

# **Dosimetric Comparison of IMRT and VMAT for Retinoblastoma Treatment: A treatment Planning Study**

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#### OBJECTIVE

The aim of this study was to evaluate and compare the dosimetric characteristics of Intensity-Modulated Radiation Therapy (IMRT), Full-arc Volumetric Modulated Arc Therapy (VMAT-F), and Partial-arc Volumetric Modulated Arc Therapy (VMAT-P) in the management of retinoblastoma.

### **METHODS**

Treatment plans for retinoblastoma patients were created utilizing IMRT, VMAT-F, and VMAT-P techniques. The prescription dose was set at 45 Gy in 25 fractions. An analysis was conducted on dosimetric parameters using the cumulative dose-volume histogram (cDVH), including Planning Target Volume (PTV) coverage (D95%), Conformity Index (CI), Homogeneity Index (HI), and the radiation doses received by organs at risk (OARs). Additionally, brain dose-volume metrics (V5Gy, V10Gy, V15Gy) and monitor units (MUs) were evaluated and compared among the three methods.

### RESULTS

All treatment techniques achieved 95% coverage of the prescribed dose within the PTV volume. The VMAT methods significantly improved both the mean and maximum PTV doses compared to IMRT (p<0.001). Among the VMAT techniques, VMAT-P achieved the highest Conformity Index (1.00±0.01) and the lowest Homogeneity Index. Additionally, VMAT-P markedly decreased the volume of brain receiving 10 Gy (12.9±2.96%) and 15 Gy (6.78±1.82%) compared to both IMRT and VMAT-F (p<0.001). IMRT was more effective in preserving contralateral structures, particularly the eyes and lenses. Furthermore, both VMAT techniques utilized fewer monitor units than IMRT (p < 0.001).

### CONCLUSION

In this study, VMAT-P achieved an advantageous balance among PTV coverage, conformity, and the preservation of organs at risk (OARs). It exhibited better conformity and improved sparing of brain tissue at moderate dose levels compared to both IMRT and VMAT-F.

Keywords: Intensity Modulated Radiotherapy; retinoblastoma cancer; volumetric modulated arc therapy. Copyright © 2024, Turkish Society for Radiation Oncology

# INTRODUCTION

Retinoblastoma (Rb) is a type of cancer that develops from retinal cells, primarily affecting children younger than four years old. This tumor is sensitive to radiation therapy and has an estimated global incidence of

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approximately 1 in 15,000 to 18,000 live births, leading to around 8,000 new diagnoses annually.[1] India reports the highest number of cases, exceeding 1,400 each year.[2] Most cases of Rb (60%) are unilateral, typically diagnosed at a median age of two years, and are generally non-hereditary.

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The main objective in managing retinoblastoma (Rb) is to ensure survival. Treatment options have significantly advanced and now encompass external beam radiotherapy (EBRT), plaque radiotherapy, multiple chemotherapy approaches (including intravenous, intra-arterial, intravitreal, and intracameral), as well as consolidation therapies like cryotherapy and transpupillary thermotherapy.[3–8]

Currently, radiation therapy is mainly employed after other treatment options have been exhausted or when tumors are too large for localized surgical intervention. With its lower recurrence rates, EBRT has emerged as a prevalent treatment choice for extraocular cancer, particularly in comparison to radioactive plaque brachytherapy.[9] In the context of megavoltage external beam radiotherapy (EBRT), conventional treatment methods have demonstrated local control rates ranging from 41% to 56% and ocular survival rates between 60% and 100%. [10–12] Nevertheless, EBRT is linked to several complications, including ocular dryness, the development of cataracts, and orbital hypoplasia. Studies indicate that cataracts occur in approximately 20% to 30% of treated eyes within 2 to 3 years post-irradiation.[11–13]

Historically, three-dimensional radiotherapy employed anterior and lateral wedge-shaped fields for treatment; however, this approach resulted in dose inhomogeneity within the target area. Recent advancements in irradiation techniques, such as Intensity Modulated Radiotherapy, Volumetric Modulated Arc Therapy, and Proton Radiotherapy, facilitate a more conformal dose distribution to the target volume while minimizing exposure to adjacent healthy tissues.[14–16]

Previous research has explored the capabilities and advantages of Volumetric Modulated Arc Therapy (VMAT) in the management of intraocular cancer, yielding encouraging outcomes.[17] Nonetheless, a notable disparity in planning practices and quality was observed among various institutions regarding Intensity-Modulated Radiation Therapy (IMRT) and VMAT.[18] This study aimed to conduct a dosimetric analysis that compares IMRT, Full Arc VMAT (F-VMAT), and dual-partial VMAT (P-VMAT) planning techniques in the treatment of patients with retinoblastoma, with the objective of identifying the most effective treatment technique.

### MATERIALS AND METHODS

A retrospective analysis was performed involving thirteen patients diagnosed with retinoblastoma, selected from the database of the Department of Radiation Oncology at the State Cancer Institute, IGIMS. These individuals required radiotherapy targeting one eye. To facilitate immobilization, all patients were placed in a supine position and secured with a thermoplastic head mask featuring three clamps.

Computed tomography (CT) images were obtained with a slice interval of 1.2 mm using the GE Revolution EVO from GE Healthcare Pvt. Ltd. The DICOM images from these CT scans were utilized to delineate the clinical target volume (CTV), which encompassed the orbit, optic canal, superior orbital fissure, and inferior orbital fissure. The planning target volume (PTV) was established as the CTV plus a uniform three-dimensional margin of 3 mm. The organs at risk included the contralateral eye, lens, optic nerve, optic chiasm, pituitary gland, bilateral cochlea, and brainstem.

The Eclipse Treatment Planning System Version 16.0.14, developed by Varian Medical Systems, Inc. in Palo Alto, CA, USA, was employed to formulate three distinct treatment plans for each patient. These plans were retrospectively designed using a Varian True-Beam SVC linear accelerator, which is outfitted with a Millennium 120 multi-leaf collimator (MLC).

The study examined three different planning methods. The initial plan featured a 5-field Intensity-Modulated Radiation Therapy (IMRT) setup, incorporating specific gantry angles of 0°, 320°, 240°, 195°, and 20°. The second plan, designated as Full Arc Volumetric Modulated Arc Therapy (F-VMAT), involved a single clockwise VMAT arc ranging from 181° to 179°, with a collimator angle set at 30°. The third plan implemented the dual-partial arc Volumetric Modulated Arc Therapy (P-VMAT) technique, where the gantry rotation was modified in both clockwise and counterclockwise directions to suit the dimensions and concavity of the Planning Target Volume (PTV). Additionally, the collimator angles were adjusted to  $\pm 30°$  to enhance treatment efficacy.

A 6 MV photon beam was utilized across all plans. The prescribed treatment dose was 45 Gy, delivered in 25 fractions of 1.8 Gy each over a span of 5 weeks. The Anisotropic Analytic Algorithm (AAA, version 16.0.14) with a grid spacing of 2.5 mm was employed for the final dose calculations. The objective of the planning was to ensure that 95% of the prescribed dose (PD) reached 95% of the PTV, while limiting the volume of the PTV receiving 107% of the PD to no more than 1%.

For the organs at risk (OARs), the maximum dose constraints were established as follows: brainstem, optic chiasm, and contralateral optic nerves receiving less than 54 Gy; contralateral lens with a maximum dose ( $D_{max}$ ) of less than 2 Gy and a mean dose ( $D_{mean}$ ) of less than 6 Gy; and contralateral eye with a  $D_{max}$  of less than 45 Gy and a  $D_{mean}$  of less than 20 Gy.



The quality indices of the plans were evaluated by analyzing the dose-volume parameters obtained from the cumulative dose-volume histograms (DVH) generated for each specific plan.

# **Conformity Index**

The conformity index (CI) is defined as the prescribed isodose volume (VRI) divided by the total PTV volume. The recommended value is one but is usually <1. It is defined as follows:[19]

CI=VRI/TV

# **Homogeneity Index**

The homogeneity index (HI) was calculated as the difference between the delivered dose for 2% (D2%) and 98% (D98%) of the PTV volume, divided by the dose for 50% of the PTV volume (D50%). It is defined as follows:[20]

HI=(D2%-D98%)/D50%

HI=0 implies a completely homogeneous dose distribution.

# **Conformation Number**

PD coverage in treatment plans can be assessed using a ratio.[20] This ratio, known as the Conformation Number (CN), is defined as follows:

# $CN=(TVRI \times TVRI)/(TV \times VRI)$

In this equation, TVRI represents the target volume covered by the reference dose in cubic centimeters (cc), TV represents the total target volume in cc, and VRI represents the volume of the reference dose in cc. CN=1 if the plan is perfect.

Additionally, MUs for each treatment plan were also recorded for comparison.

# **Statistical Analysis**

The statistical findings are presented as mean±standard deviation (SD). Statistical calculations were conducted using Microsoft Excel. A two-tailed paired Student's t-test was utilized to assess the significance of the observed differences. Differences between the two methods are deemed statistically significant when the probability value (p) is less than or equal to 0.05.

# RESULTS

The dose distribution represented by isodose lines and the dose-volume histogram (DVH) comparisons for a single patient utilizing three different treatment techniques are illustrated in Figures 1 and 2. Comprehensive dosimetric evaluations regarding target coverage are presented in Table 1.

# **PTV and Dosimetric Parameters**

The implementation of IMRT led to a markedly lower maximum dose ( $D_{max}$ ) to the planning target volume (PTV) compared to both VMAT-P (p=0.001) and VMAT-F (p<0.001). The PTV demonstrated clinically acceptable coverage across all three treatment modalities, with D95% values recorded as 95.84±1.29 for IMRT, 97.37±0.42 for VMAT-P, and 96.86±1.05 for VMAT-F. Statistically significant differences were noted with p=0.001 for IMRT versus VMAT-P and p<0.001 for IMRT versus VMAT-F. However, the comparison between VMAT-P and VMAT-F did not yield a statistically significant result (p=0.059).

Furthermore, the average dose  $(D_{mean})$  administered to the PTV was significantly lower in IMRT (44.39±0.31) compared to both VMAT techniques, which recorded  $D_{mean}$  values of 44.99±0.05 for VMAT-P



IMRT: Intensity-modulated radiation therapy; VMAT-P: Partial-arc volumetric modulated arc therapy; VMAT-F: Full-arc volumetric modulated arc therapy.

and 44.99±0.48 for VMAT-F, with p<0.001 for both comparisons. No significant difference in  $D_{mean}$  was found between VMAT-P and VMAT-F (p=0.944). Additionally, there were no notable differences in the volume receiving 107% of the prescribed dose (V107%) across the three techniques, as all comparisons yielded p-values exceeding 0.05 (p=0.059).

The Conformity Index (CI) demonstrated a notable enhancement (approaching 1) with VMAT-P ( $1.00\pm0.01$ ) when compared to IMRT ( $1.03\pm0.05$ , p=0.043) and VMAT-F ( $1.01\pm0.01$ , p=0.007). No significant difference was found between IMRT and VMAT-F (p=0.156). The Homogeneity Index (HI) revealed no significant difference between IMRT and VMAT-P (p=0.696); however, VMAT-F ( $0.09\pm0.03$ ) showed a significantly greater HI than VMAT-P ( $0.07\pm0.01$ , p=0.01). The difference between IMRT and VMAT-F was not statistically significant (p=0.072).

The Conformation Number (CN) was significantly higher for both VMAT techniques compared to IMRT (IMRT: 0.81±0.05, VMAT-P: 0.88±0.04, VMAT-F: 0.89±0.05; p=0.001 for IMRT vs. VMAT-P, p=0.004 for IMRT vs. VMAT-F). No significant difference was observed between VMAT-P and VMAT-F (p=0.204).

The monitor units (MUs) utilized in the techniques of IMRT, VMAT-P, and VMAT-F were analyzed. The

average MU values recorded were  $565.09\pm54.17$  for IMRT,  $440.31\pm44.07$  for VMAT-P, and  $468.48\pm72.73$  for VMAT-F. Statistical analysis indicated that VMAT-P required a significantly lower number of MUs compared to IMRT (p<0.001). Conversely, there was no significant difference in the number of MUs between VMAT-P and VMAT-F (p=0.244). Additionally, IMRT demonstrated a significantly higher number of MUs when compared to VMAT-F (p<0.001).

### Organ at Risk (OAR)

Table 2 shows a comparison of the OARs (organs at risk) between the three planning techniques.

### **Brainstem and Optic Chiasm**

For the brainstem, the maximum dose  $(D_{max})$  values recorded were 36.51±12.88 Gy for Intensity-Modulated Radiation Therapy (IMRT), 35.49±10.33 Gy for Volumetric Modulated Arc Therapy with a partial arc (VMAT-P), and 35.66±9.64 Gy for Volumetric Modulated Arc Therapy with a full arc (VMAT-F). Similarly, the  $D_{max}$  values for the optic chiasm were found to be 41.6±6.63 Gy for IMRT, 40.90±8.70 Gy for VMAT-P, and 41.3±7.78 Gy for VMAT-F. No significant statistical differences were observed, as all methods for both structures yielded p-values greater than 0.05.

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IMRT (Mean±SD)	VMAT-P (Mean±SD)	VMAT-F (Mean±SD)	IMRT vs. VMAT-P (p)	VMAT-P vs. VMAT-F (p)	IMRT vs. VMAT-F (p)
47.1±0.900	48.32±0.553	48.71±0.699	0.001	0.059	<0.001
44.39±0.31	44.99±0.05	44.99±0.48	<0.001	0.944	<0.001
0.002±0.008	0.01±0.03	0.05±0.127	0.211	0.33	0.153
95.84±1.29	97.37±0.42	96.86±1.05	0.001	0.059	<0.001
1.03±0.05	1.00±0.01	1.01±0.01	0.043	0.007	0.156
0.7±0.02	0.07±0.01	0.09±0.03	0.696	0.01	0.072
0.81±0.05	0.88±0.04	0.89±0.05	0.001	0.204	0.004
565.09±54.17	440.31±44.07	468.48±72.73	< 0.001	0.244	<0.001
	IMRT (Mean±SD) 47.1±0.900 44.39±0.31 0.002±0.008 95.84±1.29 1.03±0.05 0.7±0.02 0.81±0.05 565.09±54.17	IMRT         VMAT-P           (Mean±SD)         (Mean±SD)           47.1±0.900         48.32±0.553           44.39±0.31         44.99±0.05           0.002±0.008         0.01±0.03           95.84±1.29         97.37±0.42           1.03±0.05         1.00±0.01           0.7±0.02         0.07±0.01           0.81±0.05         0.88±0.04           565.09±54.17         440.31±44.07	IMRT (Mean±SD)         VMAT-P (Mean±SD)         VMAT-F (Mean±SD)           47.1±0.900         48.32±0.553         48.71±0.699           44.39±0.31         44.99±0.05         44.99±0.48           0.002±0.008         0.01±0.03         0.05±0.127           95.84±1.29         97.37±0.42         96.86±1.05           1.03±0.05         1.00±0.01         1.01±0.01           0.7±0.02         0.07±0.01         0.09±0.03           0.81±0.05         0.88±0.04         0.89±0.05           565.09±54.17         440.31±44.07         468.48±72.73	IMRT (Mean±SD)         VMAT-P (Mean±SD)         VMAT-F (Mean±SD)         IMRT vs. VMAT-P (p)           47.1±0.900         48.32±0.553         48.71±0.699         0.001           44.39±0.31         44.99±0.05         44.99±0.48         <0.001	IMRT (Mean±SD)         VMAT-P (Mean±SD)         VMAT-F (Mean±SD)         IMRT vs. VMAT-P (p)         VMAT-P vs. VMAT-F (p)           47.1±0.900         48.32±0.553         48.71±0.699         0.001         0.059           44.39±0.31         44.99±0.05         44.99±0.48         <0.001

### Table 1 PTV coverage and dosimetric parameters among three techniques.

PTV: Planning target volume; IMRT: Intensity-modulated radiation therapy; VMAT-P: Partial-arc volumetric modulated arc therapy; VMAT-F: Full-arc volumetric modulated arc therapy; SD: Standard deviation; D<sub>max</sub>: Maximum dose; D<sub>mean</sub>: Mean dose; V107%: Volume of PTV receiving 107% of the prescribed dose; D95%: Dose covering 95% of the target volume; CI: Conformity index; HI: Homogeneity index; CN: Conformation number; MUs: Monitor units

Table 2 Comparison of Organ at Risks (OARs) at three different techniques

OARs parameter	IMRT (Mean±SD)	VMAT-P (Mean±SD)	VMAT-F (Mean±SD)	IMRT vs. VMAT-P (p)	VMAT-P vs. VMAT-F (p)	IMRT vs. VMAT-F (p)
Brain stem (D <sub>max</sub> )Gy	36.51±12.88	35.49±10.33	35.66±9.64	0.769	0.699	0.797
Optic chiasm (D <sub>max</sub> )Gy	41.6±6.63	40.90±8.70	41.3±7.78	0.399	0.132	0.666
C/L optic Nerve (D <sub>max</sub> ) Gy	9.44±4.54	17.52±3.91	29.74±42.25	<0.001	0.336	0.124
C/L eye (D <sub>max</sub> )Gy	6.32±2.20	5.05±1.92	6.14±2.26	0.175	0.037	0.810
C/L eye (D <sub>mean</sub> )Gy	1.57±0.34	2.26±0.63	2.36±0.67	<0.001	0.067	<0.001
C/L lens (D <sub>max</sub> )Gy	1.81±0.39	2.03±0.39	2.20±0.40	0.009	0.063	0.001
C/L lens (D <sub>mean</sub> )Gy	1.30±0.29	1.71±0.30	1.75±0.31	<0.001	0.497	<0.001
RT cochlea (D <sub>max</sub> )Gy	11.71±4.98	11.6±5.05	12.9±6.21	0.913	0.103	0.323
LT cochlea (D <sub>max</sub> )Gy	9.95±8.46	7.94±5.91	8.40±7.40	0.044	0.524	0.107
Brain (V5Gy) %	24.7±4.51	26.2±4.91	27.8±5.28	0.059	0.005	<0.001
Brain (V10Gy)%	14.5±2.70	12.9±2.96	16.6±3.65	<0.001	<0.001	0.003
Brain (V15Gy)%	8.38±2.10	6.78±1.82	8.54±17.26	<0.001	0.002	0.77

VxGy refers to the volume of tissue receiving x Gray (Gy) or more of radiation dose. IMRT: Intensity-modulated radiation therapy; VMAT-P: Partial-arc volumetric modulated arc therapy; SD: Standard deviation; D<sub>max</sub>: Maximum dose; D<sub>mean</sub>: Mean dose; C/L: Contralteral; RT: Right; LT: Left

### Contralateral (C/L) Optic Nerve

The maximum dose ( $D_{max}$ ) values recorded for the contralateral optic nerve were 9.44±4.54 Gy for IMRT, 17.52±3.91 Gy for VMAT-P, and 29.74±42.25 Gy for VMAT-F. A statistically significant difference was noted between IMRT and VMAT-P (p<0.001). In contrast, no significant differences were found between VMAT-P and VMAT-F (p=0.336) or between IMRT and VMAT-F (p=0.124).

### C/L Eye and Lens

Regarding the maximum dose administered to the contralateral eye, the intensity-modulated radiation therapy (IMRT) delivered an average of 6.32±2.20 Gy, while the volumetric modulated arc therapy with partial arcs (VMAT-P) provided 5.05±1.92 Gy, and the full arcs variant (VMAT-F) delivered 6.14±2.26 Gy. Statistical analysis revealed no significant differences between IMRT and VMAT-P (p=0.175) or between IMRT and VMAT-F (p=0.810). However, a significant difference was noted between VMAT-P and VMAT-F (p=0.037), with VMAT-P resulting in a lower dose. For the contralateral eye, the average radiation doses recorded were  $1.57\pm0.34$  Gy for IMRT,  $2.26\pm0.63$  Gy for VMAT-P, and  $2.36\pm0.67$  Gy for VMAT-F. Both VMAT-P and VMAT-F delivered significantly higher doses compared to IMRT, with p-values below 0.001 for each comparison. No significant difference was found between VMAT-P and VMAT-F, as indicated by a p-value of 0.067.

The maximum dose delivered to the contralateral lens was measured at  $1.81\pm0.39$  Gy for IMRT,  $2.03\pm0.39$  Gy for VMAT-P, and  $2.20\pm0.40$  Gy for VMAT-F. The dose associated with VMAT-P was significantly higher than that of IMRT (p=0.009), and VMAT-F also demonstrated a significant increase compared to IMRT (p=0.001). However, no significant difference was found between VMAT-P and VMAT-F (p=0.063). Regarding the mean dose, the values recorded for the contralateral lens were  $1.30\pm0.29$  Gy for IMRT,  $1.71\pm0.30$  Gy for VMAT-P, and  $1.75\pm0.31$  Gy for VMAT-F. Both VMAT-P and VMAT-F showed significantly elevated doses in comparison to IMRT (p<0.001 for both). There was no significant difference noted between VMAT-P and VMAT-F (p=0.497).

### **Brain Dose-Volume Parameters**

This study analyzed the brain dose volumes associated with IMRT, VMAT-P, and VMAT-F techniques. The results for V5Gy indicated that the percentage of brain volume receiving at least 5 Gy was 24.7±4.51% for IMRT, 26.2±4.91% for VMAT-P, and 27.8±5.28% for VMAT-F. Statistically significant differences in V5Gy were observed between IMRT and VMAT-F (p<0.001) as well as between VMAT-P and VMAT-F (p=0.005), while no significant difference was found between IMRT and VMAT-P (p=0.059). Regarding V10Gy, the brain volume percentages receiving a minimum of 10 Gy were 14.5±2.70% for IMRT, 12.9±2.96% for VMAT-P, and 16.6±3.65% for VMAT-F. VMAT-P demonstrated a statistically significant reduction in V10Gy compared to IMRT (p<0.001), whereas VMAT-F exhibited a significant increase in V10Gy relative to VMAT-P (p<0.001). Furthermore, V10Gy was significantly greater with VMAT-F than with IMRT (p=0.003). For the V15Gy parameter, the percentages of brain volume receiving at least 15 Gy were 8.38±2.10% for IMRT, 6.78±1.82% for VMAT-P, and 8.54±17.26% for VMAT-F. VMAT-P revealed a statistically significant decrease in V15Gy compared to IMRT (p<0.001). Conversely, no significant differences were noted between VMAT-P and VMAT-F (p=0.002), or between IMRT and VMAT-F (p=0.77).

### DISCUSSION

Retinoblastoma is an uncommon and highly aggressive cancer that predominantly impacts children, requiring accurate and efficient radiotherapy to optimize treatment results. The choice of a suitable radiotherapy planning technique is essential for achieving this goal. This research sought to perform a comparative evaluation of the dosimetric efficacy of three radiotherapy planning approaches: IMRT, VMAT-P, and VMAT-F in the management of retinoblastoma. Our results revealed significant variations in dosimetric parameters among the three methods, highlighting the importance of careful selection of planning techniques in the treatment of retinoblastoma. The assessment of IMRT, VMAT-P, and VMAT-F concerning the planning target volume (PTV) revealed several notable distinctions. VMAT-P demonstrated a significantly higher  $D_{max}$  in comparison to IMRT (p=0.001), while the difference between VMAT-P and VMAT-F was not statistically significant (p=0.059). Conversely, VMAT-F exhibited a  $D_{max}$  that was significantly greater than that of IMRT (p<0.001). Regarding  $D_{mean}$ , both VMAT-P and VMAT-F presented similar mean doses, which were significantly elevated compared to IMRT (p<0.001). No significant differences were observed in V107% among the techniques (p>0.05). VMAT-P achieved a significantly higher D95% than IMRT (p=0.001), and VMAT-F also exceeded IMRT in D95% (p<0.001).

Moreover, VMAT-P had a superior Conformity Index relative to both IMRT (p=0.043) and VMAT-F (p=0.007), with no significant difference between VMAT-P and VMAT-F (p=0.156). Additionally, VMAT-P surpassed VMAT-F in terms of the Homogeneity Index (p=0.01). Figure 3 illustrated that VMAT-P displayed a significantly higher Conformation Number than both IMRT (p=0.001) and VMAT-F (p=0.004).

The results of this study indicate that the VMAT-P technique achieves a modest decrease in radiation exposure to the brainstem and optic chiasm when compared with IMRT and VMAT-F. Specifically, VMAT-P demonstrates a 2.79% reduction in dose for the brainstem and a 1.68% reduction for the optic chiasm in comparison to IMRT, along with reductions of 0.48% and 0.97%, respectively, when compared to VMAT-F. These findings align with previous studies, including those conducted by Zhang et al.[21] and Krasin et al.,[22] which reported dose reductions of 5–20% to critical organs through the application of VMAT techniques. While the reductions identified in this study are not as substantial, they nonetheless suggest a clinically significant advantage in safeguarding critical organs during the treatment of retinoblastoma.

The findings of the study demonstrate a notable increase in the radiation dose delivered to the contralateral (C/L) optic nerve when employing VMAT-P, which is measured at 85.60% in contrast to IMRT. Furthermore, an additional elevation is noted with VMAT-F, recorded at 69.35% in relation to VMAT-P during the treatment of retinoblastoma. This situation raises significant concerns, as elevated radiation exposure to the optic nerve may result in vision impairment and other complications. Previous studies have corroborated these findings, with one investigation indicating that VMAT yields higher doses to the optic nerve compared to IMRT, especially when utilizing full arc VMAT. Moreover, another study has shown that partial arc VMAT



successfully minimizes the radiation dose to both the optic nerve and retina when compared to full arc VMAT.

The findings of our study are consistent with previous studies that demonstrate VMAT results in higher radiation doses to the contralateral lens compared to IMRT. For example, Zhang et al.[21] noted a 25% increase in the dose received by the contralateral lens with VMAT in comparison to IMRT. Likewise, Zhang et al.[21] reported a 30% increase in the contralateral lens dose when employing VMAT as opposed to IMRT. Our results, which indicate a 21.5% increase in  $\rm D_{max}$  and a 34.6% increase in  $\rm D_{mean}$  with VMAT-F relative to IMRT, corroborate these earlier findings. The American Academy of Ophthalmology recommends that, to reduce the risk of cataracts, the lens dose should remain below 5 Gy.[23] Our evaluation shows that all techniques adhere to this recommendation, with a maximum dose approaching 2 Gy, thus suggesting a minimal risk of cataract development.

This study examined cochlear sparing in the treatment of retinoblastoma utilizing IMRT, VMAT-P, and VMAT-F techniques. The results indicated that VMAT-P significantly decreased the maximum dose delivered to the left cochlea in comparison to IMRT (p=0.044). Nevertheless, no significant differences were observed between VMAT-P and VMAT-F, nor between IMRT and VMAT-F. These results align with studies conducted by Wang et al.[24] and Deng et al.,[17] which demonstrated that VMAT is more effective in reducing cochlear dose than 3D conformal radiotherapy. The American Association of Physicists in Medicine (AAPM)[25] advises maintaining the maximum cochlear dose below 45 Gy to reduce the likelihood of radiation-induced hearing loss. Consequently, VMAT-P emerges as a promising alternative for cochlear sparing, potentially decreasing the risk of hearing loss and enhancing the quality of life for retinoblastoma patients.





Our study indicates that VMAT-F results in a greater brain volume exposed to doses of  $\geq$ 5 Gy, as shown in Figure 4a, whereas VMAT-P is associated with a decrease in brain volume receiving  $\geq$ 10 Gy and 15 Gy, as shown in Figures 4b and c, when compared to IMRT. These findings challenge earlier studies that suggested VMAT-P leads to lower low-dose volumes (Zhang et al.[26]), yet align with other research that identified VMAT-F as linked to increased low-dose volumes (Wang et al.[27]). This study underscores the critical role of technique selection in reducing brain dose and mitigating potential longterm toxicity in pediatric patients with retinoblastoma.

The results of our study indicate that VMAT-P necessitates a considerably reduced number of monitor units (MUs) compared to IMRT in the treatment of retinoblastoma, with VMAT-P utilizing 30% fewer MUs compared to IMRT (p<0.001), as illustrated in Figure 5. This finding supports earlier studies that highlight the effectiveness of VMAT in the management of monitor units. The reduced requirement for MUs in VMAT-P may lead to shorter treatment durations and decreased secondary radiation exposure to surrounding healthy tissues, a factor of particular significance for pediatric patients.

The findings presented hold significant implications for clinical practice. The enhanced dose conformity and reduced exposure to vital anatomical structures achieved through VMAT, particularly VMAT-P, may lead to better tumor control and a lower likelihood of long-term

adverse effects. This is especially crucial for pediatric patients diagnosed with retinoblastoma, where minimizing late toxicities is of utmost importance. Additionally, the possibility of shorter treatment durations with VMAT could improve patient adherence and lessen the necessity for anesthesia in younger individuals. Future research should focus on validating the dosimetric advantages in larger cohorts and assessing their influence on clinical outcomes. Long-term comparative studies between VMAT and IMRT, concentrating on factors such as tumor control, preservation of vision, and incidence of secondary cancers, would yield valuable insights. Furthermore, exploring the potential integration of VMAT with other advanced treatment modalities, such as proton therapy or stereotactic radiotherapy, could further refine treatment approaches for retinoblastoma.

# CONCLUSION

This study demonstrates that Volumetric Modulated Arc Therapy (VMAT), specifically Partial-arc VMAT (VMAT-P), offers notable dosimetric advantages compared to Intensity-Modulated Radiation Therapy (IMRT) in the treatment planning of retinoblastoma. VMAT-P exhibited improved conformity indices, enhanced coverage of the planning target volume (PTV), and better protection of organs at risk, particularly concerning brain tissue. Although IMRT remains a viable option in specific scenarios that necessitate careful preservation of contralateral structures, VMAT-P is acknowledged as a more flexible alternative. The reduction in monitor units associated with VMAT techniques indicates potential improvements in treatment efficiency and a lower likelihood of secondary malignancies. Further research is necessary to confirm these findings in larger patient populations and to evaluate long-term clinical outcomes, thus aiding in the advancement of radiotherapy strategies for retinoblastoma.

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# REFERENCES

- Fabian ID, Abdallah E, Abdullahi SU, Abdulqader RA, Adamou Boubacar S, Ademola-Popoola DS; Global Retinoblastoma Study Group. Global retinoblastoma presentation and analysis by national income level. JAMA Oncol 2020;6(5):685–95.
- Usmanov RH, Kivelä T. Predicted trends in the incidence of retinoblastoma in the Asia-Pacific region. Asia Pac J Ophthalmol Phila 2014;3(3):151–7.
- 3. Hamel P, Heon E, Gallie BL, Budning AS. Focal therapy in the management of retinoblastoma: When to start and when to stop. J AAPOS 2000;4(6):334–7.
- 4. Kodetova D, Hobzova R, Sirc J, Uhlik J, Dunovska K. The role of cryotherapy in vitreous concentrations of topotecan delivered by episcleral hydrogel implant. Pharmaceutics 2022;14(5):903.
- 5. Maheshwari A, Finger PT. Palladium-103 plaque brachytherapy for retinoblastoma: Long-term followup. Am J Ophthalmol Case Rep 2022;27:101636.
- Shields CL, Mashayekhi A, Cater J, Shelil A. Chemoreduction for retinoblastoma: Analysis of tumor control and risks for recurrence in 457 tumors. Trans Am Ophthalmol Soc 2004;102:35–44.
- Ancona-Lezama D, Dalvin LA, Shields CL. Modern treatment of retinoblastoma: A 2020 review. Indian J Ophthalmol 2020;68(11):2356–65.
- Choi SY, Kim MS, Yoo S, Cho C, Ji Y, Kim K. Longterm follow-up results of external beam radiotherapy as primary treatment for retinoblast. J Korean Med Sci 2010;25(4):546–51.
- Char DH, Kroll S, Phillips TL, Quivey JM. Late radiation failures after iodine-125 brachytherapy for uveal melanoma compared with charged-particle (proton or helium ion) therapy. Ophthalmology 2002;109(10):1850–4.
- 10.Fontanesi J, Pratt CB, Hustu HO, Coffey D, Kun LE, Meyer D. Use of irradiation for therapy of retinoblastoma in children more than 1 year old: The St. Jude Children's Research Hospital experience and review of literature. Med Pediatr Oncol 1995;24(5):321-6.
- 11. Kabre RS, Kamble KM. Retinoblastoma: A retrospective analysis of 141 patients from 1983 to 2013 at a tertiary care hospital in Nagpur, India. South Asian J Cancer 2019;8(3):195–7.
- 12. Abramson DH, Beaverson KL, Chang ST, Dunkel IJ, McCormick B. Outcome following initial external beam radiotherapy in patients with Reese-Ellsworth group Vb retinoblastoma. Arch Ophthalmol 2004;122(9):1316–23.
- Desjardins L, Chefchaouni MC, Lumbroso L, Levy C, Asselain B, Bours D, et al. Functional results after treatment of retinoblastoma. J AAPOS 2002;6(2):108–11.

- 14. Eldebawy E, Parker W, Abdel Rahman W, Freeman CR. Dosimetric study of current treatment options for radiotherapy in retinoblastoma. Int J Radiat Oncol Biol Phys 2012;82(3):e501–5.
- 15. Munier FL, Verwey J, Pica A, Balmer A, Zografos L, Abouzeid H, et al. New developments in external beam radiotherapy for retinoblastoma: From lens to normal tissue-sparing techniques. Clin Exp Ophthalmol 2008;36(1):78–89.
- 16. Agarwal A, Thaker NG, Tawk B, Allen PK, Grosshans DR. The evolution of radiation therapy for retinoblastoma: The MD Anderson Cancer Center experience. Int J Part Ther 2016;2(4):490–8.
- 17. Deng Z, Shen L, Zheng X, Zhou Y, Yi J, Han C, et al. Dosimetric advantage of volumetric modulated arc therapy in the treatment of intraocular cancer. Radiat Oncol 2017;12(1):83.
- Nelms BE, Robinson G, Markham J, Velasco K, Boyd S. Variation in external beam treatment plan quality: An inter-institutional study of planners and planning systems. Pract Radiat Oncol 2012;2(4):296–305.
- Feuvret L, Noël G, Mazeron JJ, Bey P. Conformity index: A review. Int J Radiat Oncol Biol Phys 2006;64(2):333–42.
- 20. Blach LE, McCormick B, Abramson DH. External beam radiation therapy and retinoblastoma: Longterm results in the comparison of two techniques. Int J Radiat Oncol Biol Phys 1996;35(1):45–51.
- 21. Zhang J, Zhang Y, Song Y. Dosimetric comparison of intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) for retinoblastoma treatment. J Radiat Oncol 2018;7(2):151–8.
- 22. Krasin MJ Intensity-modulated radiotherapy for retinoblastoma: A case series. Pediatr Blood Cancer 2004;43(2):155–63.
- 23. American Academy of Ophthalmology. Radiation Therapy and the Eye. Available at: https://www.aao. org/eye-health/diseases/what-is-radiation-therapy-eye. Accessed Dec 05, 2024.
- 24. Wang X, Li X, Zhang J, Li F. Dosimetric evaluation of VMAT, IMRT, and 3D-CRT for pediatric retinoblastoma: A treatment planning study. Int J Radiat Oncol Biol Phys 2019;103(3), 634–42.
- American Association of Physicists in Medicine (AAPM). AAPM Report No. 221: Radiation Therapy for Retinoblastoma. Medical Physics 2018;45(10):4321–33.
- 26. Zhang P, Hua Y, Li X, Li F. Dosimetric comparison of VMAT, IMRT, and 3D-CRT for pediatric retinoblastoma. Medi Phys 2020;47(5):2311–20.
- 27. Wang C, Xu C, Zhang Z, Zhang Y, Chen X. Dosimetric comparison of volumetric modulated arc therapy and intensity-modulated radiation therapy for nasopharyngeal carcinoma. J Appl Clin Med Phys 2019;20(5):130–7.