

Research Article

Simultaneous Integrated Boost Plan Comparison between Volumetric Modulated Arc Therapy (VMAT) and Intensity Modulated Radiation Therapy (IMRT) for Prostate, Seminal vesicle and Lymph Node Irradiation

 Samuel O. Adeneye,^{1,2}  Inioluwa D. Ariyo,¹  Adedayo O. Joseph,¹  Anthonia C. Sowunmi,^{1,2}
 Michael O. Akpochafor,²  Godwin Uwagba,¹  Ibrahim EL Hamamsi,¹  Abdallah E. Kotkat¹

¹NSIA-LUTH Cancer Centre, Lagos University Teaching Hospital, Idi-Araba, Lagos, Nigeria

²Department of Radiation Biology, Radiotherapy and Radiodiagnosis, College of Medicine/Lagos University Teaching Hospital, Idi-Araba, Lagos, Nigeria

Abstract

Objectives: We performed a planning study to evaluate the dosimetric differences between Volumetric Modulated Arc Therapy (VMAT) and Intensity Modulated Radiation Therapy (IMRT) using simultaneous Integrated Boost (SIB) for prostate cancer cases.

Methods: 20 prostate cancer patients scheduled for SIB-VMAT treatment on the Halcyon™ 2.0 linear accelerator were recruited for this study and SIB-IMRT plans were generated for comparison purpose. The pelvic lymph nodes (PTV46), the seminal vesicle (PTV50), and the prostate (PTV60) were simultaneously treated to 46 Gy 50 Gy, and 60 Gy delivered in 20 fractions respectively.

Results: SIB-VMAT was better due to its higher (1.41%) CI, lower (2.7%) HI, and lower (26%) GI than SIB-IMRT for PTV60. For PTV50, a higher (7.3%) CI, lower (48%) HI, and a lower (31.73%) GI for SIB-VMAT compared to SIB-IMRT. Also, for PTV46, a higher (9.4%) CI, lower (2.5%) HI, and a lower (16.4%) GI were achieved by SIB-VMAT compared to SIB-IMRT.

Conclusion: Better conformal and slightly similar homogeneous dose distribution were noticed in SIB-VMAT plans compared to SIB-IMRT plans. However, SIB-IMRT provided better OARs sparing of the bladder and the femoral heads while SIB-VMAT had better sparing for rectum.

Keywords: Halcyon, Prostate cancer, Radiotherapy, Simultaneous Integrated Boost (SIB)

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One of the most common cancers in men is prostate cancer. External beam radiation therapy, brachytherapy, radical prostatectomy, and watchful waiting are currently approved treatment choices.^[1] The term intensity

modulated radiation therapy (IMRT) refers to a technique of radiation therapy in which a nonuniform fluence is administered to the patient from any given location of the treatment beam to maximize the delivery of the composite

Address for correspondence: Inioluwa D. Ariyo, MD. NSIA-LUTH Cancer Centre, Lagos University Teaching Hospital, Idi-Araba, Lagos, Nigeria

Phone: +234 7038670743 **E-mail:** sanyainioluwa@gmail.com

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dose. Volumetric modulated arc therapy (VMAT) is a newer technique of delivering IMRT and it delivers IMRT distributions in a single rotation of the arc, varying the gantry speed and dose rate, as opposed to standard IMRT with fixed gantry beams. The planner defines the treatment parameters for plan optimization, and the optimum fluence profiles for a given set of beam directions are determined by "inverse planning".^[2]

Inverse planning is a computer algorithm that changes the beam weighting and blocking to achieve an ideal plan based on dose objectives applied to the target volume and critical organs.^[3] Treatment planning has evolved from the three-dimensional conformal radiotherapy (3D-CRT) to IMRT and VMAT and these are one of the most used treatment techniques in external beam photon radiotherapy.^[4]

VMAT plans increase the number of beam angles, and as a result can produce a more conformal dose distribution to the target volume when compared to traditional IMRT. VMAT provide very similar planning target volumes (PTV) coverage as the fixed gantry IMRT plans with improved homogeneity. They also happen to have shorter delivery time and use less monitor units than that of a fixed gantry IMRT plan.^[5,6]

Simultaneous Integrated Boost (SIB) technique delivers a higher dose to the primary tumor while keeping the overall treatment delivery time the same.^[7] Furthermore, when compared to sequential techniques, SIB technique have shown to improve plan quality. Several studies have performed dosimetric comparison of IMRT and VMAT plans in prostate cancer.^[4, 8-14] Also, recent studies on dosimetric evaluation of IMRT and VMAT plans delivering SIB in prostate cancer cases are available.^[15-18] Few studies have also been published on delivering SIB to other anatomical sites like spine, lung, breast and rectum.^[7, 19-23]

Halcyon™ 2.0 with a kV cone-beam computed tomography (CBCT) delivers a single 6MV flattening filter-free (FFF) beam with a double stack multi-leaf collimator (MLC), SX2. The width of SX2 leaves is 1 cm at the isocenter with a 0.5 cm offset at the isocenter to minimize the leakage between the proximal and distal leaves.^[24, 25]

Effective tools such as conformity indexes (CI), homogeneity indexes (HI), and gradient indexes (GI), have been proposed as a simple way to quantify the dose distribution, which reflects the conformance between the prescribed dose area and PTV, the degree of uniformity within the target, and the dose fall-off outside the target.^[26-28]

Gradient index (GI) is another tool for evaluation of radiotherapy plans and it describes the dose steepness outside the target volume and it also shows how dose outside the target is distributed optimally. GI is defined as the ratio of the volume of 50% prescribed dose to that of the pre-

scribed dose. A lower GI value means a steeper gradient of dose distribution outside the target.^[29]

Since the recent introduction of advanced treatment techniques in Nigeria, there is a dire need to report our experiences on these techniques. This dosimetric study on SIB lays the groundwork for future clinical investigations of dose escalation in prostate cancer cases, and our findings show the potential of improved treatment.

The aim of the study was to dosimetrically compare SIB-VMAT and SIB-IMRT in the delivery of SIB treatments for prostate cancer patients. Specifically, to compare the abilities of these two treatment techniques to spare the normal tissue after increasing the dosage to a daily fraction of 3 Gy to the prostate bed.

Methods

Patients

Twenty patients with prostate cancer treated with SIB-VMAT technique on the Halcyon™ machine at NSIA-LUTH Cancer Centre were replanned using SIB-IMRT by eclipse planning system (Varian Medical Systems version 15.6) for the purpose of this study. The mean age of the patients studied was 66.4 years old (range 50-80 years old). The patients were instructed to void their bladder and bowel after which they are to drink 300 ml of water 15 to 30 minutes prior to simulation in the bid to achieve a comfortably full bladder. This was done to eliminate disparities in bladder and rectal volumes between simulation and treatment. The patients were simulated in head-first supine position using a computed tomography (CT) simulator (General electric CT scanner) and were immobilized with the aid of a knee rest and foot rest for comfort and support. All CT planning scans were acquired with a slice thickness of 2.5 mm. The CT images were then transferred to the eclipse treatment planning system via Digital Imaging and Communications in Medicine "DICOM" network.

Contouring

All organs at risks (OAR) and region of interest were contoured manually from axial-CT images. The Clinical Target Volumes (CTV) were outlined by the radiation oncologist to include the prostatic fossa, seminal vesicles and the lymph nodes. The CTVs were expanded 5 mm posteriorly and 10 mm in all the other directions to form the PTV.^[30] Some of the OAR contoured and used in this study included the rectum, bladder and the femoral heads.

Treatment Planning

All patients were prescribed a dose of 46 Gy in 20 fractions at 2.3 Gy per fraction to the pelvic nodes, the seminal vesi-

cle was simultaneously treated to 50 Gy in 20 fractions delivered in 2.5 Gy per fraction while the prostate was also simultaneously treated to 60 Gy in 20 fractions delivered in 3 Gy per fraction. The Halcyon™ plans were generated with the eclipse TPS v15.6. The inverse planning technique with the photon optimizer (PO) v15.6 was used, and dose calculations were performed with the analytical anisotropic algorithm (AAA) v15.6 as well.

A total of 40 plans- 20 SIB-VMAT and 20 SIB-IMRT were studied. These plans were computed using linear accelerator photon beams with 6MV energy. Four full arcs with automatically generated 281, 326, 11, and 56 degrees of collimator angles were used for the SIB-VMAT treatment plans of the 20 patients. However, one SIB-IMRT plan using seven co-planar beams (0°, 50°, 100°, 150°, 200°, 260° and 310°) was generated for each patient for comparison purpose only (Fig. 1). Some studies reported that multiple arcs are beneficial to produce the modulation necessary to achieve optimal treatment planning goals when using SIB technique for complex target volume^[15] hence the choice of four arcs for the SIB-VMAT plans.

The SIB-VMAT and SIB- IMRT plans were planned with the aim of generating the best achievable plan per technique. The same dose constraints used in the SIB-VMAT plans were applied in the SIB-IMRT plans. The planning objectives was

to give at least 95% of the prescribed doses to at least 95% of the PTV volumes while minimizing dose to the organs at risk. Once the plans satisfy the desired coverage and constraints, no more adjustments were made. The OAR guidelines were adopted from objectives presented by Marks et al.^[31] as part of the QUANTEC analysis (Quantitative Analyses of Normal Tissue Effects in the Clinic) of normal tissue effects: that no more than 50% of the rectum should receive 50 Gy (V50Gy ≤ 50%) and a maximum dose of not more than 65 Gy to the bladder. Dose to the femoral heads was evaluated in terms of the recommendation in Vergalasova et al.'s study.^[17] That 15 % of the femoral heads should get less than 30 Gy (D15% < 30 Gy).

Plan Evaluation

Evaluation of the dose received in PTV46 (pelvic lymph nodes), PTV50 (seminal vesicle), PTV60 (prostate) and the dose received by organs at risk (bladder, rectum, left and right femoral heads) was done using a dose-volume histogram (DVH), CI, HI, GI and MU. For the PTVs, values of D98%, D50% and D2% (dose in Gy received by 98%, 50% and 2% of the target volume) were reported respectively in addition to V95% (the volume in cm³ receiving 95% of prescribed dose. The V30Gy, V50Gy (percentage volume getting 30Gy and 50 Gy respectively) and mean dose to the OARs was extracted to compare the degree of OAR sparing between SIB-IMRT and SIM-VMAT. The total number of MUs per planning technique were recorded and studied to compare the efficiency of delivery too.

The degree of conformity of each treatment technique was evaluated by calculating conformity index (CI) which is defined as the volume in cm³ encompassed by the 95% isodose divided by the PTV volume.^[32]

$$\text{The formula used is } CI = \frac{V95\%}{TV} \quad (i)$$

$$\text{The homogeneity index (HI) was calculated as } HI = \frac{D2\% - D98\%}{D50\%} \quad (ii).^{[33]}$$

The gradient index was also calculated as;

$$GI = \frac{V50\%}{V100\%} \quad (iii)$$

V50% and V100% are simply the percentage volumes of the PTV that got 50% and 100% of the prescribed dose.^[34] Higher CI and lower HI values indicated a better dose conformity and homogeneity to the targets.^[10] A GI that is closer to 1 indicates a faster dose fall off.^[29]

Statistical Methods

Numerical data were expressed as mean and standard deviation as appropriate. All analysis were performed using the paired, two-tailed Wilcoxon signed-rank test. A two-tailed p-value <0.05 was considered significant.

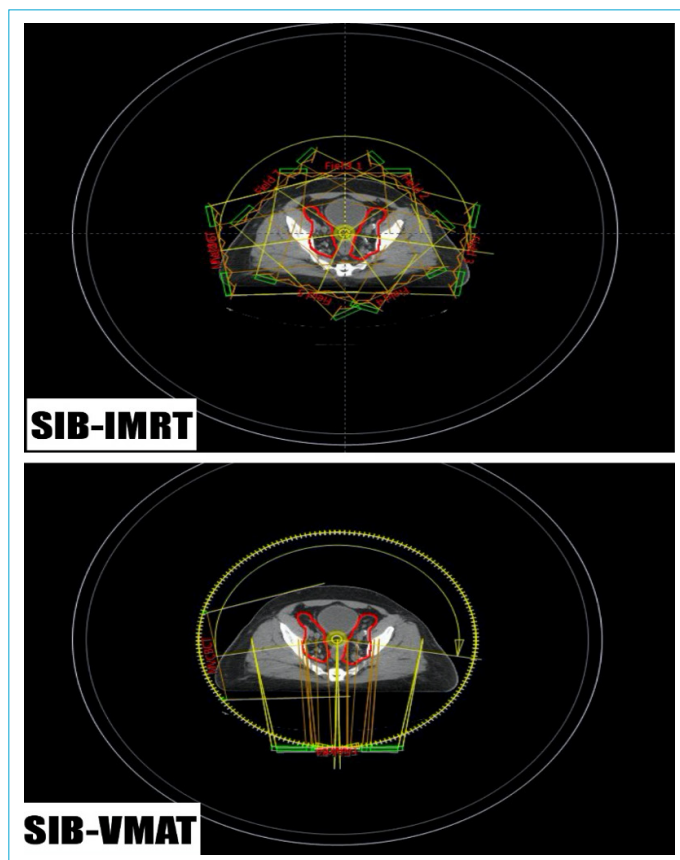


Figure 1. Field and arc arrangement for SIB-IMRT plans (top) and SIB-VMAT plan (bottom).

Results

PTV Coverage

The dose received by 95% of the PTV60 (D95%) were 58.81±0.47 Gy and 58.69±1.40 Gy, respectively, for SIB-VMAT and SIB-IMRT. This means that all two techniques allowed a good PTV60 coverage by the 95% isodose of the prescribed dose (60 Gy). Mean doses to PTV60 were 60.78±0.54 Gy and 60.74±1.52 Gy, respectively, for SIB-VMAT and SIB-IMRT as seen in Table 1.

The dose received by 95% of the PTV50 (D95%) were 49.03±0.45 Gy and 46.39±9.94Gy, respectively, for SIB-VMAT and SIB-IMRT. This means that SIB-VMAT had about 5.4% better dose coverage by the 95% isodose of the prescribed dose (50 Gy) compared to SIB-IMRT. Mean doses to PTV50 were 52.85 ±1.99 Gy and 51.56±2.96 Gy, respectively, for SIB-VMAT and SIB-IMRT. Mean doses to PTV46 (Dmean) were 46.31±1.24 Gy and 44.07±8.61Gy, respectively, for SIB-VMAT and SIB-IMRT.

Organs at Risk Sparing

Both SIB-VMAT and SIB-IMRT plans achieved the objectives for both PTV coverage and OAR sparing across all 20 patients. Table 2 shows the Wilcoxon signed rank results for

Table 2. Wilcoxon signed rank results for organs at risk (OARs) of SIB-VMAT versus SIB-IMRT (mean±standard deviation)

Target	Parameter	SIB-VMAT	SIB-IMRT	p
Bladder	D _{mean} (Gy)	39.13±3.10	35.39±5.19	0.003
	V _{30Gy} (%)	83.69±14.34	67.06±18.32	0.001
	V _{50Gy} (%)	11.04±5.75	10.67±7.93	0.16
	V _{95%} (%)	4.34±3.52	4.73±4.76	0.90
	D _{max} (Gy)	62.44±1.85	62.06±1.86	0.28
Rectum	D _{mean} (Gy)	36.41±6.03	33.67±6.72	0.006
	V _{30Gy} (%)	76.41±16.05	62.97±18.49	0.001
	V _{50Gy} (%)	11.53±6.79	11.73±9.62	0.58
	V _{95%} (%)	3.8±3.66	4.42±5.36	0.91
Left femoral head	D _{15%} (Gy)	21.28±3.74	21.23±3.48	0.97
	D _{mean} (Gy)	13.01±2.53	13.15±2.55	0.91
Right femoral head	D _{15%} (Gy)	21.31±4.29	20.90±3.90	0.48
	D _{mean} (Gy)	13.11±3.42	12.78±2.80	0.67

organs at risk (OARs) of SIB-VMAT versus SIB-IMRT (mean + standard deviation). In the SIB-IMRT plans, the average mean doses to the bladder, rectum and right femoral head were lower by 9.6%, 7.5% and 2.5%, respectively, than in the SIB-VMAT plans. However, the average mean dose to the left femoral heads was slightly lower (1.1%) in SIB-VMAT than SIB-IMRT with an insignificant p-value (0.91). SIB-VMAT showed a better rectum sparing V50Gy to be 11.53±6.79% compared to 11.73±9.62% in SIB-IMRT.

Homogeneity Index, Conformity Index, Gradient Index and Monitor Unit

The mean value of HI in PTV60 for the two techniques were slightly different (0.072 vs. 0.074) for SIB-VMAT and SIB-IMRT, respectively. CI was better in SIB-VMAT with a higher value of 0.993 compared to 0.979 for SIB-IMRT. The GI was also better in SIB-VMAT with a lower value of 1.41 compared to the 1.91 recorded for SIB-IMRT as seen in Table 3.

For PTV50, mean value of HI was about 48% lower in SIB-VMAT compared to SIB-IMRT which results in a better homogeneity with SIB-VMAT plans. CI was better in SIB-VMAT compared to SIB-IMRT (0.998 vs. 0.925) with a statistically significant p-value (0.018).

Table 1. Wilcoxon signed rank results for PTV comparisons of SIB-IMRT and SIB-VMAT (mean±standard deviation)

Target	Parameter	SIB-VMAT	SIB-IMRT	p	
PTV ₆₀	D _{2%} (Gy)	62.28±0.86	62.20±1.17	0.94	
	D _{50%} (Gy)	60.99±0.58	60.73±1.24	0.20	
	D _{95%} (Gy)	58.81±0.47	58.69±1.40	0.41	
	D _{98%} (Gy)	57.90±0.49	57.73±1.48	0.37	
	D _{mean} (Gy)	60.78±0.54	60.74±1.52	0.75	
	V _{95%} (%)	99.26±0.69	97.95±3.18	0.085	
	HI	0.072±0.01	0.074±0.02	0.18	
	CI	0.993±0.01	0.979±0.03	0.08	
	PTV ₅₀	D _{2%} (Gy)	57.14±3.6	56.98±3.56	0.91
		D _{50%} (Gy)	51.64±2.89	50.12±4.79	0.06
D _{95%} (Gy)		49.03±0.45	46.39±9.94	0.1	
D _{98%} (Gy)		48.41±0.94	48.12±0.99	0.35	
D _{mean} (Gy)		52.85±1.99	51.56±2.96	0.024	
V _{95%} (%)		99.74±0.47	92.46±19.24	0.006	
HI		0.17±0.06	0.33±0.5	0.001	
CI		0.998±0.004	0.925±0.193	0.018	
PTV ₄₆		D _{2%} (Gy)	47.69±1.20	47.97±2.22	0.31
		D _{50%} (Gy)	45.97±0.7	45.92±0.99	0.66
	D _{95%} (Gy)	44.80±0.71	42.26±9.64	0.014	
	D _{98%} (Gy)	44.32±0.74	43.86±1.11	0.04	
	D _{mean} (Gy)	46.31±1.24	44.07±8.61	0.14	
	V _{95%} (%)	97.86±4.30	88.62±25.61	0.005	
	HI	0.07±0.02	0.08±0.03	0.011	
	CI	0.979±0.043	0.887±.257	0.007	

Table 3. Gradient index, monitor unit parameters and p-value comparisons between SIB-VMAT and SIB-IMRT

Parameter	SIB-VMAT	SIB-IMRT	p
GI ₆₀	1.41±0.52	1.91±1.41	0.16
GI ₅₀	1.42±0.48	2.08±1.39	0.13
GI ₄₆	1.78±0.89	2.13±1.77	0.53
MU	184.78±16.4	305.08±82.97	0.0002

GI was better in SIB-VMAT as compared to SIB-IMRT (1.42 vs. 2.08).

The CI for PTV46 was a lot better in SIB-VMAT compared to SIB-IMRT, (0.979 vs. 0.887) with a statistically significant p-value (0.007). We also got a statistically significant result for HI (0.07 vs. 0.08) with a p-value of 0.011.

The MU generated by SIB-VMAT was lower compared to SIB-IMRT (184.78 vs. 305.08) with a statistically significant p-value of 0.0002 as seen in Table 3. In (Fig. 2), we showed the Dose-volume histogram (DVH) plan comparison between SIB-IMRT (triangles) and SIB-VMAT (squares) for the organs at risk and target volumes of one of the patients.

Discussion

In this study, we evaluated the dosimetric differences between VMAT and IMRT using homogeneity index (HI), target dose conformity index (CI), gradient index (GI) and OAR sparing for simultaneous Integrated Boost (SIB) treatment plans of prostate cancer cases. We made use of four full arcs in the SIB-VMAT plans as opposed to some published studies that used one or two full arcs in their SIB-VMAT plans.^[15, 18, 35] We also made use of seven co-planar beams for the SIB-IMRT plans.

Results in Tables 1 and 2 shows our comparison results in terms of target volumes and organs at risk. In terms of CI, HI and GI; SIB-VMAT was better due to its higher (1.41%) CI, lower (2.7%) HI and lower (26%) GI than SIB-IMRT for PTV60. For PTV50, a higher (7.3%) CI, lower (48%) HI and a lower (31.73%) GI for SIB-VMAT compared to SIB-IMRT. Also, for PTV46, a higher (9.4%) CI, lower (2.5%) HI and a lower (16.4%) GI were achieved by SIB-VMAT compared to SIB-IMRT. In terms of normal tissue sparing according to the OAR guidelines, SIB-IMRT spared the bladder and femoral heads with lower dose than SIB-VMAT which spared the rectum more. Some published works indicated in their result a significant reduction in doses delivered to the rectum using VMAT.^[9, 16]

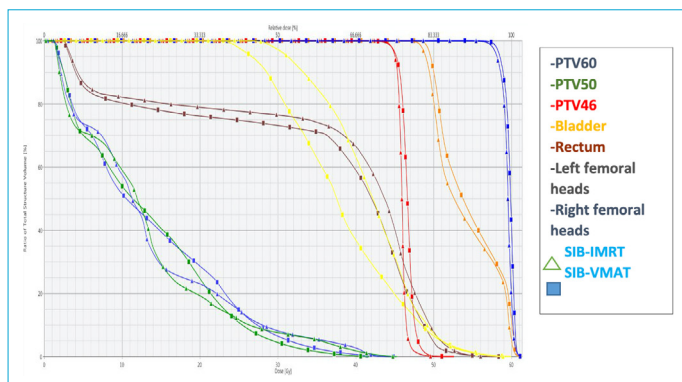


Figure 2. Dose-volume histogram (DVH) plan comparison between SIB-IMRT (triangles) and SIB-VMAT (squares) for the organs at risk and target volumes of a patient.

Comparing this study with others, the seminal vesicles were contoured as a separate target volume (PTV50) to receive a dose of 50 Gy. However, Jolly David et al.^[36] included seminal vesicle with prostate as a single target volume in their study where they compared rapid arc (RA; also known as VMAT) with IMRT plans produced for 10 randomly-selected high and intermediate risk previously treated patients with prostate carcinoma. Their result showed that the MU and estimated treatment time were considerably decreased in RA while retaining a comparable coverage of target volumes and better conformance level compared to IMRT. OAR sparing for both the rectum and the femoral heads was also enhanced in the RA plans. Another study was done using ten previously treated patients with high-risk adenocarcinoma of the prostate after laparoscopic radical prostatectomy.^[35] Their results showed that the VMAT technique provided reduced normal tissue dose and better target conformity compared to IMRT technique. According to (Fig. 3), the dose distribution for each of the target volumes in axial view created by SIB-VMAT) and SIB-IMRT plans of the same patient shows 95% prescription dose coverage.

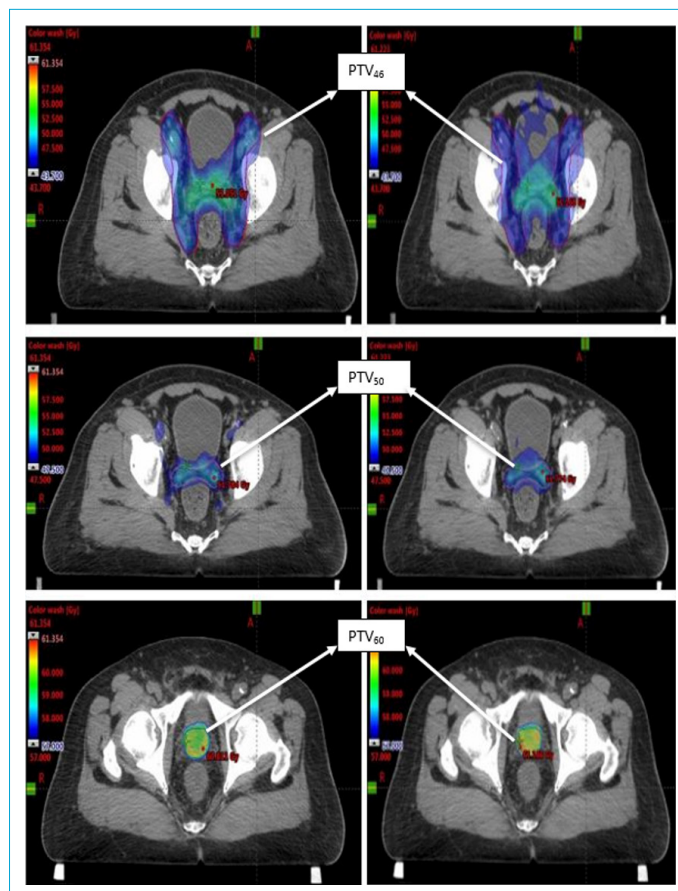


Figure 3. Dose distribution for each of the target volumes in axial view created by SIB-VMAT plan (left) and SIB-IMRT plan (right) of the same patient showing 95% prescription dose coverage.

Table 2 shows that SIB-IMRT had a lower mean dose to the rectum compared to SIB-VMAT (33.67 ± 6.72 vs. 36.41 ± 6.03) with a significant p-value of 0.006. This agrees with previous research works that had a lower mean dose to the rectum with SIB-IMRT plans.^[35, 37]

The main strengths of the study are that a relatively homogeneous RT technique was used, dose fractionation and consistent number of RT fields were presented and treatment was done with modern techniques in a single Nigerian institution. The limitations of this study however, are the undocumented follow-up and the small study population which is too small to be conclusive as regards the superiority of SIB-VMAT over SIB-IMRT in terms of conformity.

Conclusion

This study evaluated the dosimetric differences using VMAT and IMRT techniques in the delivery of SIB radiation therapy to prostate cancer patients. SIB-VMAT technique uses a smaller number of monitor units compared to SIB-IMRT. Both techniques however produced a good coverage to the target volume with SIB-VMAT having more conformal plans but slightly similar homogeneity with SIB-IMRT. They both maintained dose to OARs within acceptable tolerance levels of the institution.

Disclosures

Ethics Committee Approval: ADM/DSCST/HREC/APP/4710, 07/01/2022, Lagos University Teaching Hospital Health Research Ethics Committee.

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