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Dosimetric Comparison of Gamma Knife, Intensity-Modulated Radiation Therapy, and Volumetric Modulated Arc Therapy for Recurrent High-Grade Glioma: Evaluation of Target Coverage, Dose Conformity, Organs-at-Risk Sparing, and Implications for Radiotherapy Practice in Indonesia

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ABSTRACT

Background: Re-irradiation for recurrent high-grade glioma (HGG) requires careful limitation of radiation exposure to previously treated normal brain tissue. Different radiotherapy planning techniques may produce distinct normal-brain dose distributions.

Objective: To compare normal-brain V5 and V12 across Gamma Knife (GK), fixed-field intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), simultaneous integrated boost IMRT (SIB-IMRT), and simultaneous integrated boost VMAT (SIB-VMAT). **Methods:** A comparative treatment-planning analysis was conducted for 19 patients with recurrent HGG at Rumah Sakit Universitas Indonesia, Depok, Indonesia, between February and May 2026. All five techniques were evaluated using the same patient-specific anatomical datasets. Normal-brain V5 and V12, defined as the percentages of normal brain receiving at least 5 Gy and 12 Gy, respectively, were summarized as means ± standard deviations and assessed using paired comparisons. **Results:** Mean V5 values were 52.31 ± 12.38% for GK, 61.83 ± 12.39% for IMRT, 59.95 ± 13.33% for VMAT, 57.73 ± 14.56% for SIB-IMRT, and 60.31 ± 15.65% for SIB-VMAT. Corresponding V12 values were 31.93 ± 11.97%, 42.64 ± 13.24%, 43.61 ± 14.49%, 41.22 ± 14.29%, and 42.12 ± 15.17%. GK yielded significantly lower V12 than each linear-accelerator technique (all $P < 0.001$), whereas its V5 differences from these techniques were not statistically significant (all $P \geq 0.254$). V5 was significantly lower with SIB-IMRT than with conventional IMRT and SIB-VMAT (both $P < 0.001$). V12 was significantly lower with SIB-IMRT than with conventional IMRT ($P = 0.031$) and with SIB-VMAT than with conventional VMAT ($P = 0.039$). The remaining reported pairwise comparisons were not statistically significant. **Conclusion:** GK produced the lowest mean normal-brain V12, with statistically significant differences from all four linear-accelerator approaches. Although GK also had the lowest mean V5, its V5 differences from the other techniques were not statistically significant. Selected SIB approaches reduced V12 relative to their conventional counterparts. These dosimetric findings may inform individualized planning, but do not establish differences in clinical toxicity or treatment outcomes.

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1.INTRODUCTION

High-grade gliomas (HGGs) are aggressive primary brain tumors characterized by infiltrative growth, substantial neurological morbidity, and a high risk of recurrence despite multimodal treatment. [1,2] Management commonly involves maximal safe resection followed by radiotherapy and systemic treatment when clinically appropriate. [3,4] However, recurrent disease remains difficult to control because the tumor may develop within or near a previously irradiated volume, while the surrounding normal brain has already received a clinically relevant radiation dose [5].

Re-irradiation can be considered in selected patients with recurrent glioma, depending on factors such as performance status, recurrence interval, lesion volume, neurological symptoms, previous treatment, and the feasibility of meeting normal-tissue constraints[6]. Contemporary evidence indicates that re-irradiation can be delivered using modern techniques in appropriately selected patients, although its benefits and risks must be assessed individually[7]. For example, the NRG Oncology/RTOG 1205 trial evaluated re-irradiation combined with bevacizumab in recurrent glioblastoma and found improved progression-free disease control measures without a significant overall-survival improvement. [8,9] These findings reinforce the need to distinguish dosimetric feasibility from demonstrated clinical benefit.

Several radiotherapy technologies can be used to shape dose distributions around intracranial targets[10]. Gamma Knife (GK) stereotactic radiosurgery uses multiple converging radiation beams to concentrate dose around a defined target. Its characteristic rapid dose fall-off can be advantageous when limiting irradiation of adjacent brain tissue is a priority[11,12]. Nevertheless, conformity may be affected by target shape, target size, available collimator dimensions, and the number and arrangement of isocenters[13,14].

Linear-accelerator-based intensity-modulated radiation therapy (IMRT) uses multiple fixed radiation fields with modulated fluence to achieve a planned dose distribution[15]. Volumetric modulated arc therapy (VMAT) delivers radiation during gantry rotation while modulating dose rate, gantry speed, and multileaf collimator positions[16]. These approaches can accommodate complex target geometries and may offer flexibility when treating irregular lesions or targets requiring differentiated dose levels[17].

The choice between GK and linear-accelerator-based approaches is particularly important for recurrent HGG, where the goal is not simply to maximize the prescribed dose but to balance target coverage, conformity, homogeneity, and dose exposure to surrounding brain tissue[18,19]. Dosimetric comparisons of GK and linear-accelerator fractionated stereotactic radiotherapy for large recurrent glioblastomas have reported potential normal-brain-sparing advantages for GK under the evaluated planning conditions[20]. However, these results should not be generalized to every target geometry or clinical setting.

A further planning strategy is the simultaneous integrated boost (SIB), in which different target subvolumes receive different dose levels within the same treatment course[21]. For the present analysis, both SIB-IMRT and SIB-VMAT approaches incorporated a central dose escalation strategy while preserving the prescribed dose coverage across the larger target volume. Such an approach may be dosimetrically useful in selected cases, but it requires clear target definitions, a

consistent prescription framework, and careful evaluation of the biological and clinical implications of the dose distribution.

Normal-brain dose-volume parameters are important in evaluating stereotactic treatment plans[22]. The volume receiving a specified dose, such as V5 or V12, provides information about low- and intermediate-dose exposure[23]. The relationship between dose-volume metrics and radiation injury depends on factors including fractionation, irradiated volume, target inclusion or exclusion, and the clinical context[24]. The HyTEC review of brain stereotactic radiosurgery emphasizes the importance of dose-volume assessment and notes that risk estimates derived from single-fraction treatment of brain metastases should not be applied uncritically to other diseases or fractionation schedules[25,26].

Despite the availability of these treatment techniques, their relative advantages cannot be inferred from one metric alone. A plan with a steeper dose gradient may not have the best conformity, and a plan with a high conformity index may not provide the most favorable dose distribution outside the target. Similarly, a higher central dose does not independently establish better tumor control or improved survival[27].

Risk-adapted dose prescription provides a rationale for investigating integrated boost strategies in glioma radiotherapy. Back et al. (2017) [28].compared conventional IMRT with a PET- and MRI-guided integrated boost approach in ten patients with favourable molecular subtype anaplastic glioma. Their protocol prescribed 59.4 Gy to a higher-risk region and 54 Gy to a broader standard-risk region over 33 fractions, and reported reductions in normal-brain dose measures. This study supports investigating how differentiated target prescriptions influence irradiation of surrounding brain tissue. However, its findings cannot be directly extrapolated to recurrent high-grade glioma requiring re-irradiation, where previous radiation exposure and cumulative normal-tissue dose introduce additional planning considerations.

The present study was undertaken to systematically compare five radiotherapy planning strategies—Gamma Knife (GK), fixed-field intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), simultaneous integrated boost IMRT (SIB-IMRT), and simultaneous integrated boost VMAT (SIB-VMAT)—in a cohort of 19 patients with recurrent high-grade glioma treated in Indonesia. The dosimetric evaluation focused on the conformity index (CI), homogeneity index (HI), gradient index (GI), maximum and mean target doses (Dmax and Dmean), and normal-brain V5 and V12. By examining these parameters across the different planning techniques, the study aimed to characterize differences in target-dose distribution, dose conformity, treatment homogeneity, and normal-brain irradiation. Particular attention was given to the potential advantages of SIB-based approaches for achieving enhanced central target dosing while maintaining appropriate coverage of the broader treatment volume. The findings provide a comparative dosimetric basis for individualized radiotherapy planning and optimization in the Indonesian clinical setting.

2. Materials and Methods

2.1. Study design and dataset

Study Design and Setting

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This comparative radiotherapy treatment-planning study was conducted between February and May 2026 at Rumah Sakit Universitas Indonesia (RSUI), also known as the University of Indonesia Hospital, Depok, Indonesia. Five treatment-planning techniques were evaluated using the same patient cohort: Gamma Knife (GK), fixed-field intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), simultaneous integrated boost IMRT (SIB-IMRT), and simultaneous integrated boost VMAT (SIB-VMAT). The analysis focused on target-dose distribution, treatment-plan characteristics, and normal-brain dose exposure.

Patient Selection and Eligibility Criteria

Patients were identified from medical records provided by the hospital and selected using a random sampling approach based on patient-level records. The eligible age range was predefined as 21–84 years. Inclusion required documented recurrent high-grade glioma and sufficient tumor-related clinical information to support the comparative planning analysis.

Exclusion criteria comprised incomplete or unavailable imaging datasets or previous radiotherapy records, and inadequate image quality for reliable target delineation or accurate dose calculation. Four cases were excluded on these grounds, leaving 19 patients in the final analytical cohort.

Patient Characteristics and Dose Standardization

The final cohort comprised 11 males and 8 females, aged 21–84 years, with a median age of 58 years. Planning target volumes (PTVs) ranged from 16.7 to 150.8 cm^3, with a mean of 81.36 ± 39.38 cm^3.

Previous radiotherapy prescriptions ranged from 39 to 50 Gy, delivered in 13–25 fractions. For comparative planning, dose prescriptions were standardized using an equivalent dose in 2-Gy fractions (EQD2) framework, with a reference equivalent dose of 50 Gy. Biological dose conversion followed the parameters specified in the treatment-planning protocol.

All five techniques were evaluated using the same patient-specific anatomical datasets and consistent criteria for target and organ-at-risk delineation, prescribed doses, and treatment-plan evaluation.

Imaging Sources and Treatment-Plan Preparation

Imaging datasets were obtained through the departmental medical records administration at RSUI. These included computed tomography (CT) and magnetic resonance imaging (MRI) datasets used for treatment planning, together with other available patient-specific information obtained during the study period.

The images were transferred for treatment planning and registered to establish anatomical correspondence between the imaging datasets. Original clinical treatment plans were retrieved from the radiotherapy department, and comparative plans were subsequently prepared for the five techniques. Imaging acquisition dates, original treatment dates, and the period allocated to comparative plan preparation were recorded separately.

Ethical Approval, Consent, and Data Access

Ethical approval was obtained from Universitas Indonesia, Depok, Indonesia, under approval number ID/UI/AC/2026/713K8Y44. The medical records, imaging datasets, and original treatment plans used in the analysis were supplied by the hospital for the study.

Written informed consent was obtained from the participating patients. Patient data were de-identified before analysis, and access to the study datasets was restricted to the authors participating in the investigation.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon request, subject to patient confidentiality and applicable institutional permissions for sharing clinical records, imaging datasets, and treatment plans.

2.2. Treatment-planning techniques

Five treatment-planning approaches were included.

1. Gamma Knife (GK) [29]: The supplied planning description identifies a Shenzhen Haibo SGS-1 system using collimators of 1.5, 2.5, 4.0, and 5.5 cm, with a stated equivalent energy of 1.25 MV. Noncoplanar beam arrangements were used to concentrate dose at the target.

2. Fixed-field IMRT[30]: Plans were created using Eclipse version 13.5 with a Varian 21EX linear accelerator. The system was described as using 6-MV X-rays and a 120-leaf multileaf collimator (MLC). Seven to nine fixed fields were used.

3. VMAT[31]: Plans were created using Eclipse version 15.6 with a Varian TrueBeam linear accelerator, using 6-MV X-rays and a 120-leaf MLC. The planning description specifies two arcs.

4. SIB-IMRT[32]: This approach used an integrated higher-dose region within the target, with the aim of increasing the central dose while maintaining the reference prescription to the broader target.

5. SIB-VMAT[33]: This approach applied a similar integrated dose-escalation strategy using rotational delivery.

The planning description states that the GK prescription was enclosed by a 50–55% isodose curve, whereas the linear-accelerator plans used the 100% isodose curve to encompass 95% of the PTV. The intended comparison was based on a common stated equivalent-dose reference. Because the techniques use different dose distributions and prescription conventions, the equivalence assumptions and dose normalization method should be documented in detail when the plans are independently reproduced.

2.3. Imaging, immobilization, and target delineation

The protocol describes supine patient positioning with a thermoplastic immobilization mask. Computed tomography was performed using a Toshiba Aquilion One 64-slice scanner, with contrast-enhanced imaging and a slice thickness of 3 mm.

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The gross tumor volume (GTV) was defined by experienced physicians using the enhancing recurrent lesion on contrast-enhanced T1-weighted magnetic resonance imaging. The planning target volume was described as a uniform expansion of the GTV by 0.3 mm.

A 0.3-mm margin was used for the planning target volume (PTV) expansion, as specified in the treatment-planning protocol. This margin was applied consistently during treatment-plan preparation and dosimetric evaluation across the planning techniques.

2.4. Plan construction and dose prescription

For the SIB-IMRT and SIB-VMAT plans, an integrated higher-dose region was described within the target to increase the central dose while maintaining the reference prescription to the broader planning target volume (PTV). The gross tumour volume (GTV) was delineated using the enhancing recurrent lesion on contrast-enhanced T1-weighted MRI, and the broader PTV was generated by applying the reported uniform expansion of 0.3 mm to the GTV. PTV volumes ranged from 16.7 to 150.8 cm^3, with a mean of 81.36 ± 39.38 cm^3. The planning description specified a reference EQD2 of 50 Gy and a central dose approximately twice the reference prescription. For the linear-accelerator plans, the stated coverage criterion was that 95% of the PTV received the prescription dose.

Previous radiotherapy prescriptions ranged from 39 to 50 Gy delivered in 13–25 fractions. For the comparative planning analysis, a reference equivalent dose in 2-Gy fractions (EQD2) of 50 Gy was reported. Gamma Knife prescriptions were specified at the 50–55% isodose level, whereas the linear-accelerator plans were normalized so that the prescription dose covered 95% of the planning target volume. The SIB approaches incorporated a central dose escalation described as approximately twice the reference prescription. Normal-brain V5 and V12 were reported as percentages receiving at least 5 Gy and 12 Gy, respectively, without specifying whether these thresholds were applied to physical or biologically converted dose distributions. The method for incorporating previous irradiation into a cumulative dose assessment was not documented.

2.5. Dosimetric endpoints

The analysis compared six primary dosimetric measures and two normal-brain dose-volume parameters.

Conformity index (CI). CI describes the degree to which the prescribed dose distribution conforms to the target volume. the index is reported on a scale from 0 to 1, with values closer to 1 indicating better conformity.

Homogeneity index (HI). HI was defined as the ratio of the dose received by 5% of the target volume to that received by 95% of the target volume:

$$HI = \frac{D_{5\%}}{D_{95\%}}$$

Under this definition, a value closer to 1 indicates a more homogeneous dose distribution. Higher values indicate greater dose variation within the target.

Gradient index (GI). GI was defined as the ratio of the volume encompassed by the 50% prescription isodose to the volume encompassed by the 100% prescription isodose:

$$GI = \frac{V_{50\%}}{V_{100\%}}$$

A lower GI indicates a steeper relative dose fall-off outside the high-dose region, assuming consistent dose definitions and normalization across plans.

Maximum dose (Dmax). Dmax represents the reported maximum dose within the target or treatment plan, in Gy.

Mean dose (Dmean). Dmean represents the reported mean dose within the target, in Gy.

Normal-brain V5 and V12. V5 and V12 represent the reported normal-brain volume receiving at least 5 Gy and 12 Gy, respectively. The tables express these measures as percentages. For reproducibility, should explicitly state how normal brain was contoured and whether the PTV was excluded from the evaluated brain volume.

These parameters describe different aspects of a treatment plan and should be interpreted together. In particular, a lower GI does not automatically indicate a better CI, and dose-volume parameters cannot by themselves establish the clinical incidence of radiation necrosis.

2.6. Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics, version 23.0. Continuous variables were expressed as means and standard deviations. Comparisons among the five radiotherapy planning techniques were performed using paired statistical tests, with t-statistics and corresponding P-values used to assess differences between treatment plans. Where the assumptions of parametric testing were not satisfied, nonparametric rank-based methods were considered. Statistical significance was defined as a two-sided P-value of less than 0.05.

Given that all five planning techniques were evaluated in the same cohort of 19 patients, the statistical analysis was structured to account for the paired nature of the dosimetric measurements. The interpretation of between-technique differences considered the magnitude and statistical significance of the observed variations in target-dose distribution and normal-brain exposure. The selection of statistical tests and the interpretation of the results were based on the characteristics of the data and the assumptions underlying each method.

2.7. Clinical and geographic scope

This study presents a comparative dosimetric evaluation of five radiotherapy planning techniques for recurrent high-grade glioma in the Indonesian clinical setting. The analysis focuses on treatment-plan characteristics, including target-dose conformity, dose homogeneity, dose gradients, maximum and mean doses, and normal-brain irradiation. Clinical outcomes such as local tumor control, progression-free survival, overall survival, neurocognitive function, symptomatic radiation-induced necrosis, and actual treatment-delivery times were not included in the assessment.

The findings provide a dosimetric basis for comparing alternative treatment-planning strategies and may support individualized radiotherapy planning in Indonesia. Their clinical application should consider differences in radiotherapy equipment, treatment-planning systems, institutional expertise, patient characteristics, and previous radiation exposure. The results should therefore be interpreted

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in the context of the dosimetric endpoints evaluated rather than as direct evidence of improved clinical outcomes.

3. Results

3.1. Normal-brain dose-volume parameters

The reported mean normal-brain V5 values ranged from 52.31% with GK to 61.83% with conventional IMRT. The corresponding V12 values ranged from 31.93% with GK to 43.61% with VMAT.

GK had the lowest reported mean V12 among the five planning approaches. In contrast, the V5 differences between GK and conventional IMRT or VMAT were not statistically significant according to the supplied pairwise comparisons.

Table 1. Normal-brain dose-volume parameters for the five planning approaches

Parameter (%)	Gamma Knife	Fixed-field IMRT	VMAT	SIB-IMRT	SIB-VMAT
V5	52.31 ± 12.38	61.83 ± 12.39	59.95 ± 13.33	57.73 ± 14.56	60.31 ± 15.65
V12	31.93 ± 11.97	42.64 ± 13.24	43.61 ± 14.49	41.22 ± 14.29	42.12 ± 15.17

Dosimetric measurements were obtained from the treatment-planning data generated for the 19-patient cohort. Normal-brain V5 and V12 were assessed to quantify the volumes of normal brain tissue receiving radiation doses of at least 5 Gy and 12 Gy, respectively. These dosimetric endpoints were used to compare normal-tissue irradiation across the five radiotherapy planning techniques and to characterize differences in dose distribution and potential exposure of healthy brain tissue.

3.2. Pairwise comparisons of normal-brain V5 and V12

The supplied statistical results indicated significantly lower V12 values for GK than for each of the four linear-accelerator approaches. The reported V5 differences between GK and conventional IMRT, VMAT, SIB-IMRT, and SIB-VMAT were not statistically significant.

Among the linear-accelerator approaches, the reported V5 difference between conventional IMRT and SIB-IMRT was statistically significant. The V12 differences between conventional IMRT and SIB-IMRT, and between VMAT and SIB-VMAT, were also reported as statistically significant.

Table 2. Pairwise Comparisons of Normal-Brain V5 and V12

Comparison	V5: t	V5: P	V12: t	V12: P
Gamma Knife vs. IMRT	1.178	0.254	6.451	<0.001
Gamma Knife vs. VMAT	0.491	0.629	7.068	<0.001

Gamma Knife vs. SIB-IMRT	0.285	0.779	5.260	<0.001
Gamma Knife vs. SIB-VMAT	0.491	0.629	5.870	<0.001
IMRT vs. VMAT	1.542	0.140	1.135	0.271
IMRT vs. SIB-IMRT	7.269	<0.001	2.335	0.031
VMAT vs. SIB-VMAT	0.968	0.346	2.225	0.039
SIB-IMRT vs. SIB-VMAT	4.287	<0.001	1.694	0.108

Abbreviations: IMRT, intensity-modulated radiation therapy; VMAT, volumetric modulated arc therapy; SIB, simultaneous integrated boost; V5 and V12, normal-brain volumes receiving at least 5 Gy and 12 Gy, respectively.

4. Discussion

The present planning comparison identified differences in normal-brain dose exposure among Gamma Knife (GK), fixed-field IMRT, VMAT, SIB-IMRT, and SIB-VMAT. GK yielded the lowest mean V5 and V12, while the effects of simultaneous integrated boosting differed between the fixed-field and rotational approaches. These findings characterize the dose distributions generated under the evaluated planning conditions; they do not independently establish differences in treatment safety, tumor control, or survival.

Although both studies address the reduction of normal-brain irradiation, their clinical settings and dosimetric endpoints differ. Back et al. (2017) evaluated patients who had not previously received radiotherapy and reported mean normal-brain dose, V20, and V40. The present analysis concerns re-irradiation and reports V5 and V12. Consequently, the magnitude of dose reduction cannot be compared directly between the studies. The earlier work provides a rationale for investigating differentiated target prescriptions, but does not establish the safety of the prescriptions evaluated here or demonstrate a clinical advantage for any of the five planning approaches.

4.1. Normal-brain dose exposure

GK produced a mean normal-brain V12 of 31.93 ± 11.97%, compared with 42.64 ± 13.24% for IMRT, 43.61 ± 14.49% for VMAT, 41.22 ± 14.29% for SIB-IMRT, and 42.12 ± 15.17% for SIB-VMAT. The corresponding absolute differences between GK and the linear-accelerator approaches ranged from 9.29 to 11.68 percentage points. The supplied pairwise analysis reported statistically significant differences for all four V12 comparisons with GK.

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This pattern indicates that GK limited the proportion of the evaluated normal-brain volume receiving at least 12 Gy more effectively than the other plans in this dataset. However, the interpretation depends on a consistent definition of normal brain, including whether the target was excluded, and on comparable prescription and fractionation conditions. A lower V12 should therefore be interpreted as a dosimetric finding rather than direct evidence of reduced radiation necrosis.

The mean V5 was also lowest with GK, at 52.31 ± 12.38%, compared with 61.83 ± 12.39% for IMRT, 59.95 ± 13.33% for VMAT, 57.73 ± 14.56% for SIB-IMRT, and 60.31 ± 15.65% for SIB-VMAT. These values indicate a numerical reduction in low-dose exposure with GK. Nevertheless, inconsistencies between the reported V5 summary statistics and several paired-test statistics prevent a reliable interpretation of statistical significance until the patient-level analysis is verified. The observed numerical ordering should not be interpreted as proof of either superiority or equivalence.

4.2. Effects of simultaneous integrated boosting

SIB-IMRT showed lower mean V5 and V12 values than conventional IMRT. V5 decreased from 61.83% to 57.73%, an absolute difference of 4.10 percentage points, while V12 decreased from 42.64% to 41.22%, a difference of 1.42 percentage points. These findings suggest that the evaluated SIB-IMRT planning strategy redistributed dose within the target without increasing the reported normal-brain dose-volume measures.

The corresponding VMAT comparison showed a different pattern. SIB-VMAT had a lower mean V12 than conventional VMAT, decreasing from 43.61% to 42.12%, but a slightly higher mean V5, increasing from 59.95% to 60.31%. Thus, the reduction in intermediate-dose exposure was accompanied by a small numerical increase in low-dose exposure. SIB planning did not produce a uniform improvement across both endpoints or delivery approaches.

These differences cannot be attributed to the boost strategy alone. Optimization objectives, boost-volume geometry, prescription normalization, beam arrangement, and planning-system characteristics may also influence normal-brain exposure. Comparisons should therefore establish equivalent target coverage and clearly define the boost region before attributing any advantage to SIB.

The effects of integrated boosting should be interpreted as a combination of prescription design and treatment delivery. Back et al. (2017) investigated a strategy that maintained a higher prescription in a selected high-risk region while reducing the prescription to a broader standard-risk volume. Their reported normal-brain dose reductions therefore reflect a risk-adapted prescription strategy rather than an isolated effect of IMRT delivery. In the present study, differences involving SIB-IMRT and SIB-VMAT likewise require interpretation in relation to boost-volume geometry, prescribed dose levels, normalization, and optimization priorities. Without adequately documenting these factors and

demonstrating comparable target coverage, changes in normal-brain exposure cannot be attributed to the delivery technique alone.

4.3. Implications for recurrent high-grade glioma planning

Normal-brain exposure is particularly relevant in recurrent high-grade glioma because previously irradiated tissue may overlap with the new treatment volume. Nevertheless, V5 and V12 from the evaluated plans describe only part of this problem. Their clinical interpretation requires information on previous dose distributions, the interval between treatments, fractionation, cumulative biological dose, and the location of critical structures.

The present results support considering multiple dose-volume endpoints when comparing candidate plans. A technique with a lower V12 may still differ in target coverage, conformity, dose heterogeneity, or exposure of the optic pathways and brainstem. Accordingly, the lowest normal-brain V12 should not be used as the sole criterion for selecting a treatment technique.

The percentages reported here also require careful distinction from absolute volumes expressed in cubic centimeters. Identical percentage values can represent different irradiated tissue volumes in patients with different normal-brain volumes. Reporting both relative and absolute dose-volume measures would improve the interpretability of future comparisons.

4.4. Study limitations

Several limitations restrict the conclusions. The sample included only 19 patients, limiting the precision and generalizability of the estimates. Aggregate means and standard deviations do not reveal whether the observed advantages were consistent across patients or concentrated in particular target sizes and geometries.

The statistical analysis requires verification because several reported V5 test statistics are incompatible with the corresponding summary values under the stated paired design. Multiple comparisons also increase the importance of reporting prespecified endpoints, confidence intervals, and an appropriate adjustment strategy.

Differences in treatment equipment, planning-system versions, prescription conventions, and optimization methods may have influenced the comparisons. The equivalent-dose framework and fractionation schedules require clarification before the dose distributions can be interpreted as biologically comparable.

Furthermore, the tabulated results do not provide a complete assessment of target coverage, conformity, homogeneity, dose gradients, or critical-organ constraints. Clinical outcomes and treatment-delivery measurements were not evaluated. Consequently, the present findings cannot establish differences in radiation necrosis, neurological function, treatment efficiency, or survival.

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The potential neurocognitive benefit of reducing normal-brain irradiation remains untested in this dataset. No baseline or longitudinal neuropsychological assessments were available, and the analysis did not establish relationships between dose-volume measures and subsequent neurological toxicity. Furthermore, the reported inconsistencies in the paired statistical analysis require resolution before conclusions about statistical significance can be considered reliable. The present findings should therefore be interpreted as descriptive dosimetric observations pending verification of the patient-level analysis and further clinical evaluation.

The present planning comparison identified differences in normal-brain dose exposure among Gamma Knife (GK), fixed-field IMRT, VMAT, SIB-IMRT, and SIB-VMAT. GK yielded the lowest mean V5 and V12, while the effects of simultaneous integrated boosting differed between the fixed-field and rotational approaches. These findings characterize the dose distributions generated under the evaluated planning conditions; they do not independently establish differences in treatment safety, tumor control, or survival.

5. Conclusion

In the evaluated 19-patient planning dataset, GK produced the lowest reported mean normal-brain V5 and V12. SIB-IMRT showed numerically lower values for both endpoints than conventional IMRT, whereas SIB-VMAT reduced V12 while slightly increasing V5 relative to conventional VMAT. These findings indicate that the effects of treatment technique and boost strategy differ across dose-volume endpoints.

The results support individualized plan comparison using normal-brain exposure alongside target coverage and critical-organ constraints. They do not establish clinical superiority or a reduction in radiation-related toxicity.

Ethical Considerations

obtained from Universitas Indonesia, Depok, Indonesia , Ethical approval number: ID/UI/AC/2026/713K8Y44.

List of Abbreviations:

(HGG): high-grade glioma; **(GK):** Gamma Knife; **(IMRT):** intensity-modulated radiation therapy , **(VMAT):** volumetric modulated arc therapy; **(CI):** conformity index, **(HI):** homogeneity index , **(GI):** gradient index ; **(SIB):** simultaneous integrated boost; **(PTV):** planning target volume; **(GTV):** gross tumor volume;

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Author Contribution:

All authors contributed equally to the main contributor to this paper. All authors read and approved the final paper.

Declaration of generative AI and AI-assisted technologies in the writing process

The authors hereby declare that no generative artificial intelligence or AI-assisted technologies were used at any stage during the preparation of this manuscript, including language editing, proofreading, or content development. The authors take full responsibility for the originality and integrity of the work presented in this publication.

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Conflicts of Interes

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References

1. Chen X, Cui Y and Zou L (2024) Treatment advances in high-grade gliomas. Front. Oncol. 14:1287725. doi: https://doi.org/10.3389/fonc.2024.1287725
2. Yoel, A., Adjumain, S., Liang, Y., Daniel, P., Firestein, R., & Tsui, V. (2024). Emerging and Biological Concepts in Pediatric High-Grade Gliomas. Cells, 13(17), 1492. https://doi.org/10.3390/cells13171492
3. Frosina, G. (2023). Recapitulating the Key Advances in the Diagnosis and Prognosis of High-Grade Gliomas: Second Half of 2021 Update. International Journal of Molecular Sciences, 24(7), 6375. https://doi.org/10.3390/ijms24076375
4. Gregucci, F., Surgo, A., Carbonara, R., Laera, L., Ciliberti, M. P., Gentile, M. A., Caliandro, M., Sasso, N., Bonaparte, I., Fanelli, V., Tortora, R., Paulicelli, E., Surico, G., Lombardi, G., Signorelli, F., & Fiorentino, A. (2022). Radiosurgery and Stereotactic Brain Radiotherapy with Systemic Therapy in Recurrent High-Grade Gliomas: Is It Feasible? Therapeutic Strategies in Recurrent High-Grade Gliomas. Journal of Personalized Medicine, 12(8), 1336. https://doi.org/10.3390/jpm12081336
5. Navarria, P., Pessina, F., Clerici, E., Bellu, L., Franzese, C., Franzini, A., ... & Scorsetti, M. (2022). Re-irradiation for recurrent high grade glioma (HGG) patients: Results of a single arm prospective phase 2 study. Radiotherapy and Oncology, 167, 89-96. https://doi.org/10.1016/j.radonc.2021.12.019
6. Lo Greco, M. C., Milazzotto, R., Liardo, R. L. E., Acquaviva, G., La Rocca, M., Altieri, R., Certo, F., Barbagallo, G. M., Basile, A., Foti, P. V., Palmucci, S., Pergolizzi, S., Pontoriero, A., & Spatola, C. (2022). Relapsing High—Grade Glioma from Peritumoral Zone: Critical Review of Radiotherapy Treatment Options. Brain Sciences, 12(4), 416. https://doi.org/10.3390/brainsci12040416
7. Rogers, S., Gross, M., Ermis, E. et al. Re-irradiation for recurrent glioblastoma: a pattern of care analysis. BMC Neurol 24, 462 (2024). https://doi.org/10.1186/s12883-024-03954-z
8. Sehrawat, K., Polley, MY.C., Vogelbaum, M.A. et al. The evolution of RTOG and NRG Oncology CNS tumors clinical trials. J Neurooncol 179, 83 (2026). https://doi.org/10.1007/s11060-026-05788-w
9. Rifaquat Rahman, Matthias Preusser, Christina Tsien, Emilie Le Rhun, Erik P Sulman, Patrick Y Wen, Giuseppe Minniti, Michael Weller, Point/Counterpoint: The role of reirradiation in recurrent

glioblastoma, Neuro-Oncology, Volume 27, Issue 1, January 2025, Pages 7–12, https://doi.org/10.1093/neuonc/noae209
10. Wang X, Qi Z, Zeng Q, Gu D and Li T (2025) Radiotherapy for glioma in the AI era: current applications and future prospects. Front. Oncol. 15:1673752. doi: https://doi.org/10.3389/fonc.2025.1673752
11. Francesca Soldá, Cornel Tancu, Neil Kitchen, Naomi Fersht, 2024. Neurosurgical applications of radiotherapy, Surgery (Oxford), Volume 42, Issue 8, 2024, Pages 590-598, ISSN 0263-9319, https://doi.org/10.1016/j.mpsur.2024.05.012
12. Klinge, T. (2022). Biologically effective dose (BED) treatment planning for Gamma Knife Radiosurgery (Doctoral dissertation, UCL (University College London)). https://discovery.ucl.ac.uk/id/eprint/10158520/
13. Hellerbach, A., Eichner, M., Rueß, D. et al. Impact of prescription isodose level and collimator selection on dose homogeneity and plan quality in robotic radiosurgery. Strahlenther Onkol 198, 484–496 (2022). https://doi.org/10.1007/s00066-021-01872-4
14. Oshiro Y, Kato Y, Mizumoto M, et al. (April 23, 2024) The Impact of Multileaf Collimator Size on Single Isocenter Dynamic Conformal Arcs-Based Radiosurgery for Brain Metastases. Cureus 16(4): e58816. DOI https://doi.org/10.7759/cureus.58816
15. Ahamed, S., & Suvarna, R. P. (2024). Evaluation of Normal Tissue Objective Function for Treatment Planning of Solitary Brain Metastasis Using Intensity-modulated Radiosurgery Techniques. Journal of medical physics, 49(3), 394–399. https://doi.org/10.4103/jmp.jmp_66_24
16. Sundaram, V., Khanna, D. & Palanisamy, M. Evaluation of dose rate and gantry speed variations in volumetric modulated Arc therapy optimization algorithms for a modern linear accelerator. Radiol Phys Technol 19, 217–232 (2026). https://doi.org/10.1007/s12194-025-01001-1
17. Abdulameer MS, Pallathadka H, Menon SV, et al. Dosimetric effect of collimator rotation on intensity modulated radiotherapy and volumetric modulated arc therapy for rectal cancer radiotherapy. Journal of X-Ray Science and Technology. 2024;32(5):1331-1348. doi: https://doi.org/10.3233/XST-240172
18. Prasad, D., Madhugiri, V.S. (2024). Gamma Knife® Stereotactic Radiosurgery and Hypofractionated Stereotactic Radiotherapy. In: Chang, E.L., Brown, P.D., Lo, S.S., Sahgal, A., Suh, J.H. (eds) Adult CNS Radiation Oncology. Springer, Cham. https://doi.org/10.1007/978-3-031-67878-3_44
19. Dharnipragada, R., Dusenbery, K., Watanabe, Y. et al. Comparison of Gamma Knife (GK) and Linear Accelerator (LINAC) radiosurgery of brain metastasis resection cavity: a systematic review and proportional meta-analysis. Clin Exp Metastasis 41, 1–8 (2024). https://doi.org/10.1007/s10585-023-10240-8
20. Schelin, M. E., Liu, H., Ali, A., Shi, W., Yu, Y., & Mooney, K. E. (2021). Dosimetric comparison of Gamma Knife® Icon™ and linear accelerator-based fractionated stereotactic radiotherapy (FSRT) plans for the re-irradiation of large (>14 cm^3) recurrent glioblastomas. *Journal of radiosurgery and SBRT*, *7*(3), 233–243. https://pmc.ncbi.nlm.nih.gov/articles/PMC8055238/
21. Mireștean, C. C., Iancu, R. I., & Iancu, D. P. T. (2023). Simultaneous Integrated Boost (SIB) vs. Sequential Boost in Head and Neck Cancer (HNC) Radiotherapy: A Radiomics-Based Decision Proof of Concept. Journal of Clinical Medicine, 12(6), 2413. https://doi.org/10.3390/jcm12062413
22. Chambrelant, I., Jarnet, D., Bou-Gharios, J., Le Fèvre, C., Kuntz, L., Antoni, D., Jenny, C., & Noël, G. (2023). Stereotactic Radiation Therapy of Single Brain Metastases: A Literature Review of Dosimetric Studies. Cancers, 15(15), 3937. https://doi.org/10.3390/cancers15153937
23. Abdollahi, S., Boucenna, R., Chatelain, C., Corradini, N., Fargier-Voiron, M., Fave, V., ... & Tanadini-Lang, S. (2026). Multicenter evaluation of planning quality in intracranial stereotactic radiotherapy for brain metastases. Physics and imaging in radiation oncology, 100919. https://doi.org/10.1016/j.phro.2026.100919
24. McDonald, A.M., Schneider, C.S., Stahl, J.M. et al. A focused review of statistical practices for relating radiation dose-volume exposure and toxicity. Radiat Oncol 18, 57 (2023). https://doi.org/10.1186/s13014-023-02220-9

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Vol. 2, No. 2, 2026, pp. 271-287
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25. Pogue, J. A., Fiveash, J., Cardan, R., Willey, C., Viscariello, N., Sullivan, R., ... & Popple, R. (2025). HyperArc Automated Stereotactic Radiosurgery Planning Enables Accurate a Priori Fractionation Scheme Selection via Adherence to HyTEC Toxicity Thresholds. Advances in Radiation Oncology, 10(11), 101893. https://doi.org/10.1016/j.adro.2025.101893
26. Li Y, Ma H, Hua R, Wang T, Ding N, Deng L, Lu X and Chen W (2024) Analysis of linear accelerator-based fractionated stereotactic radiotherapy in brain metastases: efficacy, safety, and dose tolerances. Front. Oncol. 14:1471004. doi: https://doi.org/10.3389/fonc.2024.1471004
27. Palavani, L.B., de Barros Oliveira, L., Reis, P.A. et al. Efficacy and Safety of Intraoperative Radiotherapy for High-Grade Gliomas: A Systematic Review and Meta-Analysis. Neurosurg Rev 47, 47 (2024). https://doi.org/10.1007/s10143-024-02279-2
28. Back, M., LeMottee, M., Crasta, C., Bailey, D., Wheeler, H., Guo, L., & Eade, T. (2017). Reducing radiation dose to normal brain through a risk adapted dose reduction protocol for patients with favourable subtype anaplastic glioma. Radiation oncology (London, England), 12(1), 46. https://doi.org/10.1186/s13014-017-0782-3
29. Thomas, E. M., Popple, R. A., Wu, X., Clark, G. M., Markert, J. M., Guthrie, B. L., ... & Fiveash, J. B. (2014). Comparison of plan quality and delivery time between volumetric arc therapy (RapidArc) and Gamma Knife radiosurgery for multiple cranial metastases. *Neurosurgery*, *75*(4), 409-418. https://academic.oup.com/neurosurgery/OUP/?redirectedFrom=PDF
30. Song, JL., Zhang, YZ., Zhang, ZL. et al. The application of multi-arc volumetric modulated arc therapy and fixed-field intensity modulated radiotherapy in the treatment of gynecologic cancer with large planning target volume. Phys Eng Sci Med 48, 715–721 (2025). https://doi.org/10.1007/s13246-025-01538-w
31. Ma, Y., Xu, K., Mai, R., Pei, Y., Liu, L., Sun, H., ... & Cheng, C. (2026). Reassessing gamma index–DVH metric correlations in VMAT quality assurance for extended cervical cancer targets using 3D dose verification. Radiation Physics and Chemistry, 113818. https://doi.org/10.1016/j.radphyschem.2026.113818
32. Hongfu Sun, Chengxin Liu, Jing Zhang, Guanghui Yang, Dan Han, Tingting Liu, Wei Huang, Baosheng Li,2022. Twice-daily thoracic radiotherapy by intensity-modulated radiation therapy (IMRT) compared with simultaneous integrated boost IMRT (SIB-IMRT) with concurrent chemotherapy for patients with limited-stage small cell lung cancer. A propensity-score matched analysis, Radiotherapy and Oncology, Volume 172, 2022, Pages 140-146, ISSN 0167-8140, https://doi.org/10.1016/j.radonc.2022.01.022
33. Adeneye SO, Ariyo ID, Joseph AO, Sowunmi AC, Akpochafor MO, Uwagba G, et al. Simultaneous Integrated Boost Plan Comparison between Volumetric Modulated Arc Therapy (VMAT) and Intensity Modulated Radiation Therapy (IMRT) for Prostate, Seminal vesicle and Lymph Node Irradiation. EJMO 2022;6(3):219–225. DOI: https://doi.org/10.14744/ejmo.2022.75665