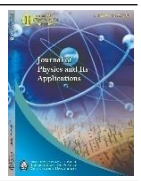
Journal of Physics and Its Applications

Journal homepage : https://ejournal2.undip.ac.id/index.php/jpa/index



A Better 3D Conformal Approach in Glioblastoma Proximates Intensity Modulated One: A Dosimetric Study

Sadiq Ullah[1], Hashir Saeed[1], Sunnia Shafiq[1*], Hafiz Khush Naseeb[2], and Hina Manzoor[1]

[1]*Department of Medical Physics, Center of Nuclear Medicine and Radiation Oncology (CENAR), Quetta, Pakistan*
[2]*Department of Nuclear Medicine, Center of Nuclear Medicine and Radiation Oncology (CENAR), Quetta, Pakistan*

**Corresponding author: Suniyakhan19@gmail.com*

ARTICLE INFO

Article history:
Received: 9 September 2024
Accepted: 21 February 2025
Available online: 31 May 2025

Keywords:
Three-Dimensional Conformal Radiation Therapy
Intensity Modulated Radiation Therapy
Glioblastoma
Monitor Units
Brain tissue

ABSTRACT

This study aimed to evaluate whether Three-Dimensional Conformal Radiation Therapy (3D-CRT) could achieve results comparable to Intensity Modulated Radiation Therapy (IMRT) in treating grade 4 glioblastoma. Treatment plans for 80 consecutive patients with grade 4 glioblastoma, treated between January 1, 2020, and July 31, 2024, were developed using 3D-CRT and IMRT. 3D-CRT utilized three to five fields with dynamic wedges and the field-in-field technique, while IMRT employed seven fields with homogeneous angles. Target coverage was set to ensure that 97% of the isodose covered 98% of the Planning Target Volume (PTV). Both 3D-CRT and IMRT achieved similar target coverage. However, IMRT showed superior homogeneity (0.053 vs. 0.097) and conformity (1.187 vs. 1.663) compared to 3D-CRT. IMRT also provided better sparing of normal brain tissue and surrounding organs, except for the contralateral eye, though it required longer treatment delivery time due to higher Monitor Units (MUs). IMRT additionally limited low-dose escalation. IMRT outperforms 3D-CRT in homogeneity, conformity, and sparing organs at risk, despite the longer treatment time. 3D-CRT may approximate IMRT when the target volume is not near critical structures but still results in greater low-dose exposure to normal brain tissue for the same target coverage.

1. Introduction

Radiation therapy seeks to provide the prescribed radiation dose to the target volume or tumor and to spare normal tissues and close by organs [1]. Intensity Modulated Radiation Therapy (IMRT), an advanced inverse planning technique, is frequently preferred over Three-Dimensional Conformal Radiation Therapy (3D-CRT) because of its greater target conformity and OAR sparing. [2-5]. Glioblastomas are mostly treated with surgery followed by radiation and chemotherapy [6]. Chemotherapy and radiation therapy after maximum surgical resection have increased survival in patients after advancements in chemotherapy and radiation therapy techniques, but unfortunately, late radiation toxicity is at high risk in these patients [7]. With the increase in long-term survival, cases of long-term radiation toxicities are observed in patients. To decrease the long-term side effects of radiation therapy more conformal and advanced techniques in radiation therapy are clinically important [8]

Several studies, including Lorentini et al. (2013), have defined dosimetric criteria for deciding between IMRT and 3D-CRT in glioblastoma therapy, emphasizing the superior dose uniformity and normal tissue protection obtained with IMRT. Radiation therapy in glioblastoma is usually delivered in 30 or 33 fractions with 2 or 1.8 Gy dose per fraction using the three-dimensional conformal radiotherapy (3DCRT) technique or intensity-modulated radiotherapy (IMRT) technique [9].

Similarly, Thibouw et al. (2018) and MacDonald et al. (2007) revealed that IMRT dramatically minimizes high-dose exposure to important structures such as the brainstem and optic chiasm while providing enough tumor coverage [6,8]. Glioblastoma is unfortunately radiation resistant with poor prognosis. Additionally, the large size of these tumors makes them difficult to plan for radiation therapy. To avoid severe toxicity, organs at risk (OARs) must be within the radiation dose limit [10]. OARs that are adjacent to planning target volume can be spared better with IMRT, as proved in many studies [11].

IMRT is a technically advanced form of 3D-CRT in which photon flux is modulated which results in better conformity of planning target volume with the sparing of adjacent critical organs [12]. The dose distribution in IMRT increases the therapeutic ratio in large tumors like glioblastomas. However, despite its advantages, IMRT needs longer treatment

delivery periods and greater Monitor Units (MUs), which might increase intra-fraction motion and total radiation exposure to normal tissues. [13]. As IMRT is an inverse planning system so the treatment planning time as compared to 3DCRT is 2 to 3 times shorter. Proper wedge and field angle selections to make isodose level conformal with planning volume and to save critical adjacent organs 3DCRT require a lot more time. In contrast, 3D-CRT, with adequate beam organization and field modulation, may approximate IMRT in some circumstances, particularly when the tumor is positioned away from important structures. [14]. In terms of monitor units delivered, IMRT always delivers a lot more MUs than 3DCRT (approximately 65% in a study of glioblastoma with all fields of 6 MV) [15]. This increases patient treatment time and the risk of intra-fraction motion. Moreover, IMRT is more conformal than 3DCRT and due to intra-fraction motion probability of missing GTV is enhanced in IMRT. The increased number of treatment fields in IMRT as compared to 3DCRT increases the time for treatment also. Previous research has concentrated on generalized dosimetric comparisons, but there has been little investigation into whether 3D-CRT may attain IMRT-like outcomes under specific clinical situations [16].

This study aims to address this gap by determining if 3D-CRT may imitate IMRT in grade 4 glioblastoma treatment while maintaining treatment efficiency and dosimetric quality. This work sheds light on how to optimize radiation treatments for glioblastoma patients depending on tumor location and clinical restrictions by analyzing dose distributions, conformity indices, and normal tissue sparing.

2. Methods

This study compares IMRT and 3D-CRT treatment plans for 80 consecutive patients diagnosed with post-surgical grade IV glioblastoma at the Atomic Energy Cancer Hospital (AECH), Centre for Nuclear Medicine and Radiotherapy (CENAR), Quetta, from January 1, 2020 to July 31, 2024. Patients were treated according to normal clinical protocols, and treatment data were analyzed retrospectively to compare dosimetric discrepancies between the two approaches.

All patients had histological evidence of grade IV glioblastoma via biopsy or post-operative tissue examination. Prior to and following surgery, contrast-enhanced MRI (T1-weighted, T2-weighted) and CT scans were used to localize and stage the tumor. Each patient underwent maximum safe resection, followed by a post-operative MRI within 48 hours to determine the degree of remaining tumor. Adjuvant chemotherapy with temozolomide (75 mg/m^2/day) was given concurrently with radiation therapy, followed by adjuvant temozolomide in a 5/28 day cycle.

For radiation therapy planning, all patients underwent CT simulation with a Toshiba Aquilion (16-slice) scanner with a 3-mm slice thickness and interval. To ensure repeatability and reduce movement, thermoplastic masks with compatible headrests were utilized to immobilize subjects in the supine position. To improve tumor visibility, intravenous Omnipaque contrast was injected.

The target volume was delineated using MRI and CT imaging, in accordance with normal radiation oncology standards. The following volumes were contoured: 1) Gross Tumor Volume (GTV), defined using post-surgical MRI, 2) Clinical Target Volume (CTV) is the GTV plus a non-uniform margin of 1-2.5 cm to accommodate for microscopic tumor spread, 3) Planning Target Volume (PTV) is CTV plus an additional buffer to account for setup uncertainties, 4) Organs at Risk (OARs) include the complete brain, normal brain (without PTV), optic chiasm, optic nerves, lenses, cochlea, parotids, and brainstem.

Treatment plans were developed using Varian Eclipse version 15.5. Patients were scheduled to receive 60 Gy in 30 fractions with either 3D-CRT or IMRT. 3D-CRT: Plans were designed with 3 to 5 fields, dynamic wedges, and the field-in-field approach to promote dose uniformity. IMRT: Plans were created using seven fields with homogenous angles and the multi-leaf collimator (MLC) sliding window approach, also known as dynamic MLC mode. Radiation therapy was delivered via a Varian Clinac iX linear accelerator with a 6 MV photon beam.

To compare IMRT and 3D-CRT plans, dose-volume histograms (DVHs) were created, and the following dosimetric characteristics were evaluated: 1) Target Coverage: Plans were normalized to ensure that 97% of the isodose covered 98% of the total PTV, 2) Homogeneity Index (HI) assessed dosage consistency within the PTV, 3) Conformity Index (CI) determined how well the treatment dose matched the target volume, 4) Organ at Risk (OAR) Dose, the mean and maximum doses for OARs were compared using IMRT and 3D-CRT.

Statistical analysis was used to establish the importance of the variations in target coverage, dosage homogeneity, conformance, and OAR sparing between the two approaches. Patient positioning was initially checked for 2 days continuously then after every 2 days. For the positioning check electronic portal imaging device (EPID) was exposed with 6 MV photons.

The whole brain, normal brain (whole brain without PTV), optic chiasm, optical nerves, optical lens, cochlea, parotids, and brainstem were contoured as organs at risk. The homogeneity index and conformity index were used to evaluate the quality of plans by using the following formulas [3].

$$\text{Homogeneity Index (HI)}: \frac{D2\% - D98\%}{D50\%} \qquad (1)$$

Where D2%, D98%, D50% are doses for 2%, 98%, and 50% of the target volumes (PTV) respectively.

$$\text{Conformity Index (CI)}: \frac{TV95\% \times PTV}{(O.V)^2} \qquad (2)$$

Where TV95% is the volume of the isodose curve which covers 95% of the prescribed dose, PTV is the planning target volume, and O.V. is the volume of the overlapping region of PTV and TV95% [17].

A linear accelerator has a millennium 120 leaf with a transmission factor of 1.5%. For better conformity 7 field plans of IMRT were made in all patients. The gantry angle between each field was the same for all fields. For fair comparison, only 6 MV beam was used. The analytical anisotropic algorithm (AAA) version 15.6.04 was used for dose calculation in all plans which is a 3D pencil beam convolution-superposition algorithm.

In all patients, volume normalization was used in which 97% of the isodose curve covered 98% of the planning target volume. These plan normalization parameters were considered constant for all IMRT and 3DCRT plans. Dose constraints provided by QUANTEC were used for all plans [18].

3. Result and Discussion

In 3D-CRT three to five fields were used with dynamic wedges, field-in-field technique, or both, while in IMRT seven fields with homogenous angles were used. For IMRT more monitor units were required than 3D-CRT per fraction. Representative sagittal isodose distributions are shown for the 3D-CRT plan in Fig. 1(a) and the IMRT plan in Fig. 1(b). IMRT displayed greater conformity and homogeneity compared to 3D-CRT, as seen in Fig. 1(b), where the 95% isodose line (green) closely follows the planned target volume (PTV) with minimum dose leakage into neighboring tissues. Fig. 1(a) (3D-CRT) demonstrates a less conformal dose distribution, with lower-dose exposure extending beyond the PTV. These findings are consistent with the findings of Lorentini et al. (2013), who emphasized that IMRT improves conformity and homogeneity through inverse planning optimization [7]. Similarly, MacDonald et al. (2007) showed that IMRT reduces the distribution of high-dose zones while preserving target coverage, which is consistent with our findings [6].

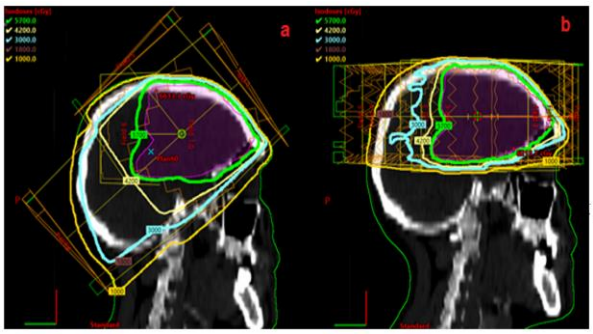


Fig. 1: a) 3D-CRT sagittal isodose distribution, b) IMRT sagittal isodose distribution

The average conformity for IMRT plans was a cut above 3D-CRT plans as manifested in both figures. Green isodose curves are showing a 95% isodose distribution. A major observation from Fig. 1(a) is that 3D-CRT produces a broader low-dose distribution, as illustrated by the 50% isodose curves (sky blue), which extends into normal brain tissue. In contrast, Fig. 1(b) (IMRT) shows a quicker dose fall-off, which limits unwanted irradiation to normal tissues. This conclusion supports the findings of MacDonald et al. (2007), who discovered that IMRT successfully limits low-dose exposure, potentially lowering late radiation toxicity [6].

Despite its benefits, IMRT is associated with a higher total dose to normal brain tissue due to the increased number of beams and monitor units (MUs). Thibouw et al. (2018) found that, while IMRT improves target conformity, it significantly increases total radiation exposure to non-target tissues due to the utilization of different beam angles [8]. Our findings support this view, since Fig. 1(b) indicates slightly higher dose deposition in the contralateral hemisphere than Fig. 1(a), though the values remain within acceptable clinical limits.

Despite its benefits, IMRT is associated with a higher total dose to normal brain tissue due to the increased number of beams and monitor units (MUs). Thibouw et al. (2018) found that, while IMRT improves target conformity, it significantly increases total radiation exposure to non-target tissues due to the utilization of different beam angles [8]. Our findings support this view, since Fig. 1(b) indicates slightly higher dose deposition in the contralateral hemisphere than Fig. 1(a), though the values remain within acceptable clinical limits.

The comparison of Fig. 1(a) and Fig. 1(b) demonstrates IMRT's dosimetric advantages in terms of target conformity and OAR sparing, making it the preferred treatment option for glioblastoma, especially when the tumor is near important structures. However, 3D-CRT remains a feasible option when shorter treatment times are required when the tumor is located far from essential organs. These findings are consistent with the findings of Wagner et al. (2009), who proposed that 3D-CRT might still mimic IMRT under certain clinical situations [4].

The conformity index and homogeneity index are two basic parameters to analyze a treatment plan. Scientists use different formulas to describe the homogeneity index but there is no ideal formula to calculate the homogeneity index [3]. According to the formulas (1&2) used in this study ideal value for the conformity index is 1 and for the homogeneity index ideal value is 0. If values increase from their ideal values, the plan becomes less conformal and homogenous. Although the target coverage of both IMRT and 3DCRT are alike the IMRT plans provided superior conformity index and homogeneity index for all cases as shown in Table 1.

Table 1: Averaged Conformity & Homogeneity Index Comparison

IMRT		**3DCRT**	
CI±SD	**HI±SD**	**CI±SD**	**HI±SD**
1.187±0.04	0.053±0.02	1.663±0.22	0.097±0.03

Planning Target Volume (PTV) can be at different regions of brain. If PTV is away from critical organs like brainstem and optic chiasm etc. then 3D-CRT can approximate IMRT in target coverage and sparing critical organs with additional benefit of less treatment time. In this study Dose Volume Histograms (DVHs) of PTV, brainstem and optic chiasm for two cases of glioblastoma are shown in Fig. 2. PTV in frontal region causes high dose to brainstem and optic chiasm and IMRT presented better sparing of critical organs. PTV in parietal and temporal region had some distance from brainstem and optic chiasm, due to which they receive minimal dose. IMRT can provide better sparing where target is close by critical organs. In opposite case 3D-CRT can proximate IMRT in target coverage and sparing normal organs. However, IMRT had an upper hand in conformity and homogeneity as discussed earlier.

Planning Target Volume (PTV) can be at different regions of brain. If PTV is away from critical organs like brainstem and optic chiasm etc. then 3D-CRT can approximate IMRT in target coverage and sparing critical organs with additional benefit of less treatment time. In this study Dose Volume Histograms (DVHs) of PTV, brainstem and optic chiasm for two cases of glioblastoma are shown in Fig. 2. PTV in frontal region causes high dose to brainstem and optic chiasm and IMRT presented better sparing of critical organs. PTV in parietal and temporal region had some distance from brainstem and optic chiasm, due to which they receive minimal dose. IMRT can provide better sparing where target is close by critical organs. In opposite case 3D-CRT can proximate IMRT in target coverage and sparing normal organs. However, IMRT had an upper hand in conformity and homogeneity as discussed earlier.

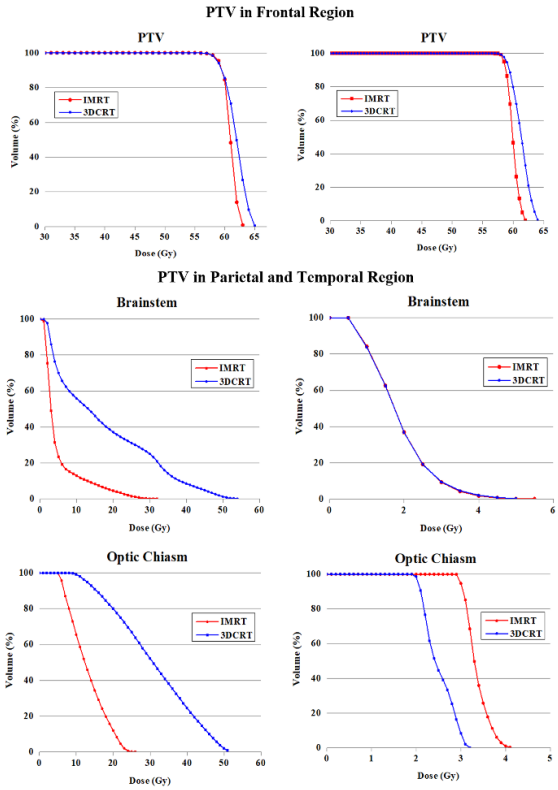


Fig. 2: DVHs comparison of PTV, Brainstem, and Optic Chiasm for PTV in different regions of Brain

Fig. 2 presents the average conformity index (CI) and homogeneity index (HI) for IMRT and 3D-CRT. Our analysis indicated that IMRT had a considerably improved conformity index (1.187 ± 0.04) compared to 3D-CRT (1.663 ± 0.22). This is similar with findings from Chan et al. (2003), who demonstrated greater dose conformity in IMRT-treated glioblastoma cases [10]. Our investigation found that IMRT had a lower homogeneity index (HI) (0.053 ± 0.02) compared to 3D-CRT (0.097 ± 0.03), indicating improved dosage uniformity. This is consistent with the findings of Amelio et al. (2010) [9]. However, Hermanto et al. (2007) discovered that IMRT's enhanced conformance can result in underdosing in the periphery of the target volume due to intra-fraction motion, a restriction that should be considered in clinical decision-making [11].

The main organs at risk involved in most GBM cases are the brain stem, optic chiasm, lens, optic nerves, cochlea, parotids, eyes, and normal brain (whole brain minus PTV). Sparing organs at risk and normal tissues is also a primary goal of any radiotherapy plan. The mean dose and maximum dose for all close by organs are shown in Fig. 3 and Fig. 4 respectively. IMRT showed better sparing of normal organs as compared to 3D-CRT both for mean and maximum doses. The contralateral eye and lens received more mean and max doses in IMRT as compared to 3D-CRT. This is because in IMRT homogenous field angles are used and in 3D-CRT contralateral eye and lens are spared by avoiding particular field angles. All other close by organs have received significantly less mean and maximum dose in IMRT plans.

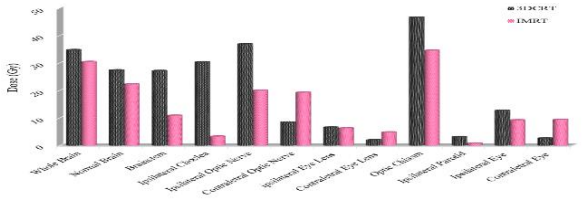


Fig. 3: Mean Dose Comparison of OARs for 3D-CRT & IMRT

Fig. 3 (Mean dosage Comparison): IMRT resulted in a lower mean dosage to most OARs, with the exception of the contralateral eye and lens, which received somewhat greater doses due to numerous beam angles. This is consistent with the findings of Zach et al. (2009), who discovered that IMRT delivers improved brainstem and optic chiasm sparing while potentially increasing dosage to distant OARs due to beam design [5].

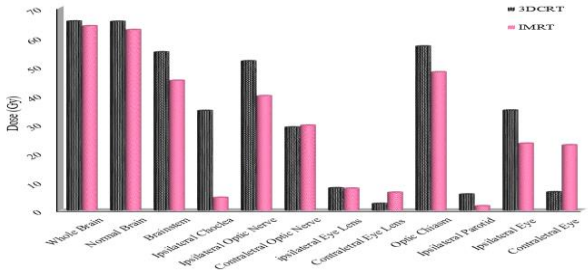


Fig. 4: Dmax Comparison of OARs for 3D-CRT & IMRT

Fig. 4 (Maximum dosage Comparison) shows that IMRT dramatically lowered the maximum dosage to the brainstem, optic nerves, and cochlea compared to 3D-CRT. Wagner et al. (2009) found a similar pattern, claiming that IMRT is more effective in sparing key structures in high-grade glioma treatments [4]. In all 80 patients together, IMRT provided a trend of scaling down healthy brain irradiation as compared to 3D-CRT. Data for normal brain irradiation is presented in Table 2. The differences were statistically significant for all dose values.

Fig. 5 shows a significant reduction in radiation dose to multiple volumes of the brain in IMRT in comparison with 3D-CRT. IMRT provided an additional benefit by limiting low-dose escalation in the normal brain. Gray bars in Fig. 5 are representing the percentage dose received by each volume of normal brain in IMRT, which are significantly low than 3D-CRT radiation doses received by each volume of brain represented by blue bars. The percentage difference in dose received by different volumes varies from 3.48% to 16.26%.

Table 2: Normal Brain Irradiation: Dosimetric Comparison

Dose Level	3D-CRT (%)	IMRT (%)	P-values	%Difference
V60	29.01	25.54	0.14	-3.48
V55	33.47	29.49	0.01	-3.98
V50	38.25	33.06	0.01	-5.19
V45	42.08	36.50	0.01	-5.58
V40	45.34	40.34	0.01	-5.00
V35	53.05	44.00	< 0.01	-9.06
V30	59.99	48.33	< 0.01	-11.66
V25	66.25	51.66	0.01	-14.59
V20	71.73	57.04	< 0.01	-14.69
V15	80.22	64.02	< 0.01	-16.21
V10	89.97	73.71	< 0.01	-16.26
V5	98.40	87.34	< 0.01	-11.07

Table 2 and Fig. 5 show a dose-volume comparison of normal brain irradiation using both procedures. Our study discovered that IMRT consistently lowered radiation exposure at all dosage levels (V5-V60) when compared to 3D-CRT. MacDonald et al. (2007) found a 3.5-15% reduction in normal brain irradiation using IMRT, which is similar with the dose reduction observed in our study [6]. Amelio et al. (2010) discovered that IMRT inhibits low-dose escalation more efficiently than 3D-CRT, which is clearly demonstrated by our findings (Fig. 5) [9].

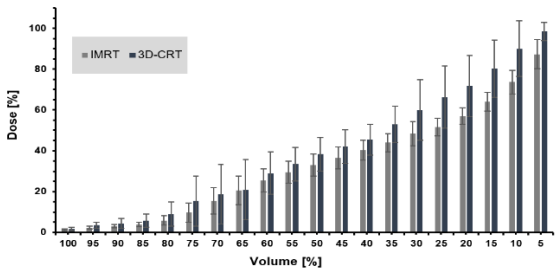


Fig. 5: Healthy brain dosimetric comparison for 3D-CRT and IMRT plans.

The results of all figures and tables show that IMRT delivers superior target conformity and OAR sparing, making it the ideal approach for glioblastoma therapy when precision is required. However, 3D-CRT remains a viable option in circumstances when shorter treatment times and lower total doses are preferred, especially when the tumor is far from important structures. These findings are consistent with Hermanto et al. (2007) and Thibouw et al. (2018), who stated that IMRT should be used sparingly, weighing the benefits against potential drawbacks such as increased integral dosage and extended treatment time [8,11].

4. Conclusions

Intensity modulated radiation therapy (IMRT) and three-dimensional conformal radiation therapy (3D-CRT) are compared in this study with an emphasis on target coverage, homogeneity, conformity, and preservation of normal tissues in the treatment of grade 4 glioblastoma. Although IMRT and 3D-CRT are well-established methods with well-defined objectives for target coverage, their performance is directly compared in this study. The results show that IMRT outperforms 3D-CRT in sparing the majority of at-risk organs and attaining improved uniformity and conformity in radiation distribution. Comparing IMRT to 3D-CRT, however, necessitates longer treatment delivery periods and lower dose escalation.

This study's main conclusion is that, even with its lengthier treatment durations, IMRT should be used in situations when precision dosage distribution and the preservation of vital organs are crucial. On the other hand, 3D-CRT might be a preferable choice when cutting down on treatment time is a top concern, particularly in situations when the target volume is not close to vital structures. The paper also makes recommendations for future research into strategies for shortening IMRT treatment durations and indicates that there may be room to improve 3D-CRT approaches to lessen low-dose escalation. This comparison offers clinicians important information about how to balance the advantages of treatment efficiency and dose precision when choosing the best course of action for patients with grade 4 glioblastoma.

Acknowledgment

We would like to express our thanks to the colleagues of the Department of Medical Physics, CENAR Hospital Quetta for their contribution.

References

[1] E. Bakiu, E. Telhaj, E. Kozma, and F. Ruci, "Comparison of 3D CRT and IMRT Treatment Plans" ACTA INFORM MED, 21, 211-212, (2013).

[2] A. Narayana, J. Yamada, S. Berry, P. Shah, and M. Hunt, "Intensity-modulated radiotherapy in high grade gliomas: clinical and dosimetric results" Radiat Oncol Biol Phys, 64, 892-897, (2006).

[3] D. Petrova, S. Smickovska, and E. Lazarevska, "Conformity Index and Homogeneity Index of the Postoperative Whole Breast Radiotherapy" Journal of Medical Sciences, 5, 736-739, (2017).

[4] D. Wagner, H. Christiansen, H. Wolff, and H. Vorwerk, "Radiotherapy of malignant gliomas: comparison of volumetric single arc technique (RapidArc), dynamic intensity-modulated technique and 3D conformal technique" Radiother Oncol, 93, 593-596, (2009).

[5] L. Zach, B. Stall, H. Ning, J. Ondos, B. Arora, and S. Uma, "A dosimetric comparison of four treatment planning methods for high grade glioma" Radiat Oncol, 4, 45, (2009).

[6] I. K. M. Lauren R. Schaff, "Glioblastoma and Other Primary Brain Malignancies in Adults" Jama, 329, 574-587, (2023).

[7] Vilashini Rajaratnam, M. M. I. M. Y. R. S. M. R., and S. P. M., "Glioblastoma: Pathogenesis and Current Status of Chemotherapy and Other Novel Treatments" Cancers, 12, 937, (2020).

[8] S. M. MacDonald, S. Ahmad, S. Kachris, B. J. Vogds, M. DeRouen, A. E. Gittelman, K. DeWyngaert, and M. T. Vlachaki, "Intensity modulated radiation therapy versus three-dimensional conformal radiation therapy for the treatment of high-grade glioma: a dosimetric comparison" Journal of Applied Clinical Medical Physics, 8, 47-60, (2007).

[9] S. Lorentini, D. Amelio, M. G. Giri, F. Fellin, G. Meliado, A. Rizzotti, M. Amichetti, and M. Schwarz, "IMRT or 3DCRT in Glioblastoma? A Dosimetric Criterion for Patient Selection" Technology in Cancer Research and Treatment, 12, 411-420, (2013).

[10] Stephen Morris, T. R. S. A. S. L., Practical Radiotherapy Planning Boca Raton: CRC Press, (2023).

[11] D. Thibouw, G. Truc, A. Bertaut, C. Chevalier, L. Aubignac, and C. Mirjolet, "Clinical and dosimetric study of radiotherapy for glioblastoma: three-dimensional conformal radiotherapy versus intensity-modulated radiotherapy" Journal of Neuro-Oncology, (2018).

[12] Aveline Marie D. Ylanan, J. S. G. P., E. M. D. C.-L. K. H. D. I. J. P. A. K. J. O. K., "Intraoperative radiotherapy for glioblastoma: A systematic review of techniques and outcomes" Journal of Clinical Neuroscience, 93, 36-41, (2021).

[13] D. Amelio, S. Lorentini, M. Schwarz, and M. Amichetti, "Intensity-modulated radiation therapy in newly diagnosed glioblastoma: A systematic review on clinical and technical issues" Radiotherapy and Oncology, 97, 361-369, (2010).

[14] M. F. Chan, K. Schupak, C. Burman, C.-S. Chui, and C. C. Ling, "Comparison of intensity-modulated radiotherapy with three-dimensional conformal radiation therapy planning for glioblastoma multiforme" Medical Dosimetry, 28, 261-265, (2003).

[15] U. Hermanto, E. K. Frija, M. J. L., E. L. Chang, A. Mahajan, and S. Y. Woo, "Intensity-Modulated radiotherapy (IMRT) and Conventional three-dimensional conformal radiotherapy for high grade gliomas: Does IMRT increase integral dose to normal brain?" Radiation Oncology, 67, 1135-1144, (2007).

[16] Daniel M. Trifiletti, M. T. M., K. J. R. E. L. P. J. A. H. M. M. K., "Treatment Planning Expansions in Glioblastoma: How Less Can Be More" International Journal of Radiation Oncology Biology Physics, 117, 293-296, (2023).

[17] L. S. Huai, Cheng, J. C. Hsien, K. S. Hsin, and L. J. J. Shenn, "Volumetric modulated arc therapy for nasopharyngeal carcinoma: A dosimetric comparison with TomoTherapy and step-and-shoot IMRT" Radiotherapy and Oncology, 104, 324-330, (2012).

[18] N. P. Brodin and W. A. Tome, "Revisiting the dose constraints for head and neck OARs in the current era of IMRT" Oral Oncology, 86, 8-18, (2018).

[19] M. Piroth, M. Pinkawa, R. Holy, G. Stoffels, C. Demirel, and C. Attieh, "Integrated-boost IMRT or 3-D-CRT using FET-PET based auto-contoured target volume delineation for glioblastoma multiforme-a dosimetric comparison" Radiation Oncology, 4, 57, (2009).