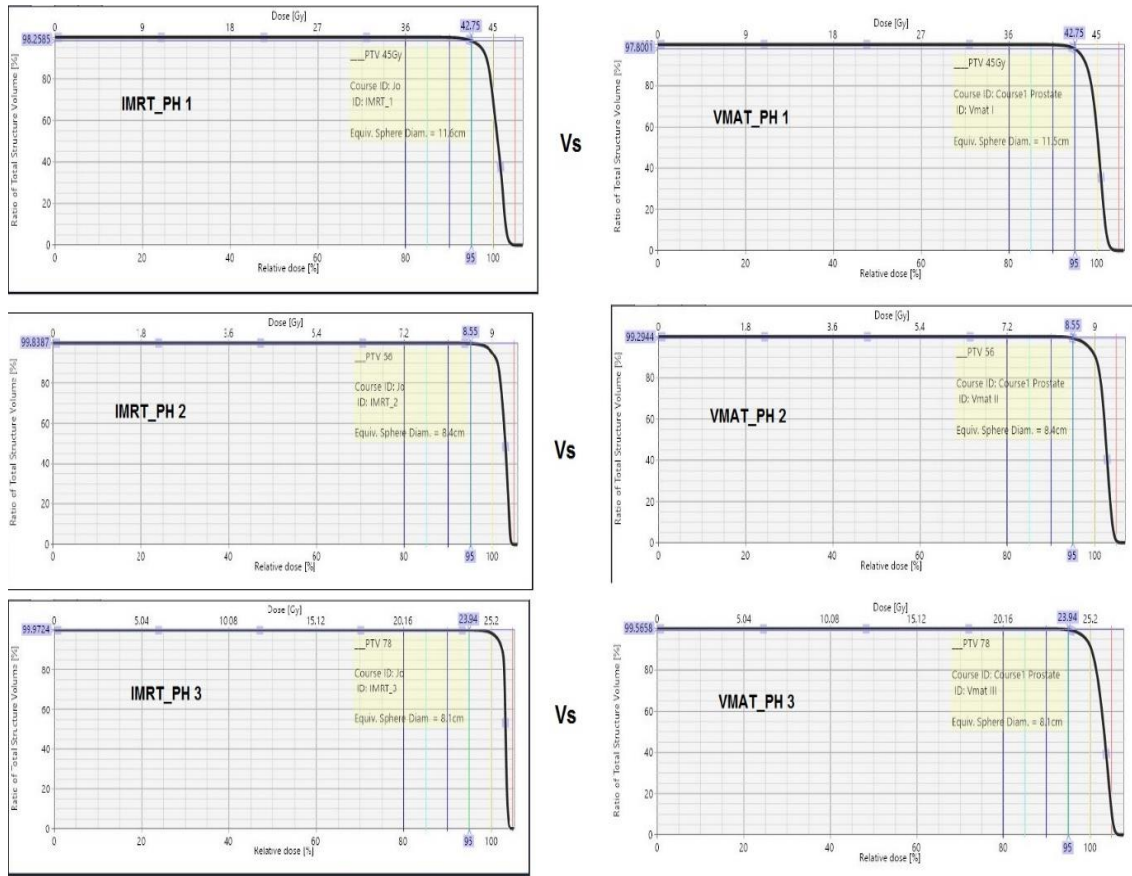


Figure 2. DVHs of IMRT and VMAT plans for a patient.

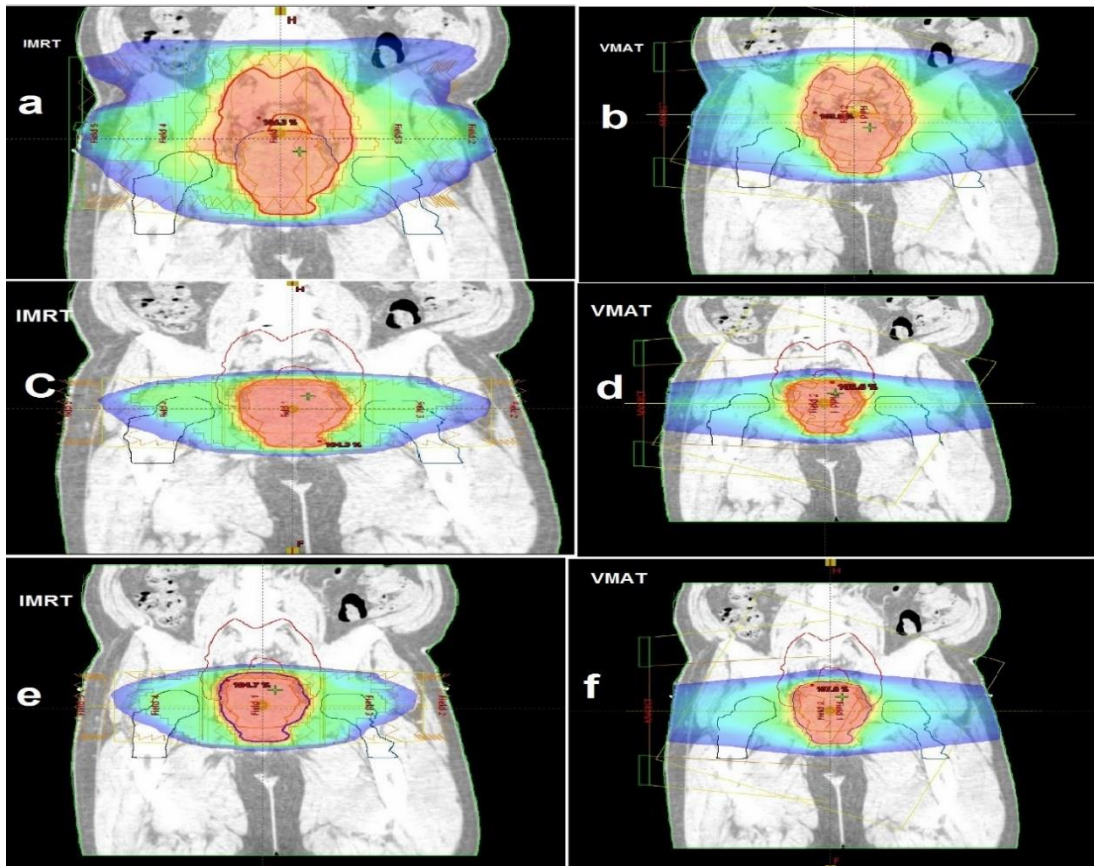


Figure 3. Frontal section illustrating dose distribution for IMRT and VMAT plans for a patient.

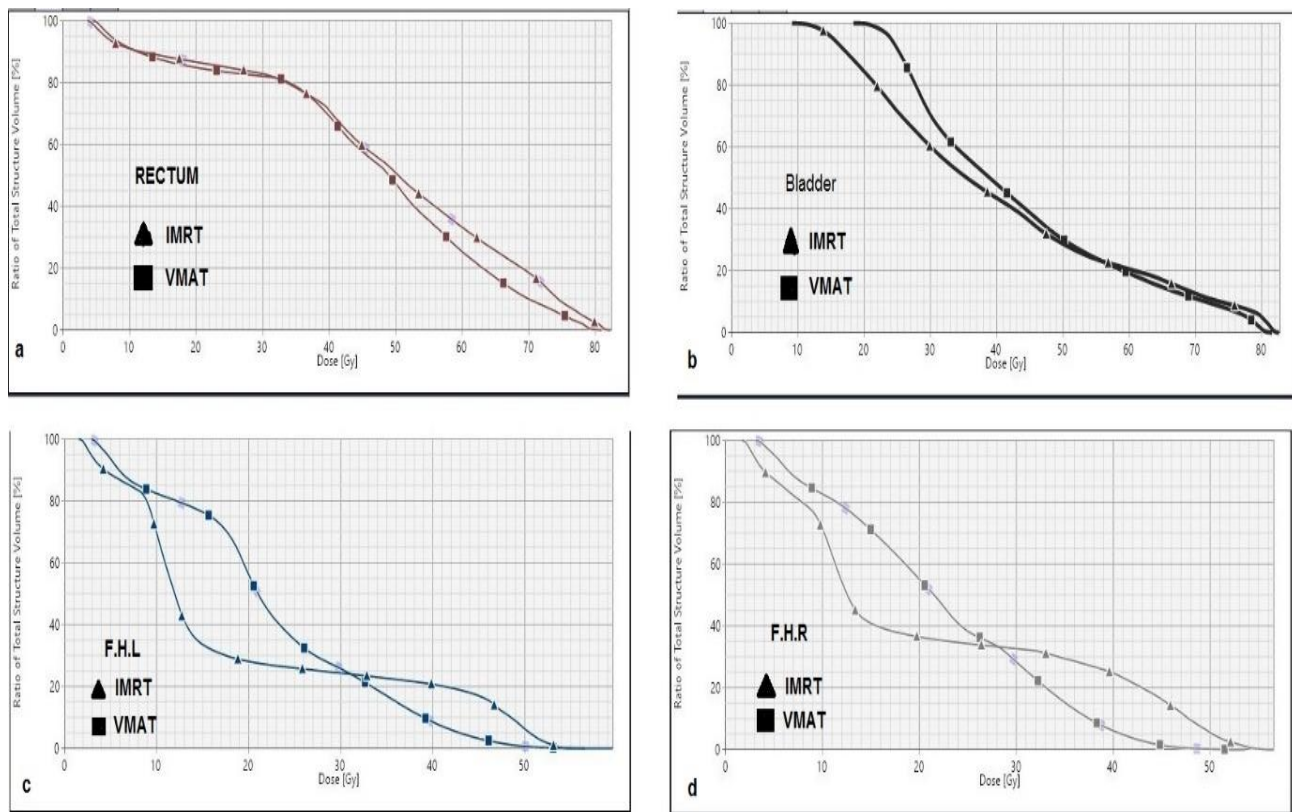


Figure 4. DVHs of OARs of IMRT and VMAT plans

Discussion

Although there has been development in treatment techniques, such as 2D to 3D-CRT, IMRT, and VMAT, radiotherapy has long been utilised to treat prostate cancer. It has also been treated in a variety of ways depending on the stage of the cancer [22], such as one phase involving only the prostate and receiving extremely high doses of 79 or 80 Gy, two phases involving both the lymph nodes and the prostate. This study divided prostate cancer treatment into three stages: lymph nodes plus seminal vesicle plus prostate in phase one, seminal vesicle plus prostate in phase two, and prostate only in phase three. The goal of this study is to examine the dosimetric parameters of these cases treated in three phases with VMAT and IMRT to see which treatment is better. In this study, each phase was examined separately, but the dose to the OARs was assessed in both directions, and a composite plan was developed for comparison with other published studies.

Conformity Index

According to our findings (Table 3), there was no statistically significant difference in the CI between the means of IMRT (1.02 0.01, 1.00 0.0, 1.02 0.05) and VMAT (1.02 0.0, 1.01 0.0, and 1.00 0.0) for all phases (PH 1, PH

2, and PH 3). PH 1, PH 2, and PH 3 had p-values of 0.285, 0.316, and 0.413, respectively, at $p < 0.05$. This contrasts with the findings of Poon *et al.* [23] and Cristofaro *et al.* [24]. The work of Poon *et al.* is divided into two phases: the lymph nodes + seminal vesicle + prostate phase, and the seminal vesicle + prostate phase. The CIs reported for phases 1 and 2 were 1.51 and 1.39, respectively, for IMRT and VMAT, and 1.13 and 1.09, respectively, for IMRT and VMAT. VMAT had better conformance of 1.39 and 1.09 than IMRT in phase one, according to Cristofaro *et al.* with a 1.6 %. A conformance index that was near to ideal was attained in this study, like that described by Poon *et al.* [23], because of the three-phase approach. Using the applicable methodology described by Knoos *et al.* we achieved a perfect conformance index in PH 2 plans prepared with IMRT and PH 3 plans planned with VMAT, which is difficult to achieve with one- or two-phase plans.

Homogeneity Index

The uniformity of dosage distribution across all instances and methodologies was highly valued in the results of this study's homogeneity index calculation. The means of the HI for all phases (PH 1, PH 2, and PH 3) of IMRT (1.07 0.01, 1.04 0.0, 1.05 0.03) and VMAT (1.06 0.01, 1.04 0.0, and 1.03 0.0) plans were not statistically significant. PH 1, PH 2, and PH 3 had p-values of 0.467, 0.834, and 0.318,

respectively, at $p < 0.05$. This was also seen in the work of Poon et al. and Kinshikar *et al.* [24]. Poon et al. measured their HI in two phases (IMRT and VMAT): phase 1 (1.08, 1.08) and phase 2 (1.03, 1.04), respectively. We learned from this study that planning with a lesser dose result in greater coverage and dose homogeneity, however it does result in a longer treatment duration in terms of number fractions.

OARs

Many studies comparing the doses delivered to the OARs by IMRT and VMAT for prostate cancer found a significant difference in dose reaching the OARs in favour of VMAT. However, when comparing plans done in one or two phases, unique behaviours were identified in the reduction of dose between both techniques in this investigation. For each phase, the Dmax (Gy), Dmean (Gy), dosage reaching the OARs, and volume receiving 20.0 Gy (V20 Gy (%)) were assessed independently and compared between the two treatment planning (TP) techniques. The plan summation for all three phases was also done for general comparison with other studies done in one and two phases, and the Dmax (Gy), Dmean (Gy), V20 Gy (%), V35 Gy (%), V50 Gy (%), V60 Gy (%), V75 Gy (%) dose reaching the OARs were examined. For PH 1 and PH 3 plans, respectively, there was a 0.1 percent and 1.6 percent reduction in the mean Dmax (Gy) reaching zero percent volume of the rectum in favour of VMAT TP, but a 2.5 percent reduction in the mean Dmax (Gy) in favour of IMRT for PH 2 plans (Table 3). Also, V20 Gy (%) of the rectum was collected and for PH 1, PH 3 plans experienced 2.9% and 4.5% reduction respectively in favour of VMAT, however, both techniques had no 20.0 Gy dose reaching the PH 2 because the prescribed dose for PH 2 is just 9.0 Gy. When compared to IMRT, the VMAT plans lowered Dmax (Gy) dosage to the bladder by 0.9, 33.4, and 3.7 %, respectively, in PH 1, PH 2, and PH 3. IMRT, on the other hand, had a lower Dmean (Gy) to the bladder of 5.9 % in PH 1 and 3.7 % in PH 2, but a larger dose in Ph 3 than VMAT. VMAT had a volume of 20.0 Gy in PH 1 and 26.5 Gy in PH 3 that was 8.1 % and 26.5 % lower than IMRT. In addition, the amount of radiation that reached the femoral heads was measured and evaluated. With VMAT, the Dmax (Gy) of PH 1, PH 2, and PH 3 were reduced by 11.3, 10.9, and 13.2 %, respectively, in the Right femoral head (RFH). VMAT lowered Dmax (Gy) to the left femoral heads by 6.7 and 28.4 % in PH 1 and PH 2, but IMRT reduced Dmax (Gy) by 43.8 % in PH 3. The volume receiving 20 Gy in the PH 1 of the Left Femoral Head (LFH) experienced a 43.9 % reduction in VMAT compared to IMRT, and no radiation was delivered to this volume in the PH 2 and PH 3 plans.

Furthermore, the composite plan of each plan was created for comparison with other studies in order to examine the dose to the OARs. When compared to VMAT, IMRT exhibited a lower Dmax (Gy) and a 45.3 % reduction in the volume receiving 60 Gy (Table 4). Myrehaug *et al.* [25] showed a 21 % decrease in the volume receiving 60 Gy (V60 Gy (percent)) of the rectum in IMRT compared to VMAT with a 21 % reduction; also, Poon et al. and Mellon et al. [26] found comparable results. We had a very high reduction figure in the V60 Gy (%), which could be attributed to the three-phase plan, as the PTVs are smaller than in the two-phase plan. However, in the rectum, VMAT reduced the volume receiving 35.0, 50.0, and 75 Gy by 11.0, 22.0, and 5.1%, respectively, compared to IMRT (Table 4). In the bladder, VMAT planning reduced Dmax (Gy) and Dmean (Gy) doses by 1.7 and 16.7 %, respectively; it also reduced volumes receiving 20, 35, 50, 60, and 75 Gy by 2.5, 34.2, 20.5, 14.4, and 11.45 %, respectively. Myrehaug et al. found a drop in VMAT in V60 Gy (%) (Table 4). Poon et al. and Kinshikar et al. had opposing viewpoints on V50 Gy (%) and V 35 Gy (%), respectively, claiming that IMRT reduced the volume of the bladder receiving those doses. The mean dose (Dmean (Gy)) for VMAT was reduced by 40% for the RFH, although the Dmax (Gy) and volumes receiving 35 and 50 percent improvements were observed at 15.7, 72, and 44 percent, respectively (Table 4). This finding matches that of Myrehaug et al. and Crowe et al., who worked on two and one phases, respectively. Also, for the LFH, the Dmax (Gy) Dmean (Gy) and volumes received 20, 35, and 50% improvement, respectively, while the Dmax (Gy) Dmean (Gy) received 14, 5, 12, 78.2, and 88.6% improvement (Table 4). Improvements in LFH were reported by Myrehaug *et al.*, Mellon *et al.* and Crowe *et al.* in one and two phases.

Despite the fact that this was the first study of its kind, the findings were comparable to those of previous research in the subject. To the best of our knowledge, there has been no new study on this issue. The clinical implications of this therapy method are currently being researched.

Conclusions

In conclusion, employing VMAT to plan high-risk prostate cancer in three phases resulted in a lower dose to OAR(s), but there was no difference in dose coverage and homogeneity between VMAT and IMRT. For high-risk prostate patients planned in three phases, VMAT proved to be better than IMRT at a lower dose to the OARs.

Abbreviations

IMRT: Intensity Modulated Radiotherapy; OAR: Organs at risk (OAR); PTV: Planning target volume; VMAT: Volumetric Modulated Arc Therapy.

Statements and Declarations

We want to make it clear that this publication has no known conflicts of interest, and that there has been no significant financial assistance for this work that could have influenced its outcome. We did not receive any funding, grants, or other forms of support during the creation of this manuscripts.

Author Contributions

The study's inception and design were helped by all the authors. Eseoghene J. Awhariado prepared the materials, Abe Adebayo and Rasak Lawal planned the cases. Dr. Salako Omolola and Dr. Adeniji Adeoluwa collected the data, and Dr. Habeebu analysed it. Dr. Samuel Adeneye wrote the first draft of the manuscript, and all contributors provided feedback on prior drafts. The final manuscript was read and approved by all the authors.

Competing Interests

The authors have declared that no competing interest exists.

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