

## RESEARCH ARTICLE

Editorial Process: Submission:08/13/2022 Acceptance:12/20/2022

# A Dosimetric Analysis of Modified Volumetric Modulated Arc Therapy for Bone Marrow Sparing Radiotherapy in Cervical Cancer-An alternative Approach to Conventional VMAT

Dharmendran Palani<sup>1\*</sup>, Kesavan Govindaraj<sup>1,2</sup>, Sowmiya Sampathrajan<sup>2</sup>, Lavanya Karunakaran<sup>3</sup>, Kadirampatti M. Ganesh<sup>4</sup>

## Abstract

**Background:** External beam radiotherapy remains the primary treatment modality in cervical cancer. Nowadays Intensity Modulated Radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) are increasingly being used to reduce normal tissue toxicity. The drawback of conventional VMAT is that a considerable volume of pelvic bone marrow receives a low dose. **aim:** We analyzed whether there was a way to reduce the volume of the low dose regions of bone marrow, and assessed the potential benefit of conventional-4Arc (C-4Arc VMAT), and Modified-4Arc (M-4Arc VMAT) over the conventional 2 ARC VMAT. **Materials And Methods:** Twelve clinically proven locally advanced cervical cancer patients treated with concurrent chemo-radiotherapy by Conventional VMAT (RapidArc) in dual rotation mode (C-2Arc VMAT) were selected for this study. C-4Arc VMAT and M-4Arc VMAT dose plans were generated for these twelve patients and these three different types of plans were evaluated for the quality and compared dosimetrically. **Results:** M-4Arc VMAT designs exhibited a greater bone marrow sparing when compared with conventional VMATs with respect to volume receiving 5Gy to 35Gy without compromising PTV dose coverage. M-4Arc VMAT plans, the bone marrow volume receiving 30 Gy (V30Gy), 40Gy (V40Gy), and mean doses were lower than the C- 4 Arc plan and a similar result was observed for V50(Gy) also when comparing with the standard 2 Arc plan. In modified VMAT plans, the rectum and bladder dose volumes were lower than standard VMAT. Similarly, the bowel bag V35(Gy), V40(Gy), V50(Gy), mean doses. The right and left femoral head doses were reduced significantly when compared to conventional VMAT plans. **Conclusion:** The M-4Arc VMAT plans are better than the C-2Arc and C-4Arc VMAT plans for reducing the dose to bone marrow by limiting the MLC field width travel.

**Keywords:** Hematologic toxicity- radiotherapy- field width- MLC- RapidArc- cervical cancer- bone marrow sparing

*Asian Pac J Cancer Prev*, 23 (12), 4323-4332

## Introduction

Cervical cancer remains a predominant cause of cancer incidence and mortality among women globally, particularly in developing nations (Arbyn et al., 2022). In comparison to radiation therapy alone, the use of combination therapeutic interventions, such as concurrent chemotherapy and radiation therapy, is advised for better tumour control and progression-free survival (Morris et al., 1999; Peters et al., 2000; Green et al., 2001). Numerous investigations have found that while the intended dose is delivered to the tumour using conventional radiation techniques, the prescription tumour dose (Lukka et al., 2002; Mell et al., 2006) irradiates a greater amount of bone marrow due to technical limitations of the treatment

technique and equipment. The most prevalent adverse effect would be the reduction in the blood cell counts produced from the pelvis and the surrounding bones as more than 50% of active bone marrow is located in the pelvis in adults (Mell et al., 2006).

Furthermore, chemotherapy increases the risk of haematological toxicity, which mandates therapeutic interruption of scheduled cycles which inhibits tumour control, and accelerates tumour growth (Vaupel et al., 2001). Contemporary approaches such as intensity modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), and volumetric modulated arc therapy (VMAT) are frequently implemented. Among them, the IMRT technique has been widely used since it has the capacity of sparing bone marrow when compared

<sup>1</sup>Research and Development Centre, Bharathiar University, Coimbatore, India. <sup>2</sup>Department of Radiotherapy, Vadamalayan Hospitals Integrated Cancer Centre, Madurai, India. <sup>3</sup>Oral and Maxillofacial Pathology, Department, Asan Memorial Dental College and Hospital, Tamil Nadu, India. <sup>4</sup>Department of Radiation Physics, Kidwai Memorial Institute of Oncology, Bengaluru, India. \*For Correspondence: pdharmendran75@gmail.com

to the 3DCRT conventional technique, which is a significant advantage (Mell et al., 2006; Hui et al., 2014). As a result, when delivering precise RT, preserving the bone marrow to as much as feasible has taken precedence (Mell et al., 2008).

With the advancement of therapeutic beam modification in IMRT/VMAT, precise radiation doses can be provided with high conformality while avoiding organ-at-risk OAR structures. Studies on prostate cancer (Mell et al., 2006; Zelefsky et al., 2012) gynaecological cancer (Lukovic et al., 2016) and head and neck cancer (Toledano et al., 2012) provide evidence on the benefits of IMRT/VMAT. When compared to IMRT, VMAT-novel radiotherapy, has a shorter treatment duration and fewer monitor units (MU) (Buckey et al., 2010; Ramiz et al., 2020).

The VMAT approach modulates the administered radiation by continuously changing the gantry speed, dosage rate, and location of the multi leaf collimator (MLC) (Otto, 2008). VMAT can provide a fraction dosage in a single rotation for a simple and small target. For complex-shaped target volumes, however, more than one rotation is required to produce IMRT-equivalent outcomes (Guckenberger et al., 2009). This is mostly due to limits applied by the dose optimization engine. planning constrains, such as MLC leaf positions and MU weights (Otto, 2008), constantly retain and quick delivery and restrict the optimization engine.

Other limitations on VMAT optimization exist in addition to MLC leaf location and MU weights. In particular, Varian Millennium MLC (Varian Medical System, Palo Alto, CA, USA) leaves are 15 cm in length (at isocenter), hence two opposed MLC leaves moving parallel to the X-jaw can only cover up to 30 cm of the field width. As a result, the X-jaw width directly regulates the speed and freedom of the MLC movement during beam modulation. The physical limitations of this machine have a direct impact on how well the larger target volume is optimized, e.g., by reducing dose rate and slowing leaf speed (Ugurlu and Temelli 2020). Furthermore, if the X-jaw opening is greater than the leaf's physical length, a single leaf cannot cover a VMAT field entirely by itself resulting in unwanted radiation dose exposure to healthy normal tissue thereby deterioration of the quality of the plans (Jang et al., 2021). The physical limits of the treatment machine, as well as the efficiency constraints of VMAT, limit the degree of freedom necessary to produce higher-quality treatment plans (Ugurlu and Temelli 2020; Jang et al., 2021; Lai et al., 2016).

These aforementioned restrictions set out the objectives of this study, which is to overcome the impact of the field width (X-jaw aperture) on VMAT plan quality by proposing an alternate technique holding the same mono-isocentric treatment method for irradiation of large targets with VMAT. This approach is referred to as applying the optimal collimator angle to different arcs to the X-jaw opening while staying within the physical length of the MLC to cover the VMAT target.

## Materials and Methods

Twelve clinically proven locally advanced cervical cancer patients who had been treated at Vadamalayan Integrated Cancer center between January to June 2022 with concurrent chemoradiotherapy by Conventional VMAT RapidArc in dual rotation mode (C-2Arc VMAT) were selected for this study. The previously treated CT dataset was selected to generate Conventional-4Arc VMAT (C-4Arc VMAT) and modified-4Arc (M-4Arc VMAT) rotation.

### Simulation

All patients were positioned in supine, on universal base-board with, immobilizer using 6-clamp abdomen and thigh immobilization cast, for better reproducibility during treatment delivery. Patients are instructed to maintain full bladder and empty rectum prior to the scan and initiation of therapeutic procedures. Axial Computed tomography (CT) images scanned superiorly from first lumbar vertebra to inferiorly 4 cm below the perineum, with 3 mm slice thickness and 500 mm field of view were acquired (Discovery IQ GE Medical System.)

### Target volume definition

The acquired images were transferred to treatment planning system (TPS) (Eclipse Version 13.6.5 Varian Medical system) and the delineation of gross tumor volume (GTV), clinical target volume (CTV) and the organ at risks (OARs) were done on the CT images (Lim et al., 2011).

The planning target volume (PTV) was determined by a uniform expansion of 6mm in all directions around the CTV which has been contoured and verified on the CT images by an experienced radiation oncologist. And the rectum, bladder, bowel sac (peritoneal cavity), right and left femoral head and bone marrow were added. The pelvic bone inner table in the CT image is delineated as bone marrow and its boundaries are defined from 2 cm above to 2 cm below the PTV (Mahantshetty et al., 2012). This volume is used for the planning of this study.

### Dose constraints for PTV and Organ at risk (OAR)

Dose planning was performed without compromising PTV coverage, taking into account of all dose constraints. PTV volume of 95% (V95) received by 95% of the prescription dose. Dose constraints for bowel bag V45Gy<195 cc and in, rectum; bladder is V40Gy<50-60% and for both femoral heads V30Gy<20%. The dosimetric constraints for the bone marrow was V10Gy and V20Gy should be less than 90% and 75% of bone marrow volume respectively.

### VMAT Planning techniques

Three different VMAT plans were created for each patient using commercially available TPS (Eclipse TPS version 13.6.5, Varian Medical System, Palo Alto, CA, USA). The dose specification for PTV was 50 Gy in 25 fractions. For each patient, the three schedules had a 6 MV clinical photon beam with a selected dose rate of 600 MU/min from the TPS. All plans made with 60 pairs of Varian Millennium 120 multi-leaf collimators (5 mm spatial resolution at 20 cm in the center and 10 mm

spatial resolution at 10 cm outside). The Arc Geometry Tool (AGT) was used for identifying the center of the target, the start angle, stop angle, optimal opening, and the collimator angle. One set of double arcs plans were created such a way that one arc in a clockwise (CW) direction and another arc in a counter-clockwise (CCW) direction using AGT for the C-2Arc VMAT plan as shown in Figure 1 (A), similarly, to create the C-4Arc VMAT plan, two more arcs added to the C-2Arc VMAT plan, CCW and other CW direction as shown in Figure 1 (B).

M-4Arc plans were created by copying the C-4Arc VMAT plan, with modified collimator angle. In arcs 1 and 2, the collimator was rotated to  $\pm 20^\circ$  to reduce the X-jaw field opening from its target width to length of an MLC. For the second set of arcs (3 and 4), the collimator was rotated to an angle of  $\pm 90^\circ$  to change the orientation of the MLC and to widen Y-jaw pair to cover the entire target width as shown in Figure 1 (C). The X-jaw remains asymmetrically open position to cover from the top half of the target to the third arch and from the bottom half of the target to the fourth arch. The length of the 3<sup>rd</sup> and 4<sup>th</sup> arc fields was further kept within the physical limits of the MLC. An overlap of 2 cm field transitions was maintained between the two arcs (arcs 3 and 4) to achieve better modulation in the field transitions. The same planning objectives were used in optimization for all three types of VMAT plans, and the final doses for these three types of plans were calculated using an anisotropy analysis algorithm (AAA) with a grid size of 2.5 mm.

#### Dosimetric comparisons between the three VMAT plans

Dosimetric comparisons between the conventional (2Arc) method, the increased arc number 4Arc method, and the modified effective field width method to assess the impact of the VMAT plan quality from a quantification perspective of minimum dose of PTV coverage and OAR was analyzed. The assessed dose-volume histogram (DVH) variables of the PTV were: Mean dose (Dmean), Median dose (Dmedian), near minimum dose (D98%), dose received by 95% of PTV (D95%), near maximum dose (D2%) of the prescription dose. similarly, the Volume

enclosed in the isodose were V107%, V98%, and V95%. homogeneity index (HI), and conformity index (CI) were calculated using formulas 1 and 2 recommended by the ICRU report no.83 and Paddick proposed conformity index.

$$HI = (D_2\% - D_{98}\%) / (D_{50}\%) \quad (1)$$

$$CI_{\text{Paddick}} = (TV_{\text{PIV}})^2 / (TV \times \text{PIV}) \quad (2)$$

where  $D_2\%$ ,  $D_{98}\%$ , and  $D_{50}\%$  doses of the prescription isodose. The smaller the HI value, the more uniform the target dose. TV is the Target volume; TVPIV is the target volume covered by the prescription isodose Volume, and PIV represents prescription isodose volume. The closer the CI value is to 1, the better the conformality of the target volume is. The dosimetric evaluation of rectum and bladder was analyzed using mean Dose (Dmean), volume received 30Gy (V30Gy), 40Gy (V40Gy), 50Gy (V50Gy) and near maximum dose (D2%). For femoral heads, (V30Gy, V40Gy, V45Gy) and near maximum (D2%) dose was used for evaluation. For the bowel bag (V30Gy, V35Gy, V40Gy, V45Gy) and near maximum (D2%) doses were used for analysis. The plan comparison was performed for the bone marrow doses using the (Dmean), (V5Gy, V10Gy, V15Gy, V20Gy, V30Gy, V40Gy, V45Gy, V50Gy)

#### Statistical analysis

The Wilcoxon Signed Ranks Test was performed, to compare the M-4Arc VMAT plan with other methods of the plans. The statistical significance level was set to a p-value <0.05. All these comparative statistical analyses were computed using IBM SPSS statistics version 26.0.0.

## Results

#### PTV coverage and its quality index

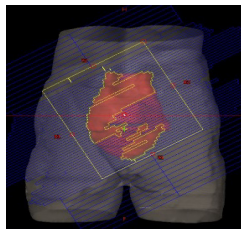
Table 1 shows the quality indices and dose coverage to PTV for the twelve patient plans. The dose coverage of the

Table 1. Dosimetric Parameters Comparison among C-2Arc VMAT , C-4Arc VMAT and M-4Arc VMAT Technique for PTV (mean standard deviation and the level significant)

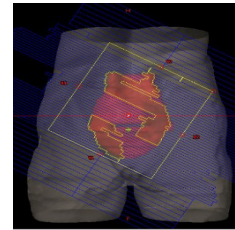
	C-2Arc VMAT	M-4Arc VMAT	C-4Arc VMAT	p-value	
				C-2Arc Vs M-4Arc	C-4Arc Vs M-4Arc
D98 (GY)	47.33±0.894	47.43±0.4	46.94±1.5	0.754	0.505
D2 (GY)	52.66±0.630	52.65±0.30	52.46±0.2	0.61	0.213
D95 (GY)	48.41±0.642	48.48±0.29	48.027±1.25	0.875	0.388
V95 (%)	97.56±1.81	97.75±0.93	96.16±4.56	0.53	0.48
V98 (%)	91.69±3.15	91.96±1.60	89.68±6.9	0.937	0.388
V107 (%)	0.69±1.45	0.237±0.40	0.059±0.08	0.79	0.155
Mean Dose (GY)	50.75±0.28	50.58±0.16	50.48±0.35	0.084	0.541
Median Dose (GY)	50.85±0.28	50.683±6.96	50.63±0.22	0.084	0.814
CI	0.7266±0.046	0.7224±0.039	0.7169±0.023	0.53	0.657
HI	0.105±0.024	0.103±0.01	0.108±0.0315	0.754	0.937
MU	583.75±69.67	653.5±165.63	884.58±124.56	0.002*	0.003*

The asterisk \*mark show the significant p-value.

(A)

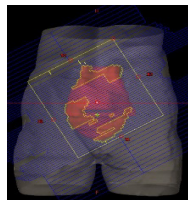


1<sup>st</sup> Arc CW, Collimator: 30°

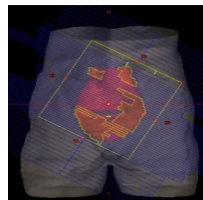


2<sup>nd</sup> Arc CCW, Collimator: 330°

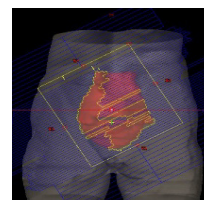
(B)



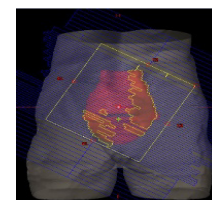
1<sup>st</sup> Arc CW, Collimator: 30°



2<sup>nd</sup> Arc CCW, Collimator: 330°

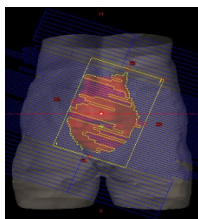


3<sup>rd</sup> Arc CW Collimator: 30°

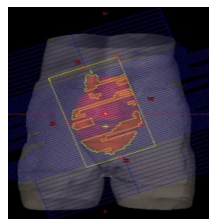


4<sup>th</sup> Arc CCW, Collimator: 330°

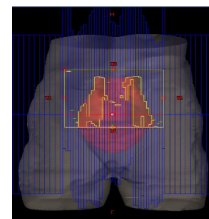
(C)



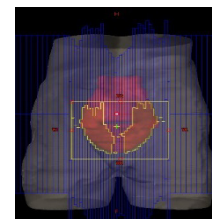
1<sup>st</sup> Arc CW, Collimator: 30°



2<sup>nd</sup> Arc CCW, Collimator: 20°



3<sup>rd</sup> Arc CW, Collimator: 90°



4<sup>th</sup> Arc CCW, Collimator: 90°

Figure 1. Volumetric Modulated Arc Therapy (VMAT) Plans Optimized with 2 to 4 Arcs and Different Field Sizes for Cancer Cervix Radiation Therapy. (A) Beam setup of conventional-2Arc VMAT (C-2Arc VMAT) plans. (B) Beam setup of conventional-4Arc VMAT (C-4Arc VMAT) plans (C) Beam setup of modified-4Arc VMAT (M-4Arc VMAT) plans

PTV did not show any statistically significant differences for the three-bone marrow sparing VMAT plans. Figure 3 depicts the average PTV dose coverage of these three strategies. The red round dot lines represent the M-4Arc VMAT plan DVH, the blue dash-dot line represents the C-4Arc VMAT plan DVH, and the yellow square dot line

represents the C- 2Arc VMAT Plan DVH.

*Comparison of dosimetric parameters of the Bone Marrow with the standard VMAT plans*

The dose volume lines were shown marginal difference between these three different type of plans

Table 2. Dosimetric Analysis of C-2Arc and C-4Arc VMAT Plans Compared with M-4Arc VMAT Plans for Bone Marrow

	C-2Arc VMAT	M-4Arc VMAT	C-4Arc VMAT	p-value	
				C-2Arc Vs M-4Arc	C-4Arc Vs M-4Arc
V5 (%)	95.85±2.37	94.38±3.35	95.79±2.64	0.0229*	0.0076*
V10 (%)	87.04±4.6	83.29±5.47	85.79±4.73	0.0096*	0.0229*
V15 (%)	78.66±5.25	73.69±5.47	76.35±5.80	0.0096*	0.0597
V20 (%)	69.57±5.76	62.56±4.66	65.30±7.70	0.0047*	0.0995
V30 (%)	47.48±6.76	40.21±3.52	44.27±7.50	0.0029*	0.0150*
V40 (%)	29.21±5.47	24.73±4.12	27.34±4.93	0.0022*	0.0342*
V45 (%)	21.02±4.67	17.59±3.94	19.72±3.95	0.0022*	0.1579
V50 (%)	9.11±3.24	7.93±3.31	8.86±1.713	0.2393	0.4328
Mean (GY)	29.2±2.38	26.82±1.56	28.13±2.53	0.0029*	0.0120*

The asterisk \*mark show the significant p-value.



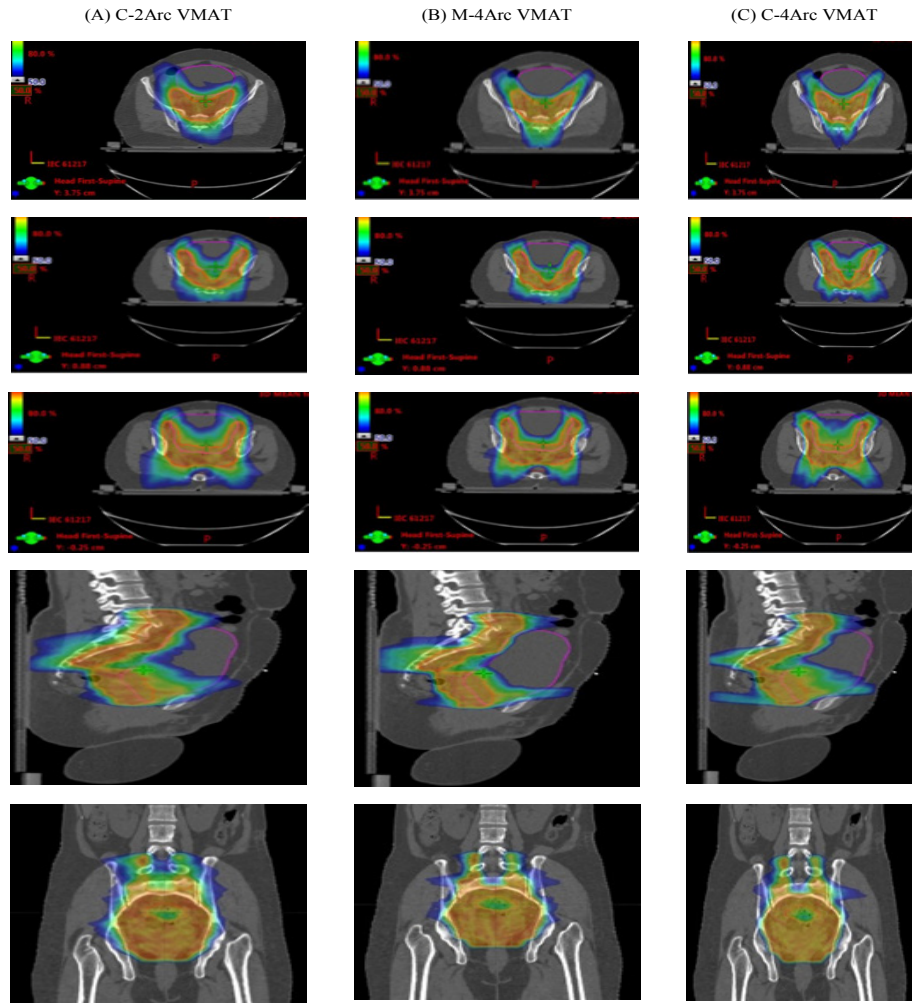


Figure 2. Comparison of Representative Dose Distributions in Axial, Coronal, and Sagittal Volumetric Modulated Arc Therapy (VMAT) Plans for a Cervix. (A, C) The dose was optimized using a fully opened field size (Conventional-VMAT) to cover the planning target volume and (B) an optimal beam opening technique (modified-VMAT). 50% Isodose displayed as a color-wash, red for planning target volume.

particularly the dose volume region from 5Gy to 35Gy, which demonstrates a significant difference compared to the standard VMAT Technique (Figure 4, Table 2). Except for the V50Gy dose volume, the dose volume of

bone marrow is statistically significant in relation to the amount of dose reduction when compared to standard VMAT (Table 2).

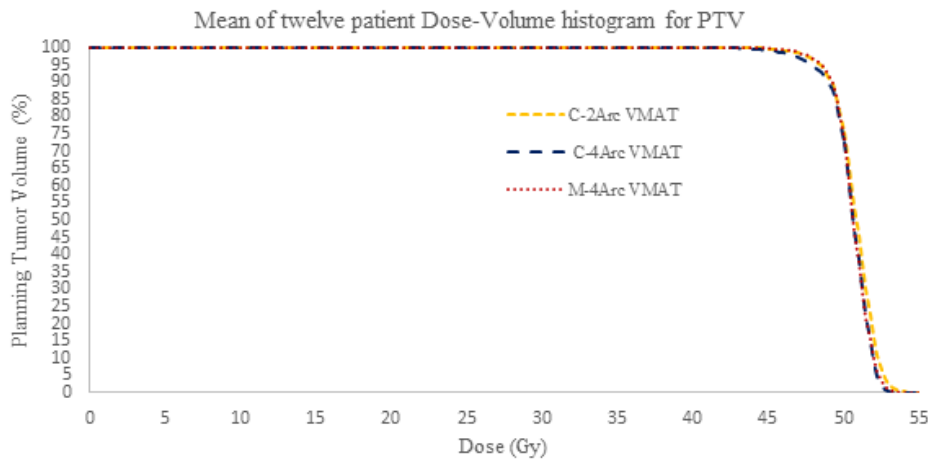


Figure 3. Comparison of PTV DVH of M-4Arc VMAT Plan Vs C-2Arc and 4Arc VMAT Plans

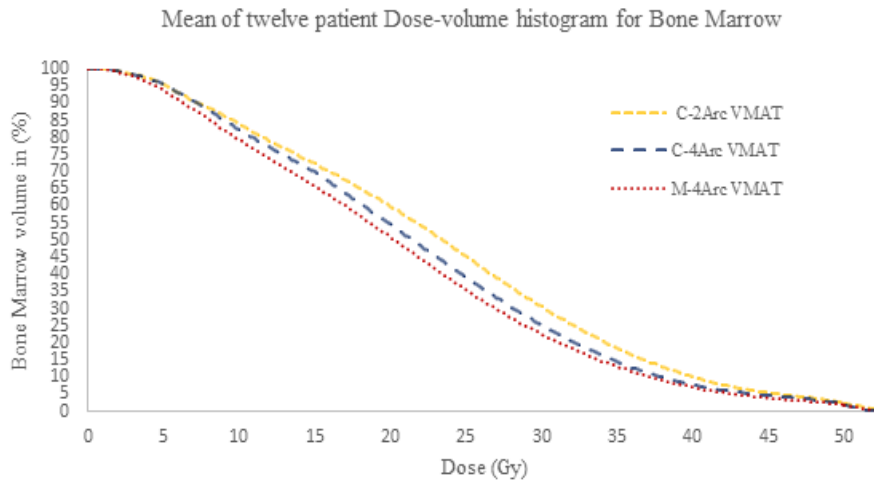


Figure 4. Comparison of Bone Marrow DVH of M- 4Arc VMAT Plan Vs C-2Arc and C-4Arc VMAT Plans

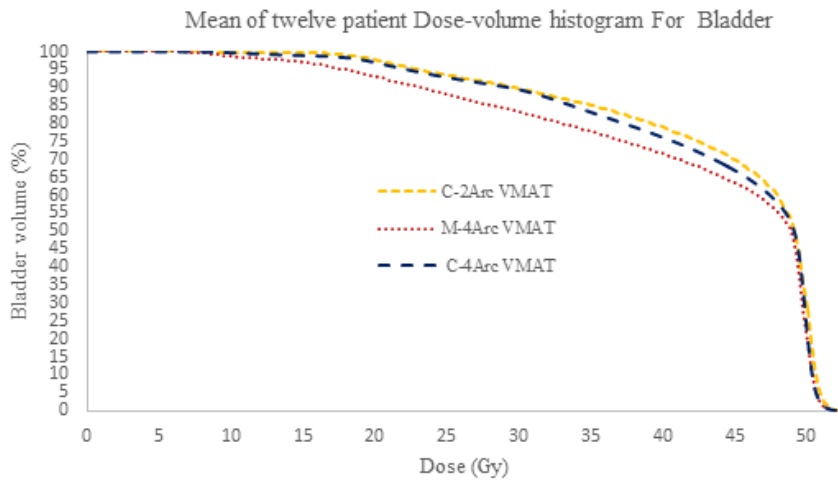


Figure 5. Comparison of Bladder DVH of M-4Arc VMAT Plan Vs C-2Arc and C-4Arc VMAT Plans

*Comparison of dosimetric parameters of the OARs for the three VMAT plans*

The dose distributions of the three method VMAT plan comparison was shown in Figure 2, M- 4Arc VMAT showed superior high dose gradients in a representative

target volume. The mean and standard deviation of the dose-volume parameters for the bladder M-4Arc VMAT plan are much lower than those for the other two plans and the similar results were obtained for V30(Gy), V40(Gy), and V50(Gy) which is significantly lower than

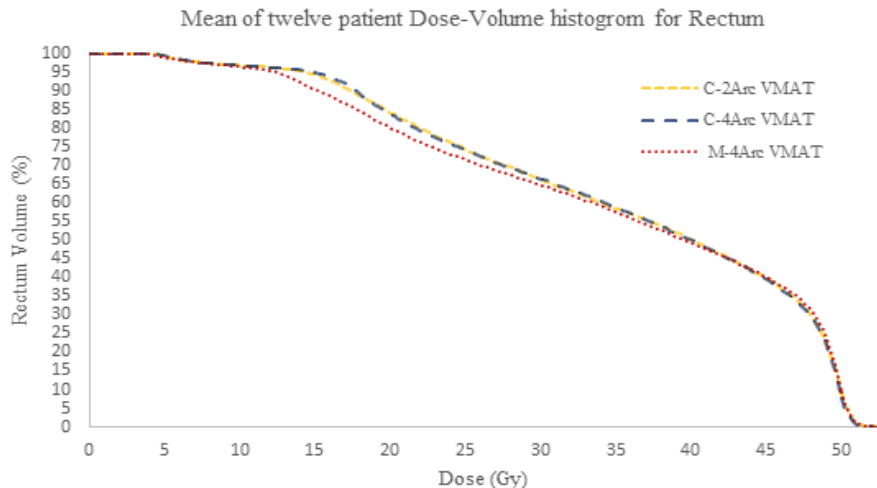


Figure 6. Comparison of Rectum DVH of M-4Arc VMAT Plan Vs C-2Arc and C-4Arc VMAT Plans

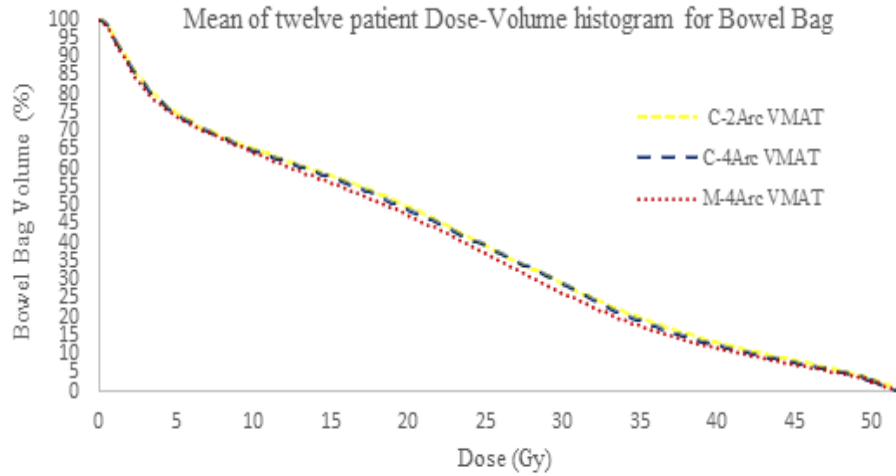


Figure 7. Comparison of Bowel Bag DVH of M-4Arc VMAT Plan Vs C-2Arc and C-4Arc VMAT Plans

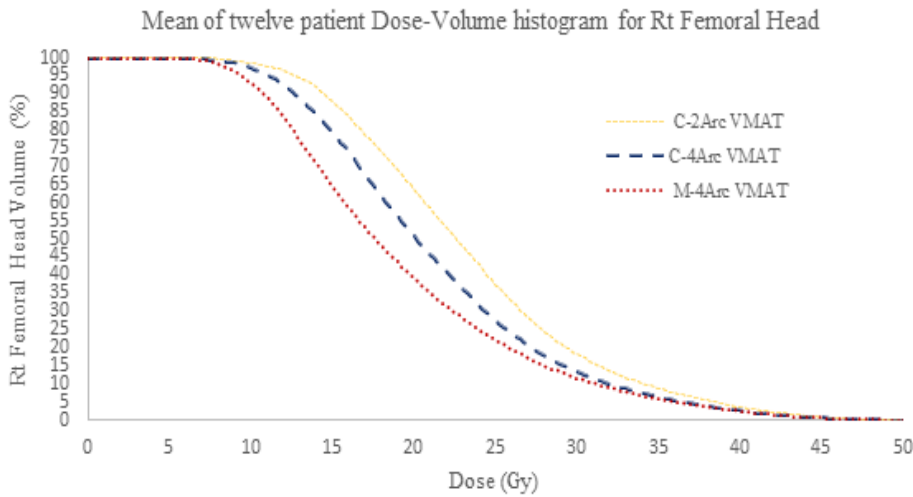


Figure 8. Comparison of Rt Femoral Head DVH of M-4Arc VMAT Plan Vs C-2Arc and C-4Arc VMAT Plans

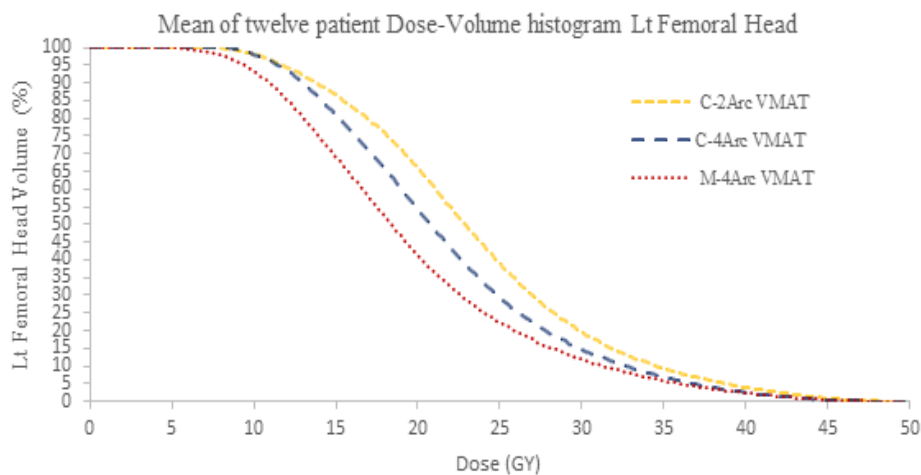


Figure 9. Comparison of Lt Femoral Head DVH of M-4Arc VMAT plan Vs C-2Arc and C-4Arc VMAT Plans

C-2Arc VMAT plan (Table 3, Figure 5). Comparing the three methods, the dose volumes of the rectum V30(Gy), V40(Gy), V50(Gy), D2% and mean dose did not show a significant dose variation. The M-4Arc VMAT method

was a good option for controlling the low-dose region (Figure 6). For analyzing bowel bag, the dose reduction was well respected in the M-4Arc VMAT plan (Figure 7) and in V35(Gy), V40(Gy), V50(Gy), and Dmean dose

Table 3. Dosimetric Analysis of C-2Arc and C-4Arc VMAT Plans Compared with M-4Arc VMAT Plans for OARs Bladder, Rectum, Bowel Bag, Lt Femoral Head and Rt Femoral Head.

OARs		C-2Arc VMAT	M-4Arc VMAT	C-4Arc VMAT	p-value	
					C-2Arc Vs M-4Arc	C-4Arc Vs M-4Arc
Bladder	V30 (Gy)	86.34±13.99	83.21±15.40	89.47±11.80	0.0712	0.0186*
	V40 (%)	74.71±18.33	71.55±16.47	76.09±15.66	0.0597	0.0121*
	V50 (%)	26.04±14.55	18.51±6.69	21.23±6.40	0.0499*	0.1823
	D2 (Gy)	51.02±0.39	51.26±1.19	50.86±0.35	0.6377	0.61
	Mean (Gy)	43.58±4.51	42.39±5.19	44.02±3.86	0.0597	0.0096*
Rectum	V30 (%)	66.19±10.55	64.69±13.35	66.38±10.48	0.3465	0.2094
	V40 (%)	50.00±9.74	49.48±13.20	49.82±10.27	0.7537	0.8753
	V50 (%)	8.58±3.85	8.99±6.24	7.66±4.04	0.6379	0.5829
	D2 (Gy)	50.58±0.35	50.58±0.38	50.54±0.32	0.5828	0.5631
	Mean (Gy)	36.22±3.11	35.58±4.26	36.21±3.13	0.1549	0.1952
Bowel Bag	V30 (CC)	642.25±188.3	583.9±161.07	629.01±215.69	0.1579	0.3465
	V35 (CC)	434.29±144.33	384.85±117.9	406.4±156.32	0.0342*	0.4328
	V40 (CC)	285.59±100.93	251.39±83.80	258.37±113.25	0.0186*	0.5303
	V45(CC)	177.45±68.59	154.48±56.67	155.83±79.96	0.0186*	0.5303
	D2 (Gy)	49.76±2.19	49.4±2.36	48.65±3.63	0.0995	0.6949
	Mean (Gy)	20.41±3.66	19.55±3.65	19.96±3.80	0.0096*	0.3078
Rt Femoral Head	V30(%)	18.56±	11.36±5.26	13.14±6.66	0.0047*	0.2393
	V40(%)	4.07±	2.37±1.96	2.45±2.30	0.0076*	0.666
	V45(%)	0.98±	0.53±0.90	0.62±0.92	0.0367*	0.6353
	D2(Gy)	41.60±2.93	39.48±3.72	39.21±4.28	0.0150*	0.5303
	Mean (Gy)	23.59±2.83	19.26±2.74	21.21±3.53	0.0047*	0.0342*
Lt Femoral Head	V30(%)	19.53±10.55	11.89±4.65	14.64±6.08	0.015*	0.158
	V40(%)	4.28±2.56	2.38±1.49	2.43±1.4	0.034*	0.814
	V45(%)	1.07±1.00	0.49±0.54	0.38±0.52	0.11	0.61
	D2(Gy)	41.56±3.56	20.06±1.93	38.46±6.26	0.002*	0.003*
	Mean (Gy)	23.66±3.55	19.84±2.27	21.86±2.99	0.010*	0.06

The asterisk \*mark show the significant p-value

variations were significantly lower than C- 2Arc VMAT (Table 3). When comparing the M-4Arc VMAT to the C-2Arc VMAT, similar dose reductions were observed for the right and left femoral heads (Figure 8 and 9).

### Discussion

By comparing bone marrow sparing utilizing C-2Arc VMAT, C-4Arc VMAT, and M-4Arc VMAT planning, this study purpose was to lower the dose volume to pelvic bone marrow. Instead of using a relatively limited range of predefined angles, M-4Arc VMAT can use the gantry, collimator, and field size that are most suited for the patient Compared to the conventional arc angles established by the TPS (Lai et al., 2016). Additionally, the optimization for M-4Arc VMAT has different methodology from standard VMAT optimization in terms of dynamically adjusted leaf speed and dose rate. For site-specific requirements, it is crucial to determine the optimal gantry angle, field size, and collimator angle (Lai et al., 2016).

The findings presented in Table 3 reveals that the 4Arc plan has a higher quality overall compared to the

2Acr plan. The addition of two rotational arcs was a smart improvement to make to this layout (Guckenberger et al., 2009). In a similar manner, the quality of the 4Arc plan deteriorates as the target volume increases. The data shown in Table2 substantiates this conclusion. The p-values for the mean dose and bone marrow dose volume dosimetry parameters are clearly visible. These values demonstrate considerable changes that are heavily influenced by the field width (Ugurlu and Temelli, 2020). A large volume complex-shaped target encircled by bone marrow volume presents this issue. Therefore, we recommended using a single isocentric combination of two Arc 90-degree collimators as well as two Arc 20-degree and 340-degree collimators with a limited field width in order to irradiate a target that was significantly larger. The 90-degree collimator, which covers nearly half the field and has a field overlap of two Arcs, helps to minimize the MLC travelling distance, which enables greater modulation and the leaf’s ability to move all around the target, this provides more expected dose distribution than is visible in the view. The MLC side jaws limited field width size also adds more power to the dose modulation.



Numerous studies show that VMAT helps to save bone marrow, minimizing hematological toxicity (HT) (Deng et al., 2017; Jayapalan et al., 2017; chigurupalli et al., 2019). In our study, we compared C-2Arc VMAT, C-4Arc VMAT, and M-4Arc VMAT to spare bone marrow in patients undergoing a radiotherapy for advanced cervix cancer. Multiple arc VMAT is recommended for better target coverage (Guckenberger et al., 2009). All our plans obtained clinically acceptable PTV doses, and we did not find any statistically significant differences. It was found that for OAR doses, the M-4Arc VMAT plan approach reduced the dose significantly, notably for bone marrow, which is a surrogate for the target volume. On the contrary, this planning method had significant dose reduction.

VMAT plans that use small field size or half-field method have a increased MU, which means more radiation beam ON time due to the aperture size reduction (Ugurlu and Temelli 2020). MU results in a rise in scatter, which may raise the risk of secondary cancer in healthy tissue (Hall and Wu, 2003; Hall,2006). In order to irradiate a larger target with VMAT, it is necessary to make use of bigger fields. This is a prerequisite for the process. When this is done, there is a chance that healthy normal tissue and OARs will be subjected to direct irradiation. Due to the physical limitations of the present treatment machines, the MLC leaves cannot adequately modulate bigger fields (Ugurlu and Temelli, 2020). Consequently, this has been addressed in our study, 90 degree collimator rotation and a roughly half-field plan combination provides additional openness to cover the Y-jaw direction without exceeding the MLC limits. The two asymmetrically oriented opening arcs filled the whole PTV at the same moment, resulting in a significant MU reduction. For the bone marrow dose, this method has shown a statistically significant dose reduction.

Traditional full-field methods are not able to provide clinically acceptable plans for large targets compared to small targets (Jang et al., 2021). However, contemporary pelvic irradiation for gynecological cancers and late-stage prostate necessitates extensive bone marrow-sparing fields. Gynecological malignancies show that the combination of the small field and 90-degree collimator rotated half field method can produce mono-isocentric and effective treatment plans with the VMAT technique. Traditional full-field with jaw-tracking is an alternative for larger targets. Since these licenses are pricey, most clinics don't offer them.

Our small field optimized collimator approach has been enhancing the quality of VMAT plans for bigger targets due to the effect of field width. Clearly, in the near future, this study could establish the M-4Arc VMAT standards for bone marrow sparing gynecological tumors. The radiation dose received by the pelvic Bone Marrow and its related VMAT technical merit of bone marrow sparing can be analyzed using advanced quantitative image analysis.

### Author Contributions Statement

All authors contributed efficiently to the research and approved the manuscript.

### Acknowledgements

None.

### References

- Arbyn M, Weiderpass E, Bruni L, et al (2020). Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health*, **8**, 191-203.
- Buckey C, Swanson G, Stathakis S, Papanikolaou N. (2010). Dosimetric comparison between 3D conformal and intensity-modulated radiation therapy for prostate cancer. *J Radiotherapy Pract*, **9**, 77-5.
- ChigurupalliK, VashisthaA, Patel D, et al (2019). Retrospective Dosimetric analysis of Bone marrow sparing vs non bone marrow sparing Image Guided Volumetric Modulated Arc Therapy in intact Carcinoma Cervix patients. *J Curr Med Res Opinion*, **2**, 288-2.
- Deng X, Han C, Chen S, et al (2017). Dosimetric benefits of intensity-modulated radiotherapy and volumetric-modulated arc therapy in the treatment of postoperative cervical cancer patients. *J Appl Clin Med Phys*, **18**, 25-1.
- Guckenberger M, Richter A, Krieger T, et al (2009). Is a single arc sufficient in volumetric-modulated arc therapy (VMAT) for complex-shaped target volumes?. *Radiother Oncol*, **93**, 259-5
- Green JA, Kirwan JM, Tierney JF, et al (2001). Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. *Lancet*, **358**, 781-6.
- Hall EJ, WuCS (2003). Radiation-induced second cancers: the impact of 3D-CRT and IMRT. *Int J Radiat Oncol Biol Phys*, **56**, 83-8.
- Hall EJ (2006). Intensity-modulated radiation therapy, protons, and the risk of second cancers. *Int J Radiat Oncol Biol Phys*, **65**, 1-7.
- Hui B, Zhang Y, Shi F, et al (2014). Association between bone marrow dosimetric parameters and acute hematologic toxicity in cervical cancer patients undergoing concurrent chemoradiotherapy: comparison of three-dimensional conformal radiotherapy and intensity-modulated radiation therapy. *Int J Gynecol Cancer*, **24**, 1648-2.
- Jayapalan K, Shetty J, Rao S, Hegde S, Shambhavi (2017). Dosimetric Advantage of VMAT Technique in Bone Marrow Sparing Than IMRT in Treatment of Cervical Cancer. *Int J Health Sci Res*, **7**.
- Jang H, Park J, Artz M, et al (2021). Effective Organs-at-Risk Dose Sparing in Volumetric Modulated Arc Therapy Using a Half-Beam Technique in Whole Pelvic Irradiation. *Front Oncol*, **11**.
- Lai Y, Chen Y, Wu S, et al (2016). Modified Volumetric Modulated Arc Therapy in Left Sided Breast Cancer After Radical Mastectomy With Flattening Filter Free Versus Flattened Beams. *Medicine (Baltimore)*, **95**, e3295.
- Lim K, Small W Jr, Portelance L, et al (2011). Gyn IMRT Consortium. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy for the definitive treatment of cervix cancer. *Int J Radiat Oncol Biol Phys*, **79**, 348-5.
- Lukka H, Hirte H, Fyles A, et al (2002). Cancer Care Ontario Practice Guidelines Initiative Gynecology Disease Site Group. Concurrent cisplatin-based chemotherapy plus radiotherapy for cervical cancer--a meta-analysis. *Clin Oncol (R Coll Radiol)*, **14**, 203-2.
- Lukovic J, Patil N, D-souza D, et al (2016). Intensity-Modulated Radiation Therapy Versus 3D Conformal Radiotherapy for Postoperative Gynecologic Cancer: Are They Covering the

- Same Planning Target Volume?. *Cureus*, **8**, e465.
- Mahantshetty U, Krishnatry R, Chaudhari S, et al (2012). Comparison of 2 contouring methods of bone marrow on CT and correlation with hematological toxicities in non-bone marrow-sparing pelvic intensity-modulated radiotherapy with concurrent cisplatin for cervical cancer. *Int J Gynecol Cancer*, **22**, 1427-34.
- Mell LK, Kochanski JD, Roeske JC, et al (2006). Dosimetric predictors of acute hematologic toxicity in cervical cancer patients treated with concurrent cisplatin and intensity-modulated pelvic radiotherapy. *Int J Radiat Oncol Biol Phys*, **66**, 1356-65.
- Mell LK, Tiriyaki H, Ahn KH, et al (2008). Dosimetric comparison of bone marrow-sparing intensity-modulated radiotherapy versus conventional techniques for treatment of cervical cancer. *Int J Radiat Oncol Biol Phys*, **71**, 1504-10.
- Morris M, Eifel PJ, Lu J, et al (1999). Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med*, **340**, 1137-43.
- Otto K, (2008). Volumetric modulated arc therapy: IMRT in a single gantry arc. *Med Phys*, **35**, 310-7.
- Peters WA, Liu PY, Barrett RJ, et al (2000). Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *J Clin Oncol*, **18**, 1606-13.
- Ramiz A H, Afifi S, Almousa A, et al (2020). Volumetric-modulated arc therapy versus intensity-modulated radiotherapy for localized prostate cancer: a dosimetric comparative analysis of moderate hypofractionated radiation. *Oncol Radiotherapy*, **14**.
- Toledano I, Graff P, Serre A, et al (2012). Intensity-modulated radiotherapy in head and neck cancer: results of the prospective study GORTEC 2004-03. *Radiother Oncol*, **103**, 57-2.
- Ugurlu BT, Temelli O (2020). The impact of the field width on VMAT plan quality and the assessment of half field method. *J Appl Clin Med Phys*, **21**, 115-2.
- Vaupel P, Thews O, Hoeckel M (2001). Treatment resistance of solid tumors: role of hypoxia and anemia. *Med Oncol*, **18**, 243-9.
- Zelevsky MJ, Kollmeier M, Cox B, et al (2012). Improved clinical outcomes with high-dose image guided radiotherapy compared with non-IGRT for the treatment of clinically localized prostate cancer. *Int J Radiat Oncol Biol Phys*, **84**, 125-9.



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.