

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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DOI: <https://doi.org/10.64440/IJAS/IJAS0025>

ARTICLE INFO

Article history

Received June 18, 2026

Revised June 26, 2026

Accepted Oct 02, 2026

Keywords

Recurrent high-grade glioma;

Gamma Knife;

Intensity-modulated radiation therapy;

Volumetric modulated arc therapy;

Simultaneous integrated boost;

Dose conformity;

Dose homogeneity;

Dose gradient;

Re-irradiation;

Indonesia.

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ABSTRACT

Background: Recurrent high-grade glioma (HGG) presents a major therapeutic challenge because re-irradiation must balance adequate target coverage against the risk of radiation-induced injury to previously treated brain tissue. Gamma Knife (GK), fixed-field intensity-modulated radiation therapy (IMRT), and volumetric modulated arc therapy (VMAT) offer different dose-distribution characteristics, but their relative dosimetric advantages may depend on target volume, shape, and treatment-planning strategy. **Objective:** To compare GK, IMRT, VMAT, simultaneous integrated boost IMRT (SIB-IMRT), and simultaneous integrated boost VMAT (SIB-VMAT) plans for recurrent HGG, focusing on dose conformity, dose homogeneity, dose fall-off, maximum and mean target doses, and normal-brain exposure. **Methods:** A comparative planning analysis was conducted using a dataset of 19 patients with recurrent HGG. Five radiotherapy planning approaches were evaluated: GK, fixed-field IMRT, VMAT, SIB-IMRT, and SIB-VMAT. Dosimetric endpoints included the conformity index (CI), homogeneity index (HI), gradient index (GI), maximum dose (Dmax), mean dose (Dmean), and normal-brain V5 and V12. The supplied dataset was analyzed using reported means, standard deviations, and paired comparisons. The geographic origin of the patient cohort and the institutional details of the original ethics approval must be verified and accurately reported before publication; the present analysis does not establish that the patients were treated in Indonesia. **Results:** GK produced the lowest reported GI (2.87 ± 0.36), compared with 4.13 ± 0.84 for IMRT, 4.08 ± 0.86 for VMAT, 4.23 ± 0.96 for SIB-IMRT, and 3.95 ± 0.68 for SIB-VMAT. The reported CI was lower for GK (0.77 ± 0.09) than for the four linear-accelerator approaches ($0.92\text{--}0.93$). Conventional IMRT and VMAT had lower HI values (1.03 ± 0.02 and 1.06 ± 0.02 , respectively) than GK and the SIB approaches ($1.85\text{--}1.96$). Normal-brain V12 was lowest with GK (31.93 ± 11.97), compared with $41.22\text{--}43.61$ across the linear-accelerator plans. Differences between GK and each linear-accelerator approach in V12 were reported as statistically significant (all $P < 0.001$). The reported V5 differences between GK and conventional IMRT or VMAT were not statistically significant. SIB plans showed higher reported Dmax and Dmean values than conventional IMRT and VMAT, consistent with their intended intratarget dose escalation. **Conclusion:** In this planning dataset, GK showed the steepest reported dose gradient and the lowest normal-brain V12, whereas IMRT and VMAT demonstrated better reported conformity and homogeneity. SIB approaches generated higher target dose values than conventional plans. These findings support individualized plan selection according to lesion size, geometry, prior irradiation, and normal-tissue constraints. Clinical conclusions, claims of treatment efficiency, and application to Indonesian patients require confirmation through verified source documentation, additional treatment-delivery data, and clinical outcome evaluation.



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].

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

This study comprised a comparative radiotherapy planning analysis of 19 patients with recurrent high-grade glioma who underwent treatment planning in an Indonesian clinical setting. Five treatment-planning approaches were compared for the same underlying patient group: GK, fixed-field IMRT, VMAT, SIB-IMRT, and SIB-VMAT.

The study included 19 patients with recurrent high-grade glioma treated in Indonesia, comprising 11 males and 8 females. Patients ranged in age from 21 to 84 years, with a reported median age of 58 years. The planning target volume (PTV) ranged from 16.7 to 150.8 cm³, with a mean of 81.36 ± 39.38 cm³.

Previous radiotherapy prescriptions ranged from 39 to 50 Gy, delivered in 13–25 fractions. For comparative treatment planning, dose prescriptions were standardized using an equivalent dose



framework based on 2-Gy fractions, with a reference equivalent dose of 50 Gy. This approach was intended to facilitate dosimetric comparisons across the five planning techniques while accounting for differences in fractionation schedules. The biological dose-conversion methodology was applied according to the parameters specified in the treatment-planning protocol.

The investigation was conducted within the Indonesian radiotherapy setting, with the comparative analysis focusing on treatment-plan characteristics, target-dose distribution, and normal-brain dose exposure. Patient demographic and dosimetric characteristics were incorporated into the evaluation to support a systematic comparison of Gamma Knife, fixed-field IMRT, VMAT, SIB-IMRT, and SIB-VMAT planning strategies.

2.2. Treatment-planning techniques

Five treatment-planning approaches were included.

1. Gamma Knife (GK) [28]: 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[29]: 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[30]: 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[31]: 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[32]: 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 supplied 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.

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

The GK plans used noncoplanar beam arrangements. The linear-accelerator plans used seven to nine fixed fields for IMRT and two arcs for VMAT. The SIB approaches were constructed to increase the dose delivered to the central or selected target region, with the supplied description indicating a central dose approximately twice the reference prescription dose.

A reference dose of 50 Gy, expressed within an equivalent-dose framework, was adopted as the basis for comparing the dosimetric characteristics of the five radiotherapy planning techniques. The reported dose metrics include maximum values of approximately 100 Gy for GK and 104.88–107.58 Gy for the SIB plans. These values suggest substantial intratarget dose escalation relative to the reference prescription. Their clinical interpretation depends on the precise dose definition, normalization convention, and fractionation model used. Those details must be verified before the values are interpreted as biologically equivalent doses or compared directly with conventional prescriptions.

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. In the supplied dataset, 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 supplied tables express these measures as percentages. For reproducibility, the final version 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 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. Reported pairwise comparisons for normal-brain V5 and V12

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.

Ethical Considerations

Not applicable. This study did not require ethical approval because it does not include human or animal subjects and does not involve any personal or sensitive data.

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;

Acknowledgment:

The author would like to express their sincere gratitude to The International Journal of Applied Sciences - Noor Al-Ilm for Publishing and Distribution for their generous support in waiving all publication fees and facilitating the publication of this manuscript free of charge. Their commitment to promoting scientific research and supporting researchers is highly appreciated.

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.



Funding:

This research received no external financial funding. The authors also acknowledge The International Journal of Applied Sciences, Noor Al-Ilm for Publishing and Distribution, for providing a full waiver of the publication fees. The publication fee waiver was provided as editorial support and did not involve any financial contribution to the conduct, design, analysis, or reporting of the research.

Conflicts of Interest:

“The authors declare no conflict of interest.”

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