

## I. Biological Sciences

### Article. 2

# Comparative Analysis of Full Arc and Partial Arc VMAT Techniques for Prostate Cancer SBRT: Evaluating Plan Quality and Treatment Delivery Parameters

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#### **Abstract:**

This study presents a comprehensive investigation of the radiotherapy plan quality and treatment delivery parameters of two distinct volumetric-modulated arc therapy (VMAT) approaches, full arc and partial arc, for prostate cancer stereotactic body radiation therapy (SBRT). Fifteen retrospective prostate cancer patients were included in this study. Following the Radiation Therapy Oncology Group (RTOG) 0938 protocol guidelines, thirty treatment plans were generated utilizing two full arcs and two partial arcs VMAT. Dosimetric parameters were evaluated, such as target coverage, dose conformity, and organs at risk (OARs) doses. Also, the treatment delivery parameters, including monitor units (MU), modulation factor (MF), and beam on time (BOT) were analyzed to assess the efficiency of each approach. The present study's findings revealed that both techniques achieved the constraints outlined in RTOG 0938. However, a statistically significant difference was observed between the two approaches. The full arc plans demonstrated superior target coverage, conformality, steeper dose gradient, and lower dose to femoral heads compared to the partial arc plans. On the other hand, the partial arc plans exhibited better sparing of the bladder and rectum. Also, the partial arc plans required fewer MU, resulting in a faster treatment time. Ultimately, the study concluded that the partial arc VMAT approach, utilizing a 10 MV flattening filter-free (FFF) beam, is the most effective technique for prostate SBRT, as it significantly enhances the sparing of organs at risk (OARs) and improves treatment delivery parameters.

**Keywords:** Prostate SBRT; Dosimetric comparison; VMAT; Partial arc; Full arc

## 1 Introduction

Prostate cancer is the most prevalent malignancy among males and a significant public health concern worldwide. According to the American Cancer Society, there were an estimated 299,010 new cases of prostate cancer diagnosed in the United States in 2024. It is also the second leading cause of cancer-related deaths in males, following lung cancer, accounting for approximately 11% of estimated deaths (Siegel et al. 2024). While there are several treatment regimens for prostate cancer, radiation therapy is often utilized as a primary treatment, either through external beam radiotherapy (EBRT) or brachytherapy. Radiation therapy is particularly preferred when surgery may not be suitable or desired by the patient. It involves using high-energy radiation beams to destroy cancer cells while minimizing damage to surrounding healthy tissues. Another advantage of radiotherapy that draws patients is that it can be delivered as an outpatient procedure, allowing patients to continue their regular routines and quality of life during treatment. Additionally, an advanced method called stereotactic body radiation therapy (SBRT) offers another advantage for prostate cancer patients by reducing the number of treatment sessions from approximately 38 in conventional radiotherapy to about five sessions with a high dose per fraction (Haque et al. 2017; Alongi et al. 2013; Poon et al. 2021; Jackson et al. 2019).

SBRT is a radiation method that administers a concentrated dose of radiation to a specific area other than the brain using only a few treatment sessions. This approach achieves a high biologically effective dose, effectively targeting the intended area while minimizing radiation exposure to the surrounding healthy tissues due to its rapid dose fall-off (Benedict et al. 2010). For patients with low to intermediate-risk localized prostate cancer, SBRT has become more popular as a tolerable, safe, and effective therapeutic option. SBRT can be delivered through different machines such as CyberKnife (CK), Helical Tomotherapy (HT), or linear accelerators (LINACs). However, the linear accelerator is the most common EBRT machine due to its versatility in delivering conventional and hypofractionation (SBRT) treatment using different techniques. The volumetric modulated arc therapy (VMAT) is one of the LINAC techniques, and it is widely employed in SBRT due to its ability to achieve the treatment objectives of SBRT with high precision and accuracy (Scobioala et al. 2019; Seppälä et al. 2017; Serra et al. 2022; Bijina et al. 2020).

VMAT is an advanced radiation therapy technique that utilizes a linear accelerator equipped with a multi-leaf collimator (MLC) and a rotating gantry to deliver radiation precisely and efficiently. It represents an innovative form of intensity-modulated radiation therapy (IMRT) optimization, enabling the delivery of radiation doses via dynamic modulated arcs. With VMAT, the radiation beam continuously revolves around the patient, adapting to the tumor's contours through MLC shaping. This dynamic delivery allows for modulation of dose intensity and

adjustment of the beam's shape during administration, enabling effective tumor targeting while sparing surrounding healthy tissues (Otto 2008). VMAT also offers the advantage of shorter treatment times compared to other techniques, which is particularly desirable in the case of SBRT (Weyh et al. 2013). Within VMAT, two commonly used methods are full arc and partial arc approaches. The full arc VMAT involves a continuous rotation of the treatment machine around the patient to deliver radiation from all angles. In contrast, the partial arc VMAT limits the gantry rotation to a specific arc range.

Several studies have compared IMRT to VMAT for prostate cancer. However, according to our knowledge, limited research remains focused on determining the optimal beam arrangement specifically for prostate irradiation using VMAT (Bartlett et al. 2023; Elith et al. 2014; Rana and Cheng 2013; Sasaki et al. 2020). This study aims to assess and compare the plan quality and treatment delivery parameters of prostate SBRT in two VMAT approaches: one utilizing two full arcs and the other employing two partial arcs. The study provides valuable information and insights regarding selecting the most suitable planning approach for prostate SBRT by evaluating and comparing these parameters.

## 2 Materials and methods

### 2.1 Treatment design

This study utilized computed tomography (CT) data sets from fifteen patients diagnosed with low or intermediate-risk prostate cancer. The patient's simulation was conducted using the SOMATOM Definition AS CT simulator. The patients were scanned and treated in a supine position with a full bladder and empty rectum during imaging and treatment delivery. Knee and ankle supports were utilized to ensure stability and comfort and minimize the movement. After that, the patient's skin was marked with three radiopaque markers using external lasers. The simulation spanned from the upper abdomen to below the level of the lesser trochanter of the femur, with a slice thickness of 2 mm.

The CT images were then transferred to the planning system, where the radiation oncologist employed the Varian contouring tool to contour the target area and organs at risk (OARs) according to RTOG 0938 (Lawton 2012). The clinical target volume (CTV) was delineated as the prostate. The planning target volume (PTV) was defined as the CTV plus a posterior margin of 3 mm (towards the rectum) and 5 mm in the other direction.

Regarding OARs, all of them were contoured as a solid organ. The femoral heads were contoured from the acetabulum to the inferior aspect of the pubic symphysis. The circumference of the rectum and its entirety were outlined. It was contoured from the anus (at the level of the ischial tuberosities) up to the rectosigmoid flexure. The bladder was delineated

from the dome to its base. Additionally, the penile bulb was also contoured as an organ at risk.

## 2.2 VMAT plans

Two VMAT plans were created for each patient using Eclipse™ v.17 treatment planning system (Varian Medical Systems, Palo Alto, CA, USA). The first plan utilized two full coplanar arcs, one arc ranging from 181 to 179 degrees (clockwise) and the other arc in the reverse direction (anti-clockwise). The second plan utilized two partial coplanar arcs, rotating from 220 to 140 degrees and vice versa. Those partial arcs were designed to avoid radiation delivery through the rectum from the posterior direction. The collimator rotation angles for all plans were set to 30 and 330 degrees to minimize the tongue and groove effect.

All plans were created using a 10 MV flattening filter-free (FFF) photon beam with a 2400 MU/min dose rate. This beam energy selection aligns with our previous study findings, which recommended using VMAT with 10 MV (FFF) for treating prostate cancer patients with SBRT. This approach provides the fastest delivery while maintaining the highest plan quality (El-Sayed et al. 2024). The plans were designed to be treated on a TrueBeam machine with a 120-leaf millennium MLC. The dose prescription for each plan was 36.25 Gy delivered in five fractions. The plans were optimized using a photon optimizer, and the optimization objectives were set to ensure that 95% of PTV received 100% of the prescribed dose while adhering to OAR constraints specified in the RTOG 0938 guidelines, as shown in Table 1. Acuros external beam algorithm was used for the final dose calculation with a 2mm grid size. Both plans were generated with the same isocenter and optimization objective to avoid inter-planning variability-biased planning.

## 2.3 Plan Comparison

The full arc and partial arc plans were compared quantitatively regarding PTV coverage and OAR doses using dose-volume histogram (DVH) parameters. For the PTV, parameters such as maximum dose (D.03cc), D95, and D2cm were evaluated. In terms of OARs, the plan comparison was done based on the dose constraints of each OAR as specified in Table 1. The mean dose of the rectum and bladder were also compared. Furthermore, quality indices including conformity, Paddick conformity, homogeneity, and gradient index were compared based on the guidelines set by the International Commission on Radiation Units and Measurements (ICRU) (Menzel 2010; Wilke et al. 2014). The conformity index (CI) was determined as the ratio of the prescribed isodose volume to the target volume (PIV/TV). The Paddick conformity index (PCI) was calculated as  $TV_{PIV}^2$  divided by  $(TV \times PIV)$ , where  $TV_{PIV}$  represents the target volume covered by the prescription isodose volume. The CI and PCI characterize the degree to which the high-dose region conforms to the PTV. Where the ideal value of those indices is one. The homogeneity index (HI) was computed as the ratio

of (D2% - D98%) to D50%, where D2%, D98%, and D50% correspond to the dose received by 2%, 98%, and 50% of the target volume, respectively. HI characterizes the uniformity of the absorbed dose distribution within the target volume. An HI closer to zero indicates that the absorbed dose distribution is almost homogeneous. The gradient index (GI) was determined as the ratio of the volume of half the prescription isodose to the volume covered by the prescription isodose.

Furthermore, the beam on time (BOT) of the plans was compared. It was measured as the time from the initiation of the first beam to the completion of the last beam using the QA mode. Additionally, the number of monitor units (MU) and the modulation factor (MF) were compared. The modulation factor was calculated by dividing the total number of monitor units per fraction by the prescribed dose per fraction in cGy.

**Table 1 Dose constraints according to RTOG 0938**

Structure	Dosimetric parameter	Criteria
PTV	D <sub>0.03cc</sub>	≤ 38.78 Gy (107% of prescription dose)
	D <sub>95%</sub>	≥ 36.25 Gy (100% of prescription dose)
Rectum	D <sub>1cc</sub>	≤ 38.06 Gy (105% of prescription dose)
	D <sub>3cc</sub>	≤ 34.43 Gy (95% of prescription dose)
	D <sub>10%</sub>	≤ 32.625 Gy (90% of prescription dose)
	D <sub>20%</sub>	≤ 29.00 Gy (80% of prescription dose)
	D <sub>50%</sub>	≤ 18.125 Gy (50% of prescription dose)
Bladder	D <sub>1cc</sub>	≤ 38.06 Gy (105% of prescription dose)
	D <sub>10%</sub>	≤ 32.625 Gy (90% of prescription dose)
	D <sub>50%</sub>	≤ 18.125 Gy (50% of prescription dose)
Femoral	D <sub>max</sub>	≤ 29.36 Gy (81% of prescription dose)
Heads	D <sub>10cc</sub>	≤ 19.57 Gy (54% of prescription dose)
	D <sub>max</sub>	≤ 36.25 Gy (100% of prescription dose)
Penile bulb	D <sub>3cc</sub>	≤ 19.57 Gy (54% of prescription dose)

**D<sub>x%</sub>**; dose received by at least x% of the volume, **D<sub>max</sub>**; maximum point dose

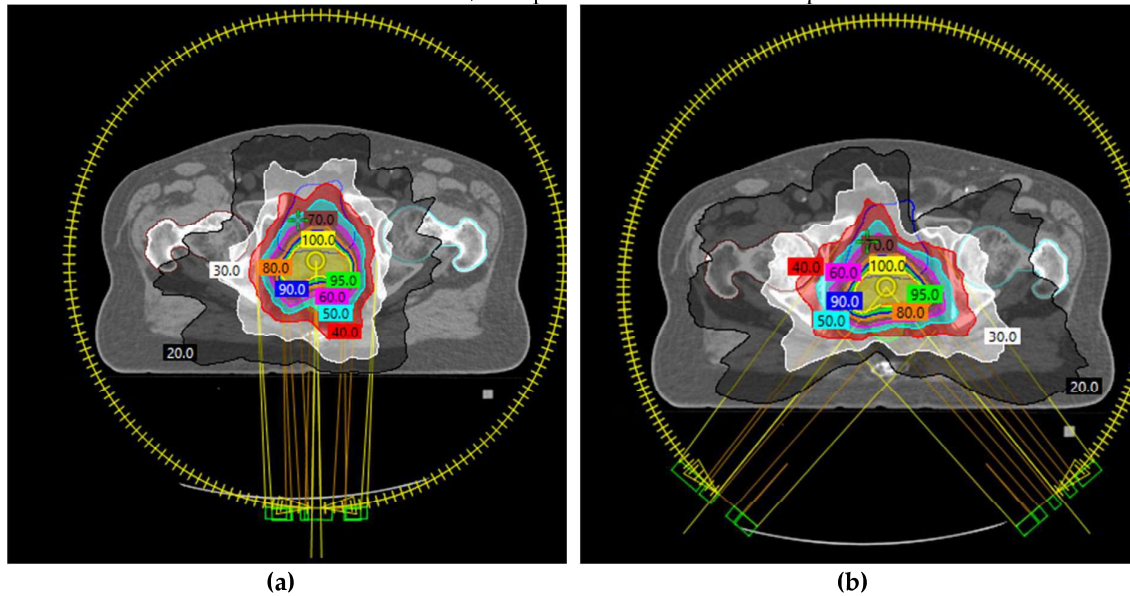
#### 2.4 Statistical analysis

The data was analyzed using the Statistical Package for Social Sciences (SPSS) software (v.20.0; IBM, New York). First, the normality test was performed using the Shapiro-Wilk test ( $p > 0.05$ ) to check the normality of the data. If the data was normally distributed, the standard two-tailed paired t-test was used. Otherwise, a paired Wilcoxon signed-rank test was used. A p-value  $< 0.05$  was set as the threshold for statistically significant differences. Finally, the data was presented as mean  $\pm$  standard deviation.

#### 3 Result

The analysis of 15 treatment plans comparing partial and full arcs demonstrated that both approaches achieved adequate dose conformity to

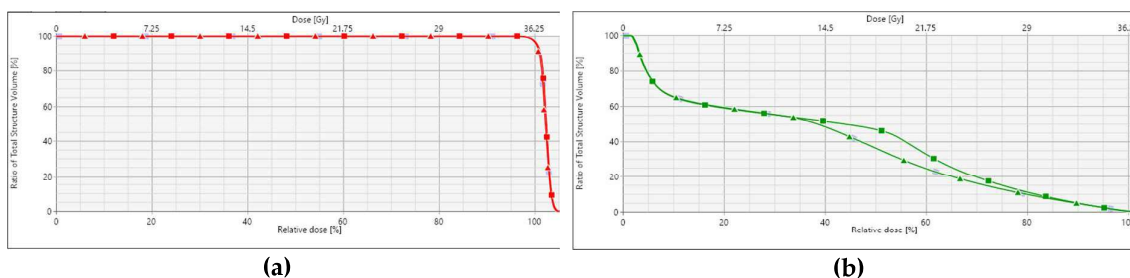
the target volume and yielded comparable dosimetric data. **Fig. 1** illustrates the dose distribution achieved by both plans for the same patient, while **Fig. 2** presents the DVH comparison considering the PTV, rectum, bladder, femoral heads, and penile bulb for the same patient.

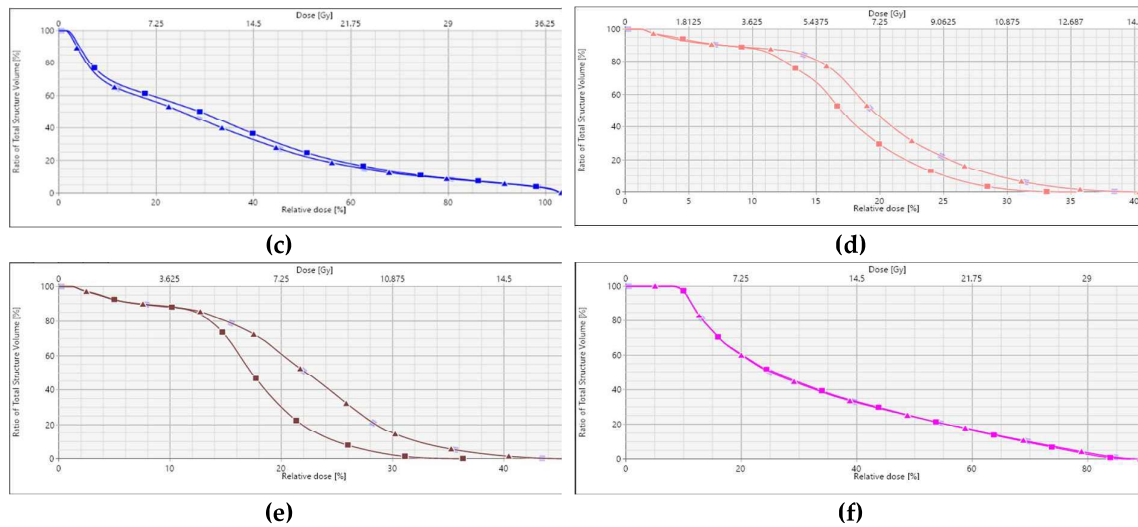


**Fig. 1** The dose distribution achieved by a full arc (a) and partial arc (b) VMAT for the same patient

**Table 2** provides dosimetric values for the PTV and OARs. For all cases, both plans met the constraints of the RTOG 0938 protocol for prostate SBRT. Regarding PTV coverage, the full arc plan exhibited a significantly higher value of  $D_{95\%}$  compared to the partial arcs, indicating superior coverage with the full arc approach. On the other hand, the partial arcs demonstrated a lower max dose than the full arc plan, although this difference was not statistically significant. The  $D_{2cm}$  value was lower in the full arc plan than in the partial arcs, but no significant difference was observed.

For the conformity indices (CI and PCI), the full arcs provided significantly higher values compared to the partial arcs, indicating that the full arcs approach achieved better dose conformity to the target volume. However, no significant differences were observed in the homogeneity index (HI), suggesting comparable dose homogeneity between the two plans.





**Fig. 2** The DVH comparison between full arc (triangles) and partial arc (squares) for the PTV (a), rectum (b), bladder (c), Lt.Femur (d), Rt.Femur (e), and penile bulb (f)

Regarding the gradient index (GI), the full arcs exhibited a significantly lower value compared to the partial arcs, indicating a steeper dose gradient and improved dose fall-off around the target volume with the full arc plan.

**Table 2** Mean dosimetric values of PTV, plan quality indices, and OARs parameters for full arc and partial arc plans

Structure	parameter	Full arc	Partial arc	P-value
PTV	D <sub>95%</sub> (Gy)	36.39 ± 0.09	36.33 ± 0.09	0.001*
	D <sub>0.03cc</sub> (Gy)	38.22 ± 0.14	38.16 ± 0.11	n
	D <sub>2cm</sub> (Gy)	21.93 ± 1.14	22.6 ± 0.82	n
	CI	1.01 ± 0.07	1.02 ± 0.07	0.035*
	PCI	0.94 ± 0.06	0.93 ± 0.06	0.006*
	HI	0.05 ± .003	0.05 ± .004	n
	GI	4.15 ± 0.32	4.27 ± 0.25	0.000*
Rectum	D <sub>1cc</sub> (Gy)	35.56 ± 0.72	35.67 ± 0.74	0.009*
	D <sub>3cc</sub> (Gy)	32.61 ± 1.52	32.83 ± 1.49	0.026*
	D <sub>10%</sub> (Gy)	29.66 ± 1.34	29.73 ± 1.64	n
	D <sub>20%</sub> (Gy)	24.73 ± 1.03	24.41 ± 1.55	n
	D <sub>50%</sub> (Gy)	16.14 ± 0.28	15.38 ± 1.35	0.012*
	Mean dose (Gy)	15.8 ± 1.17	15.47 ± 1.46	0.052*

Bladder	D <sub>1cc</sub> (Gy)	37.34 ± 0.14	37.3 ± 0.14	0.041*
	D <sub>10%</sub> (Gy)	27.13 ± 3.1	26.96 ± 3.3	n
	D <sub>50%</sub> (Gy)	11.14 ± 4.81	10.85 ± 4.86	n
	Mean dose (Gy)	13.16 ± 3.56	12.83 ± 3.56	0.004*
Rt. Femur	D <sub>max</sub> (Gy)	14.37 ± 1.89	17.13 ± 1.6	0.001*
	D <sub>10cc</sub> (Gy)	10.65 ± 1.51	12.87 ± 1.74	0.000*
Lt. Femur	D <sub>max</sub> (Gy)	14.14 ± 1.8	16.77 ± 1.95	0.000*
	D <sub>10cc</sub> (Gy)	10.54 ± 1.7	12.43 ± 1.83	0.000*
Penile bulb	D <sub>max</sub> (Gy)	20.13 ± 9	20.43 ± 9	n
	D <sub>3cc</sub> (Gy)	1.66 ± 2	1.67 ± 2	n

D<sub>x%</sub>; dose received by at least x% of the volume, cc; cm<sup>3</sup>, D<sub>xcc</sub>; dose received by at least x cm<sup>3</sup> of the volume, CI; conformity index, PCI; paddick conformity index, HI; homogeneity index, GI; gradient index, D<sub>max</sub>; maximum point dose, n; no significant difference, \*; values with statistically significant difference (p < 0.05)

In terms of OAR doses, significant differences were observed between the full arcs and partial arcs plans for various parameters. For the rectum, both D<sub>1cc</sub> and D<sub>3cc</sub> were significantly lower in the full arcs plan than the partial arcs, indicating reduced radiation exposure at a high dose level with the full arcs approach. The partial arcs plan also showed a significantly lower value of D<sub>50%</sub> compared to the full arcs plan as shown in Fig. 1. Additionally, the mean dose to the rectum was significantly lower in the partial arcs plan compared to the full arcs plan, indicating improved sparing of the rectum with the partial arcs. However, no significant difference was observed in D<sub>10%</sub> between the two plans, and D<sub>20%</sub> was lower in the partial arcs plan without statistical significance.

Regarding the femoral heads, both the maximum dose and D<sub>10cc</sub> were significantly lower in the full arcs plan than the partial arcs, indicating improved sparing of the femoral heads with the full arcs approach. For the penile bulb, there was no statistically significant difference observed between the full arc and partial arc plans for the maximum dose and D<sub>3cc</sub>. However, it is important to note that the full arc plan consistently provided lower values for both parameters compared to the partial arc plan.

Finally, in terms of treatment delivery parameters, the partial arcs required significantly lower MU, MF, and BOT compared to the full arcs as shown in Table 3, indicating more efficient treatment delivery with the partial arc approach.



**Table 3 Treatment delivery parameters of full arc and partial arc**

Treatment Delivery Parameters	Full arc	Partial arc	P-value
MU	2194.47 ± 106.84	2164.73 ± 105.11	0.018*
MF	3.03 ± 0.15	2.99 ± 0.15	0.018*
BOT (sec)	125.60 ± 0.51	100.13 ± 0.35	0.000*

MU; monitor units, MF; modulation factor, BOT; beam on time, \*; Values with statistically significant difference (p < 0.05)

#### 4 Discussion

Several studies have explored the use of VMAT in SBRT and its efficacy compared to alternative treatment modalities or techniques. Alongi et al. (2013) conducted their study to assess the feasibility and early side effects of prostate SBRT using VMAT and FFF beams. Their findings indicated that SBRT with RapidArc and FFF beams was feasible, efficient, and well-tolerated in the acute setting for prostate cancer patients. In another study by Scobioala et al. (2019), a comparison was made between CK and other techniques such as HT, intensity-modulated radiation therapy (IMRT), and VMAT for prostate SBRT. The study revealed that there was no clear dosimetric advantage that favored CK or any other technique for the SBRT of low-grade prostate cancer. This study aimed to determine the better choice beam arrangement for VMAT plans in prostate SBRT by comparing the outcomes of partial arcs and full arcs plans for the same group of patients. The aim was to identify which technique provided the greatest benefit regarding treatment efficacy and delivery for prostate SBRT.

The analysis of the treatment plans revealed several important findings. Regarding the dosimetric results, both approaches demonstrated adequate dose conformity to the target volume, but there were differences in target coverage, OAR sparing, and treatment delivery parameters. These differences can be explained by the modulation capabilities associated with each plan.

The present study's findings demonstrated that the full arc plans achieved superior target coverage (higher D95%) than the partial arc. This can be attributed to the continuous rotation and modulation capabilities of the full arc plans. The ability to modulate the intensity of the radiation beam throughout the 360-degree arc allows for a more precise delivery of radiation dose, resulting in improved target coverage. Also, the full arc plans demonstrated better dose conformity (higher CI and PCI) and steeper dose fall-off (lower GI) around the target volume. Where the modulation capabilities of the full arc plans enable planers to shape the radiation beam and conform it closely to the target volume, resulting in improved dose conformity and dose fall-off.

On the other hand, the partial arc plans achieved a lower maximum dose to the PTV compared to full arc due to the limited range of angles, typically less than 360 degrees, from which the radiation beam approaches the target volume. By limiting the range of angles, the partial arc plan avoids certain beam orientations that may result in higher dose deposition in the PTV. These higher-dose regions can occur when the beam approaches the target volume from more perpendicular angles, leading to a higher dose concentration within a specific area. In contrast, the full arc plan allows the radiation beam to approach the PTV from a wider range of angles, including more perpendicular orientations. This broader range of beam angles can result in a higher maximum dose in certain regions of the PTV, especially those areas that receive a higher dose contribution from multiple beam angles.

Regarding OARs, the results highlight the advantages of each treatment technique in minimizing radiation exposure to specific dose levels in the rectum and bladder. The full arc plan showed advantages in reducing high-dose exposure to the rectum, as evidenced by lower D1cc and D3cc values. On the other hand, the partial arc plan demonstrates benefits in reducing radiation exposure to the low and mid-dose levels of the rectum (Fig. 1), as indicated by lower D20% and D50% values as well as mean dose. Also, the partial arc plan proved effective in reducing radiation exposure to the high-dose region of the bladder, as reflected in lower D1cc values. However, no significant differences were observed in D10% and D50% values, suggesting comparable radiation doses to the mid-dose regions of the bladder between the two plans, favoring the use of the partial arc. Additionally, the mean dose delivered to the bladder was lower in the partial arc plan with a significant difference compared to the full arc plan, indicating overall improved sparing of the bladder in the partial arc plan. Therefore, the findings highlight the effectiveness of both plans in mitigating radiation exposure to specific dose regions in the rectum and bladder.

Those findings can be attributed to the modulation capabilities and beam delivery characteristics of each plan. The full arc plan, with its continuous modulation and beam delivery from a wider range of angles, offers better control and avoidance of high-dose regions in the rectum, leading to lower D1cc and D3cc values. On the other hand, the limited range of angles in the partial arc plan allows for focused beam delivery, reducing radiation exposure to specific regions for the bladder and the rectum. The differences in D20% and D50% values suggest that the partial arc plan achieves relatively lower radiation doses in the low-dose and mid-dose regions of the rectum and bladder.

In evaluating the femoral heads, the partial arc plan exhibited a significant dose increment compared to the full arc plan. This can be attributed to the

utilization of anterior and lateral regions in the partial arc plan, which compensated for avoiding the posterior region. However, it is important to note that despite the increased dose, both plans successfully adhered to the constraints outlined in the RTOG 0938 guidelines. Conversely, when considering the dose delivered to the penile bulb, no significant difference was observed between the two treatment plans. This lack of difference can be attributed to the anatomical location of the penile bulb, situated outside the PTV region. Consequently, the penile bulb was not directly influenced by utilizing a full arc or avoiding specific sectors in the partial arc.

The results obtained in the present study were in line with the results reported by Rana and Cheng (2013), which indicate that the partial arc technique increases the dose delivered to the femoral heads while simultaneously reducing doses to the bladder and the rectum. Additionally, their results stated that these improvements in organ sparing were achieved without compromising the treatment plan's conformity or the target's homogeneity. In contrast, the results of the present study did not align with those presented by Sasaki et al. (2020) who examined the impact of rectal gas on the dose distribution of prostate cancer and OARs utilizing both full arc and partial arc VMAT techniques. The authors concluded that there were no significant differences in the dose distribution for the CTV and OARs across the four treatment planning techniques assessed.

The full arc plan required a higher number of MU due to the continuous rotation of the gantry, leading to a longer treatment time and the need for modulation throughout the entire 360-degree rotation. On the other hand, the partial arc plans demonstrated more efficient treatment delivery with significantly lower MU, MF, and BOT. The partial arc plans exhibited a 20% decrease in BOT compared to the full arc plan, indicating faster treatment delivery, reduced treatment time, and potentially lower resource utilization with the partial arc approach. These findings highlight the advantages of the partial arc technique regarding treatment efficiency and resource optimization, offering potential benefits in clinical workflow management and patient throughput.

## 5 Conclusion

In summary, both the full arc and partial arc plans demonstrated the ability to achieve sufficient coverage of the PTV and meet the OAR constraints outlined in the RTOG 0938 guidelines. However, the full arc plans exhibited superior PTV coverage, while the partial arc plans demonstrated better sparing of the rectum and bladder. Moreover, the partial arc plans showed advantages in terms of reducing monitor units (MU) and beam-on time (BOT). Based on these findings, we strongly recommend the utilization of the partial arc for prostate SBRT, as it offers improved sparing of critical structures and efficient treatment delivery.

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### Conflict of interest

The authors declare that they have no competing interests

### Author contributions

Sherif M. El-Sayed and Dina M. Abdelaziz designed this study, and Sherif M. El-Sayed, Reem H. El-Gebaly, Mohamed M. Fathy, Dina M. Abdelaziz wrote the main manuscript, performed the experiments, and prepared Figs. All authors reviewed the manuscript. All authors read and approved the final manuscript.

### Data availability

All data needed to support the conclusions are included in this article. Additional data related to this paper can be requested from the author ([sherif.mohammed@baheya.org](mailto:sherif.mohammed@baheya.org))

### Consent for publication

Not applicable

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