Volume 23, No 4 | International Journal of Radiation Research, October 2025

Significant decrease in the radiation low-dose delivered to normal tissue in a novel cervical cancer VMAT plan using sub-arc collimator angle optimization

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► ***Original article***

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Received: May 2024
Final revised: October 2024
Accepted: January 2025

Int. J. Radiat. Res., October 2025; 23(4): 1079-1084

DOI: 10.61186/ijrr.23.4.35

Keywords: *Radiotherapy, cervical cancer, volumetric modulated arc therapy, collimator angle optimization, normal tissue protection.*

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ABSTRACT

Background: Traditionally, volumetric modulated arc therapy (VMAT) plans have depended on a predefined gantry range and a fixed collimator angle. Herein, we develop a novel sub-arc collimator angle optimization (SACAO) method for VMAT in cervical cancer. ***Materials and Methods:*** Twenty patients with cervical cancer were retrieved in the retrospective planning study. Two plans for traditional optimization were generated using dual arcs with two static collimator angles of 0˚and 45˚(named $VMAT_{\_0}$ and $VMAT_{\_45}$, respectively). A new plan was also developed using SACAO (named $VMAT_{\_SACAO}$). The dynamic gantry range segmentation of the full arc was calculated according to the continuity of the best conformity index (CI). The dose-volumetric parameters, average x-jaw size, and total monitor units (MUs) were compared. ***Results:*** The HI (uniformity index) and CI (conformity index) were improved in $VMAT_{\_SACAO}$ compared to $VMAT_{\_0}$ and $VMAT_{\_45}$. The average x-jaw size of $VMAT_{\_SACAO}$ was lower than $VMAT_{\_0}$ and $VMAT_{\_45}$ (18.7 ± 0.9 cm^2, 20.7 ± 1.1 cm^2, and 20.2 ± 1.0 cm^2), as well as the total MUs (402 ± 19.0, 450 ± 18.8, and 432 ± 18.5). The average low-dose delivered to normal tissue was lowest in VMAT_SACAO compared to $VMAT_{\_0}$ and $VMAT_{\_45}$ (15.8 ± 0.4 Gy, 18.6 ± 0.3 Gy, and 17.0 ± 0.4 Gy). ***Conclusion:*** Compared to the two VMAT plans, the $VMAT_{\_SACAO}$ improved the HI and CI, decreased the low-dose delivered to normal tissue, the V50, V45, and V15 of the small bowel, and the total MUs when applied in treating cervical cancer patients.

INTRODUCTION

Volumetric-modulated arc therapy (VMAT) has emerged as a crucial method for treating cervical cancer, thanks to its capability to deliver precise doses to the targeted area while protecting adjacent healthy tissues [1, 2]. By employing a range of variables, such as rotation of the gantry and couch, gantry rotation speed, and the movement of the multileaf collimator (MLC)-VMAT optimizes radiation delivery, enhancing treatment efficiency and quality [3-6]. A critical aspect of this optimization is collimator rotation, which allows for the adaptation of the MLC to create a tailored dose distribution that minimizes exposure to organs at risk (OAR) [7-10].

The selection of optimal collimator angle in VMAT planning remains a subject of debate [11-14]. Studies by Tsurumaki [13] and Treutwein [14] have indicated that a 45-degree collimator angle is often effective for treating prostate cancer and be suitable for most cases. Additionally, Ahn [9] and Knill [15] demonstrated that optimizing the collimator angle in sections can improve both the efficiency of radiation delivery and the quality of dosimetric results. Research into dynamic optimization of collimator angles and collimator trajectory, tailored to the specific anatomy of the target, has also been extensively explored, revealing potential improvements in dose distribution and treatment efficiency [16, 17]. Moreover, the integration of advanced optimization strategies, such as three-dimensional integrated optimization of dynamic axes and dynamic rotation of the treatment couch in VMAT (DCR-VMAT), has been investigated in previous studies [18, 19]. These methods highlight the potential for further refining treatment delivery by dynamically adjusting couch and MLC angles.

In cervical cancer treatments, the challenge of minimizing low-dose radiation exposure to normal tissues is particularly pertinent, as surrounding

[DOI: 10.61186/ijrr.23.4.35]

organs in the pelvic cavity are often vulnerable to radiation-induced toxicity. This low-dose exposure, often known as the "low-dose bath," can increase the risk of complications and long-term side effects [20, 21]. Therefore, effective strategies to reduce this low-dose deposition are essential for improving patient safety and treatment efficacy.

To address this issue, we introduce a novel sub-arc collimator angle optimization (SACAO) method tailored specifically for cervical cancer in VMAT planning. This technique involves dividing the treatment arc into sub-arcs and calculating variable collimator angles based on optimal conformity indices derived from the perspective of the beam's-eye view (BEV). By concentrating on the unique anatomical characteristics of each patient, our method seeks to substantially reduce the low-dose radiation exposure to surrounding healthy tissues while maintaining effective target coverage. We will evaluate and compare dose-volume histogram (DVH) parameters, low-dose delivered to normal tissue, average x-jaw size, and monitor units (MUs) across different VMAT plans, ultimately assessing the potential of SACAO to enhance treatment outcomes in cervical cancer patients.

Notably, the SACAO method has previously been applied in the context of multiple brain targets and irregularly shaped targets, demonstrating its efficacy in protecting normal tissues surrounding the target areas [9, 22, 23]. This study represents the first application of the SACAO method in pelvic radiation therapy, with the length of the sub-arcs being patient-specific, thereby offering further potential to reduce low-dose exposure to tissues outside the target area.

MATERIALS AND METHODS

Patient selection

Twenty cervical cancer patients were retrospectively selected. The research received approval from the Ethics Committee of Zhongnan Hospital of Wuhan University (Approval Number: 20230612K, dated 2023.06.30). All patients received a prescribed dose of 50.4 Gy delivered in 28 fractions or 45 Gy administered over 25 fractions. The PTV volumes ranged from 880.6 cc to 1237.7 cc, with an average volume of 1099.3 cc. Detailed information is provided in table 1.

Table 1. Patient characteristics.

Patient number	Age	FIGO stage	Target Volume (cm^3)	Prescription (Gy/Fraction)	Patient number	Age	FIGO stage	Target Volume (cm^3)	Prescription (Gy/Fraction)
1	56	IIb	1013.9	50.4/28	11	56	IIa	880.6	45/25
2	62	IIa	1175.1	50.4/28	12	59	IIIb	1226.1	50.4/28
3	58	IIb	1215.4	45/25	13	61	IIIc	1137.7	50.4/28
4	69	IIc	1158.2	50.4/28	14	64	IIc	999.5	45/25
5	72	IIa	1094.1	50.4/28	15	50	IIb	1159.3	45/25
6	69	IVa	1137.4	50.4/28	16	39	IIc	1146.6	45/25
7	45	IIIc	957.5	50.4/28	17	70	IIIa	1029.4	50.4/28
8	70	IIa	1222.3	45/25	18	73	IIb	1091.6	45/25
9	66	IIb	935.2	50.4/28	19	62	IIa	1146.1	45/25
10	63	IVa	1226.1	50.4/28	20	60	IVa	1237.7	50.4/28

FIGO stage: International Federation of Gynecology and Obstetrics stage.

SACAO method

The SACAO method was developed utilizing a treatment planning software (Eclipse™ 13.5, Varian Medical Systems, Palo Alto, CA) and linear accelerator (Varian 23 IX, Varian Medical Systems, Palo Alto, CA) equipped with MLC. Three steps were followed to calculate the adaptive gantry range and variable collimator angle:

Step 1: CT images and structures were exported in Digital Imaging and Communications in Medicine (DICOM) format, and the targets were reconstructed by MATLAB (R2017b, Mathworks, Inc., Natick, MA) with our designed code. A total of 360 frames of target projection images were generated for each gantry angle.

Step 2: MLC shapes for each projection were optimized based on the MLC conformity index (MCI) following the equation (1), defined as the ratio of the BEV projection area to the MLC area. The optimal collimator angle was selected for each projection to maximize tissue sparing.

Step 3: A curve was drawn with the gantry angle as the X-axis and the ideal collimator angle corresponding to each gantry position as the Y-axis. Based on the continuity of the collimator angle, the complete arc was segmented into several sub-arcs. If a sub-arc was shorter than 30°, it was merged with an adjacent sub-arc. The collimator angle assigned to each sub-arc was then selected according to the maximum MCI value from the integrated projections.

$$MCI = \frac{A_{TP}}{A_{MLC}} \quad (1)$$

Where; A_{TP} represents the BEV projection area of the PTV for each projection, and A_{MLC} denotes the area defined by the MLC.

VMAT planning

For each patient, three VMAT plans were created: $VMAT_{\_SACAO}$, $VMAT_{\_0}$, and $VMAT_{\_45}$. In $VMAT_{\_SACAO}$, sub-arcs were designed according to the SACAO methodology, while $VMAT_{\_0}$ and $VMAT_{\_45}$ used fixed

[DOI: 10.61186/ijrr.23.4.35]

collimator angles of 0° and 45°, respectively. All plans were computed using the anisotropic analytic algorithm (AAA), with a 2.5 mm dose grid. Each plan was normalized for 95% coverage of the PTV.

Plan comparison

Plan comparison included dose-volume histogram (DVH) analysis for the PTV and organs at risk (OARs). Parameters such as D95, D98, D50, D2, HI, and CI for PTV were evaluated, along with normal tissue metrics (Dmax, Dmean). Additional analyses were conducted for the small intestine, rectum, bladder, femoral heads, and bone marrow, as well as average low-dose exposure to normal tissues. MUs and x-jaw sizes were also analyzed.

Statistical analysis

Data were evaluated using SPSS version 22.0. A two-sample paired t-test and a three-sample ANOVA were utilized. Statistical significance was established at $P < 0.05$.

RESULTS

Plan parameters of the 20 patients

The sub-arc number, sub-arc length, and the collimator angle associated with each sub-arc for the 20 patients with SACAO are shown in table 2. There were 6 sub-arcs for 14 patients and 5 sub-arcs for 6 patients; the average number of sub-arcs was 5.7. The longest sub-arc length was 131° and the shortest was 30°, with an average value of 63.16°. The average x-jaw size of $VMAT_{SACAO}$ was smaller than that for either $VMAT_{0}$ or $VMAT_{45}$ (18.7 ± 0.9 cm^2, 20.7 ± 1.1 cm^2, and 20.2 ± 1.0 cm^2, respectively).

Table 2. The averaged x-jaw size of $VMAT_{SACAO}$, $VMAT_{0}$ and $VMAT_{45}$.

Patient number	Arc length (°)/ Collimator angle (°)						x-jaw size (mean ± SD, cm^2)		
	Arc1	Arc2	Arc3	Arc4	Arc5	Arc6	$VMAT_{SACAO}$	$VMAT_{0}$	$VMAT_{45}$
1	82/25.5	31/345.4	72/24.2	54/351.3	31/33.4	90/352.7	18.2±0.7	19.1±1.2	19.8±1.4
2	76/23.5	46/340.2	62/21.2	60/348.0	40/28.0	76/346.5	18.2±0.5	21.0±1.3	19.6±1.1
3	72/30.2	45/335.2	70/18.5	66/350.0	36/31.9	71/350.3	19.8±1.0	22.3±1.5	22.3±1.3
4	80/25.0	30/340.5	74/16.8	62/348.2	32/30.8	82/348.2	18.2±0.8	19.8±1.2	19.0±1.2
5	78/20.1	30/315.8	80/20.8	70/342.6	35/21.4	67/328.2	17.4±0.6	20.0±0.9	19.1±0.8
6	86/18.2	30/340.2	76/22.0	68/345.4	36/24.5	64/332.2	19.4±0.7	21.1±1.0	20.8±1.0
7	96/16.5	30/330.2	60/35.4	78/338.5	30/19.4	66/340.4	18.6±0.7	21.0±1.1	20.6±0.8
8	95/20.5	36/342.8	78/324.4	62/340.1	30/20.3	59/334.8	19.3±0.8	22.3±1.9	21.2±1.7
9	68/24.4	30/326.1	87/30.5	74/345.2	30/18.5	71/342.4	17.8±0.5	19.3±1.2	19.4±0.9
10	90/20.1	34/345.2	76/325.2	68/350.4	34/25.2	58/335.0	18.3±1.2	20.0±1.5	19.7±1.3
11	92/21.8	30/337.6	78/20.1	88/348.2	38/24.2	34/340.2	17.2±0.8	19.5±0.8	19.2±0.8
12	96/28.4	35/334.2	70/318.5	92/338.2	32/30.5	35/332.5	18.9±1.0	20.4±1.7	19.8±1.7
13	83/32.1	30/346.2	80/320.8	45/346.5	36/25.0	86/330.2	20.8±1.5	23.3±2.2	22.7±2.0
14	86/35.0	32/350.0	73/25.2	65/350.0	35/26.2	69/325.6	18.2±0.7	20.8±0.9	19.5±0.8
15	124/34.6	70/348.2	68/323.8	30/347.6	68/28.3		17.9±0.9	20.2±1.5	20.1±1.5
16	118/26.7	82/342.4	78/26.2	36/345.2	46/26.1		19.4±0.8	21.1±1.8	20.1±1.3
17	131/25.6	75/340.2	72/316.5	30/342.8	52/18.4		19.6±1.1	21.2±1.2	20.6±1.3
18	125/24.8	76/336.8	80/24.5	36/339.2	43/16.5		19.7±1.2	22.5±1.6	21.2±0.9
19	84/23.2	30/330.2	78/30.2	64/341.7	104/17.6		17.9±0.7	19.3±1.1	19.3±0.8
20	74/31.8	30/342.4	67/28.2	72/352.2	117/18.7		18.3±0.6	20.2±1.2	20.0±1.2

x-jaw: The tungsten collimator in the x-axis direction of the linear accelerator. VMAT_SACAO: Volumetric Modulated Arc Therapy with Sub-Arc Collimator Angle Optimization, VMAT_0: VMAT with a collimator angle of 0°, VMAT_45: VMAT with a collimator angle of 45°.

Dosimetric parameters

The 2D dose distribution of $VMAT_{0}$, $VMAT_{45}$, and $VMAT_{SACAO}$ is shown in figure 1. The results of the DVH parameters, MUs, and average x-jaw size are shown in table 3. There were no significant differences in the D_2, D_{50}, D_{98}, and D_{95} values of the PTVs among the three groups ($P > 0.05$). A notable difference was observed in the HI and CI index values between the three plans, where those of $VMAT_{SACAO}$ were superior, followed by $VMAT_{45}$, and then $VMAT_{0}$ (0.05 ± 0.08, 0.85 ± 0.03; 0.06 ± 0.01, 0.84 ± 0.02; 0.06 ± 0.03, 0.81 ± 0.03, respectively). $VMAT_{SACAO}$ reduced the maximum dose for the small intestine significantly compared to $VMAT_{0}$. No statistically significant differences were found in the mean dose, V50, V45, and V15 values of the small intestine, the max dose and average dose received by the rectum, V30 for the left and right femoral heads, V50 of the bladder, or V30 of the bone marrow among the three plans. To minimize the low radiation dose received by surrounding healthy tissue, $VMAT_{SACAO}$ proved to be superior, followed by $VMAT_{45}$, and then $VMAT_{0}$ (15.8 ± 0.4 Gy, 17.0 ± 0.4 Gy, 18.6 ± 0.3 Gy, respectively). $VMAT_{SACAO}$ could significantly reduce the MUs compared to $VMAT_{45}$ and $VMAT_{0}$ (402 ± 19.0 MUs, 432 ± 18.5 MUs, and 450 ± 18.8 MUs, respectively).

[DOI: 10.61186/ijrr.23.4.35]

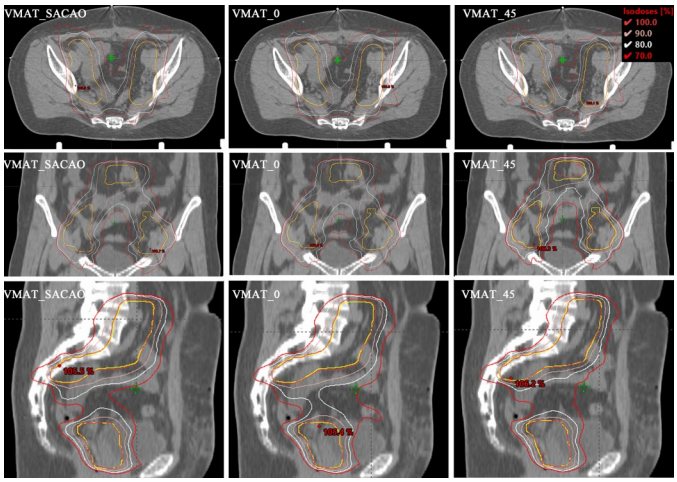

Figure 1. Two-dimensional dose distribution maps in the axial, coronal, and sagittal planes for the three treatment plans: Volumetric Modulated Arc Therapy with Sub-Arc Collimator Angle Optimization ($VMAT_{SACAO}$), VMAT with a collimator angle of 0° ($VMAT_{0}$), and VMAT with a collimator angle of 45° ($VMAT_{45}$). The dose distributions are presented to illustrate the differences in target coverage and normal tissue sparing among the plans.

Table 3. The details and statistical analysis results for dose parameters, MUs and averaged x-jaw size.

		VMAT_SACAO	$VMAT_{0}$	$VMAT_{45}$	variance	P value		
		mean±SD	mean±SD	mean±SD		VMAT_SACAO vs VMAT_0	VMAT_SACAO vs VMAT_45	VMAT_0 vs VMAT_45
PTV50.4	D50(Gy)	53.0±0.6	53.2±0.6	52.8±0.5	0.288	0.501	0.186	0.263
	D2(Gy)	54.7±0.6	54.7±0.7	54.5±0.7	0.168	0.392	0.162	0.195
	D98(Gy)	50.0±0.5	50.1±0.7	50.0±0.3	0.400	0.324	0.819	0.294
	D95(Gy)	50.6±0.3	50.7±0.4	50.4±0.1	0.165	0.335	0.246	0.142
	HI	0.05±0.08	0.06±0.01	0.06±0.01	< 0.001	<0.001	<0.001	0.001
	CI	0.86±0.03	0.82±0.03	0.84±0.02	< 0.001	<0.001	0.001	<0.001
Small bowel	Dmax(Gy)	49.5±0.3	50.5±0.3	49.9±0.3	0.023	0.014	0.343	0.005
	Dmean(Gy)	26.5±0.8	26.5±0.8	26.5±0.8	0.221	0.059	0.193	1.000
	V50(cm3)	46.7±29.3	60.0±29.4	53.4±27.6	0.031	0.021	0.038	0.061
	V45(cm3)	81.0±39.0	103.9±45.6	95.7±38.3	0.036	0.027	0.035	0.054
	V15(cm3)	320.9±150.7	440.4±126.7	427.5±148.4	0.028	0.019	0.028	0.062
Rectum	Dmax(Gy)	48.1±0.4	48.4±0.4	48.1±0.4	0.187	0.187	0.758	0.151
	Dmean(Gy)	38.0±0.3	39.5±0.3	37.6±0.3	0.131	0.107	0.621	0.073
Left femoral head	V30(%)	16.5±2.9	18.7±3.7	16.4±3.4	0.099	0.082	0.934	0.095
Right femoral head	V30(%)	16.8±4.8	16.1±6.0	18.7±3.1	0.377	0.712	0.249	0.197
Bladder	V50(%)	39.9±17.0	43.1±13.1	37.1±16.2	0.126	0.367	0.079	0.091
Bone marrow	V30(%)	55.0±6.5	53.3±6.2	54.8±8.1	0.915	0.727	0.793	0.820
MUs		402±19.0	450±18.8	432±18.5	0.001	0.007	0.010	0.047
Low-dose to normal tissue	(Gy)	15.8±0.4	18.6±0.3	17.0±0.3	0.037	0.049	0.048	0.212
Averaged x-jaw size	(cm2)	18.7±0.9	20.7±1.1	20.2±1.0	<0.001	<0.001	<0.001	<0.001

MU: monitor units, x-jaw: The tungsten collimator in the x-axis direction of the linear accelerator, $VMAT_{SACAO}$: Volumetric Modulated Arc Therapy with Sub-Arc Collimator Angle Optimization, $VMAT_{0}$: VMAT with a collimator angle of 0°, VMAT_45: VMAT with a collimator angle of 45°.

DISCUSSION

In this research, we suggested employing the SACAO algorithm for optimizing collimator angles in VMAT plans for cervical cancer. Our approach involves dynamically determining the quantity of sub-arcs and their respective collimator angles, which are specifically adapted to the unique anatomical characteristics of each patient's lesions. The dosimetric analysis conducted on a cohort of 20 patients demonstrated that the SACAO algorithm significantly reduced the low-dose exposure to normal tissue and enhances target conformity and spares OAR more effectively than conventional VMAT techniques with a fixed collimator of 0° and 45°.

The challenge of minimizing low-dose radiation exposure to normal tissues remains a significant concern in optimizing VMAT compared to IMRT. This exposure is primarily caused by dynamic gantry rotation around the patient, continuous beam modulation, and insufficient optimization of treatment parameters [24, 25]. Recent studies have suggested that optimizing collimator parameters can mitigate this issue and enhance plan quality. Techniques such as dynamic collimator angle optimization, collimator trajectory optimization, sub-arc collimator angle optimization, and dual collimator systems have shown promise in achieving this goal [16-19, 26]. For instance, Zhang [16] introduced a method for optimizing collimator trajectories based on principal component analysis (PCA) for spinal cord treatments, providing greater flexibility that improves target coverage while protecting the spinal cord in paraspinal SBRT plans. Similarly, MacDonald [18] proposed strategies that utilize automated fixed couch trajectories alongside dynamic collimator

[DOI: 10.61186/ijrr.23.4.35]

movements to minimize radiation exposure to non-target tissues. Murtaza [19] and colleagues emphasized that dynamically adjusting the collimator during treatment can yield better dose distributions in the pelvic region by aligning the MLC with the trajectory of the prostate. Additionally, Bijina *et al*. [26] found that a double collimator system significantly reduces the mean doses received by OARs compared to a single collimator system. However, despite these advancements, many of these techniques require sophisticated equipment that may not be accessible to all hospitals. In contrast, our SACAO method is compatible with conventional linear accelerators, making it more accessible to a broader range of institutions.

In recent years, the SACAO method, which provides an enhanced degree of flexibility in collimator angle for each sub-arc, has been applied to multiple brain targets and irregularly shaped lesions, demonstrating its efficacy in protecting the surrounding normal tissues [9, 10, 22, 23]. Our findings align with previous studies, such as those by Ahn *et al*. [9] and Kim *et al*. [10], which emphasized the importance of selecting optimal collimator angles and dividing a complete arc into multiple predefined uniform sub-arcs for irregularly shaped targets and multiple brain targets. They observed that VMAT plans utilizing shorter angular segments may provide clinical advantages for treating multiple brain targets and irregularly shaped lesions. Furthermore, Shen *et al*. [22] and Huang *et al.* [23] suggested that if the segmentation of the sub-arc could be individually determined instead of using a basic uniform division, it would enhance the quality of the plan even further. They discovered that the SACAO method may improve the conformity index, homogeneity index, and gradient index of the tumor targets while protecting surrounding healthy tissues during the treatment of several brain metastases using stereotactic radiosurgery (SRS). Additionally, SACAO provides the opportunity to enhance the effectiveness of treatment by optimizing the area of exposure and MUs. In our study, based on the SACAO method proposed by Shen *et al.* [22], we applied it to VMAT plan optimization for cervical cancer and found that collimator-optimized plans resulted in reduced complexity of MLC movement, smaller x-jaw sizes, fewer MUs, and reduce the exposure to lower doses of radiation in surrounding healthy tissues, aligning with findings from earlier research.

Although the SACAO plan features a reduced x-jaw size and shorter radiation beam delivery duration; however, the average overall treatment time for VMAT_SACAO increased by about 1.1 times compared to the traditional two full arcs plan for each patient, primarily due to the waiting time for collimator angle preparation between sub-arcs, which could decrease delivery efficiency. The overall treatment time has not been mentioned or recorded in other studies.

Nevertheless, this study has certain limitations. Firstly, our comparative analysis of treatment plans was conducted in a theoretical context and not on actual accelerators, necessitating further empirical validation. Secondly, while increasing the number of sub-arcs can improve dosimetric outcomes, it may also prolong treatment times, potentially affecting patient throughput. Fortunately, the reduction in MUs associated with the SACAO method could mitigate this concern to some extent, and future studies should quantify total treatment times more accurately.

CONCLUSION

In this study, the 360-degree full arc was divided into several sub-arcs using the SACAO method. The results show that when compared to traditional dual-full arc plans employing fixed collimator angles, the novel VMAT_SACAO plan proposed herein can significantly reduce both the quantity of MUs and the radiation exposure to normal tissue as well as improve the dosimetric indexes of HI and CI in the target area.

ACKNOWLEDGEMENTS: The authors would like to thank the Department of Radiation and Medical Oncology at Zhongnan Hospital of Wuhan University, as well as all colleagues for their help and guidance.

FUNDING: This work was partially supported by Natural Science Foundation of Hubei province (grant numbers 2018CFB561), and Zhongnan Hospital of Wuhan University Science, Technology, and Innovation Seed Fund (grant numbers ZNPY2016043), and Science and technology innovation cultivation fund of Zhongnan Hospital (grant numbers CXPY2022063).

CONFLICT OF INTEREST STATEMENT: Declared none.

ETHICAL CONSIDERATIONS: The study was approved by the Ethics Committee of Zhongnan Hospital of Wuhan University (Approval Number: 20230612K, dated 2023.06.30).

AUTHOR CONTRIBUTIONS: C.C. and W.X. contributed to the conceptualization and design of the study, conducted data analysis, and drafted the manuscript. J.S., C.X., Y.Z., X.W., J.Z., D.J. were responsible for data collection and interpretation, as well as revising the manuscript for important intellectual content. Y.Z., H.L. and H.Y. provided critical feedback on the study design and methodology and helped with the final editing of the manuscript. All authors read and approved the final manuscript.

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[DOI: 10.61186/ijrr.23.4.35]

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[DOI: 10.61186/ijrr.23.4.35]