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ARAŞTIRMA MAKALESİ / RESEARCH ARTICLE

Comparison of Hippocampus Doses in Hypofractionated Gamma Knife and Linac-Based Radiosurgical Treatment Plans for Patients with Intracranial Metastatic Tumors

İntrakraniyal Metastatik Tümörlü Hastalarda Hipofraksiyone Gamma Knife ve Lineer Hızlandırıcı Tabanlı Radyocerrahi Tedavi Planlarında Hipokampus Dozlarının Karşılaştırılması

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ABSTRACT

Introduction: The aim of this study is to retrospectively compare Gamma Knife radiosurgery and LINAC-based fractionated stereotactic radiosurgery treatment plans in patients with metastatic brain tumors, with a particular focus on the radiation dose delivered to the hippocampus.

Material and Methods: Twenty-four patients treated at Gazi University, Faculty of Medicine Gamma Knife Unit were included. GK plans were generated with 27 Gy in 3 fractions to the 50% isodose. Corresponding LINAC plans were created in Eclipse to match the GK target dosing. Evaluation of target and hippocampal dosimetry was performed using dose–volume histogram (DVH) analysis. Initial plans did not include sparing the hippocampus.

Results: GK plans generally resulted in lower hippocampal doses, especially when targets were fewer and distant from the hippocampus. LINAC plans tended to show higher values; however, re-optimization with the hippocampus as an organ-at-risk effectively reduced doses. Four GK and five LINAC plans exceeded a hippocampal V3 of 3 Gy, while V20 was zero for both systems. The mean Dmax was 141.88 ± 37 cGy for GK and 164.26 ± 33.3 cGy for LINAC, indicating a significant difference (p = 0.002).

Conclusion: Although hippocampal dose thresholds related to neurocognition remain uncertain, GK may offer an advantage for lesions near the hippocampus, whereas optimized LINAC planning can also maintain acceptable hippocampal doses.

Keywords: Hippocampus dose, gamma knife radiosurgery, linear accelerators, hypofractionation

ÖZ

Giriş: Bu çalışmanın amacı, metastatik beyin tümörlü hastalarda Gama Knife radyocerrahisi ve LINAC tabanlı fraksiyonlu stereotaktik radyocerrahisi tedavi planlarını, özellikle hipokampusa verilen radyasyon dozuna odaklanarak, retrospektif olarak karşılaştırmaktır.

Materyal ve Metodlar: Gazi Üniversitesi Tıp Fakültesi Gama Knife Ünitesinde tedavi gören 24 hasta çalışmaya dahil edildi. GK planları, %50 izodoza 3 fraksiyonda 27 Gy dozunda oluşturuldu. GK hedef dozlamasına uyacak şekilde Eclipse'te karşılık gelen LINAC planları oluşturuldu. Hedef ve hipokampal dozimetri değerlendirmesi, doz-hacim histogramı (DVH) analizine dayanarak gerçekleştirildi. İlk planlar hipokampusu korumayı içermiyordu.

Bulgular: GK planları genellikle daha düşük hipokampal dozlarla sonuçlandı, özellikle hedefler daha az sayıda ve hipokampustan uzakta olduğunda. LINAC planları daha yüksek değerler gösterme eğilimindeydi; ancak hipokampüsün risk altındaki bir organ olarak ele alınarak yapılan yeniden optimizasyon, dozları etkili bir şekilde azalttı. Dört GK ve beş LINAC planı, 3 Gy'lik bir hipokampal V3 değerini aşarken, her iki sistem için de V20 sıfırdı. Ortalama Dmax, GK için 141.88 ± 37 cGy ve LINAC için 164.26 ± 33.3 cGy olup, anlamlı bir fark olduğunu göstermektedir (p = 0.002).

Sonuç: Nörokognisyonla ilgili hipokampal doz eşikleri belirsizliğini korusa da, GK hipokampüse yakın lezyonlar için bir avantaj sunabilirken, optimize edilmiş LINAC planlaması da kabul edilebilir hipokampal dozları koruyabilir.

Anahtar Sözcükler: Hipokampus dozu, gama knife radyocerrahisi, lineer hızlandırıcılar, hipofraksiyonasyon

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Introduction

In the adult population, brain metastases are the most prevalent intracranial tumors, affecting roughly one-fifth to two-fifths of patients with systemic malignancies during the course of their disease (1). As advances in modern oncology have extended survival through the widespread integration of targeted therapies, immunotherapy, and personalized systemic treatments, the incidence, visibility, and clinical importance of intracranial metastatic disease have continued to grow (2). With patients living longer and facing an elevated risk of neurologic morbidity, the therapeutic focus in neuro-oncology has shifted toward balancing effective local tumor control with the preservation of cognitive and neurological function. Consequently, minimizing treatment-related neurotoxicity while maintaining optimal intracranial disease control has become a critical goal in contemporary practice (3).

Owing to its capacity to administer ablative radiation with high conformality and rapid dose fall-off, stereotactic radiosurgery (SRS) plays a central role in the management of brain metastases (4). Among currently available SRS technologies, Gamma Knife (GK) and linear accelerator (LINAC)-based systems represent the two most widely used platforms worldwide. Although both modalities achieve stereotactic precision, they differ substantially in their underlying physics, beam collimation and geometry, dose-delivery mechanisms, and treatment planning algorithms (5). These technical differences can lead to variations in dose fall-off, conformity, and the distribution of low-dose spillage, which may be particularly relevant when treating lesions situated near functionally sensitive neural structures.

Among the critical organs at risk, the hippocampus is particularly important because of its essential role in memory processing, learning, and spatial orientation. Importantly, the hippocampus is recognized as one of the most radiosensitive regions of the brain. A substantial body of experimental and clinical research has demonstrated that even relatively low doses of radiation can result in structural and functional hippocampal injury, contributing to measurable neurocognitive decline—most prominently deficits in memory and executive functions (6).

Preservation of hippocampal integrity has therefore become a major consideration in cranial radiotherapy, especially for patients with good prognostic factors and expected long-term survival. The increasing recognition of neurocognitive outcomes as a key endpoint in oncologic care underscores the need for treatment strategies that maximize hippocampal sparing when clinically feasible.

Fractionated stereotactic radiosurgery (FRx-SRS) has gained prominence as an alternative to single-fraction SRS, particularly for large lesions, tumors located near critical structures, or cases in which normal tissue tolerance is a concern. Fractionation offers radiobiological advantages, such as greater repair of sublethal injury in healthy tissue, potentially reducing the risk of radiation-induced toxicity while preserving local tumor control (7). Despite the expanding clinical use of FRx-SRS, there is a notable paucity of comparative data evaluating how GK and LINAC-based systems differ in their dosimetric impact on the hippocampus during fractionated treatment.

Given the increasing emphasis on neurocognitive preservation and the growing population of patients eligible for SRS-based approaches, understanding the hippocampal dose characteristics of different radiosurgical platforms is of significant clinical importance. Therefore, the present study aims to retrospectively compare GK and LINAC-based FRx-SRS treatment plans in patients with metastatic brain tumors, with a particular focus on hippocampal dose parameters. By analyzing dose-volume histograms (DVHs) and hippocampal protection indices, this study seeks to identify key dosimetric differences between the two systems. These findings may help inform platform selection and treatment planning strategies that optimize hippocampal sparing without compromising efficacy in local tumor control.

Material and Methods

Patient Selection

This retrospective analysis comprised patients with metastatic brain tumors treated with stereotactic radiosurgery at the Gazi University, Faculty of Medicine, Gamma Knife Unit between January 2020 and December 2024. Patient characteristics are summarized in Table 1. Eligibility criteria included age ≥18 years, histopathological confirmation of an extracranial primary malignancy, and the availability of high-resolution magnetic resonance imaging (MRI) and computed tomography (CT)-based treatment planning data. Patients who had previously undergone whole-brain radiotherapy, had lesions involving the hippocampal region, or had poor image quality were excluded from the study. The study was approved by the Gazi University, Faculty of Medicine, Clinical Research Ethics Committee on November 25, 2025, at its 18th meeting, with/protocol number 1968. As informed consent was not obtained, a statement should be included indicating that the ethics committee granted a waiver of informed consent. Also, written informed consent was obtained from the patient for the publication of this case report, including all relevant clinical data and accompanying images.

Treatment Planning

The treatment plans of 24 patients with metastatic brain tumors included in the study were retrospectively evaluated at the Gazi University, Faculty of Medicine Gamma Knife Unit. Treatment plans were prepared using the Eclipse planning module with a LINAC-based SRS system, based on Magnetic Resonance (MR) and Computed Tomography (CT) images of the same patients, to cover the same volume.

Table 1. Patient demographics

Patient No	Gender Male 0, Female 1	Age	Target Volume (cc)	Diagnosis	Localization	Prescription Dose (Gy)
1	0	73	2.25	Lung Cancer	Left temporal	27
2	0	66	3.68	Lung Cancer	Left temporal	27
3	0	55	5.1	Lung Cancer	Left temporal	27
4	0	74	6.7	Lung Cancer	Left occipital	27
5	1	67	8.7	Breast Cancer	Left temporooccipital	27
6	0	66	11.03	Lung Cancer	Left temporal	27
7	0	55	13.6	Lung Cancer	Rigt temporoparietal	27
8	0	58	16.9	Lung Cancer	Rigt temporoparietal	27
9	0	65	1.24	Lung Cancer	Rigt temporoparietal	27
10	1	68	1.02	Breast Cancer	Left temporoparietal	27
11	1	38	4.02	Breast Cancer	Left frontal	27
12	1	47	0.79	Breast Cancer	Left temporoparietal	27
13	1	58	0.41	Breast Cancer	Right temporal	27
14	0	61	0.5	Lung Cancer	Left cerebellar	27
15	0	66	0.9	Lung Cancer	Rigt temporoparietal	27
16	1	74	1.6	Breast Cancer	Left cerebellar	27
17	1	75	0.9	Breast Cancer	Left occipital	27
18	1	71	1.6	Breast Cancer	Left occipital	27
19	0	69	8.7	Lung Cancer	Left cerebellar	27
20	0	59	9.3	Lung Cancer	Left cerebellar	27
21	0	58	11.3	Lung Cancer	Left temporal	27
22	1	67	9.4	Breast Cancer	Right temporal	27
23	1	69	7.8	Breast Cancer	Right temporal	27
24	1	66	9.9	Breast Cancer	Rigt temporoparietal	27
25	1	68	11.2	Breast Cancer	Left temporal	27

In Gamma Knife planning, a total dose of 27 Gy in 3 fractions was prescribed for each lesion. Planning was optimized to cover the entire target volume with a 50% isodose. During target volume determination, contrast-enhanced T1-weighted MR images and planning CT images were fused to define the GTV (Gross Tumor Volume). The planning target volume (PTV) was created by adding an isotropic margin of 1–2 mm to the GTV, depending on immobilization accuracy and system sensitivity.

LINAC-based SRS plans were created to be compatible with GK plans. In this process, the Eclipse Treatment Planning System (version 16.1) was used to obtain an equivalent tumor dose distribution for the same target volumes, and optimization was performed using a high-definition multileaf collimator (HD-MLC). For dose calculation, both Gamma Knife and LINAC treatment plans were normalized to ensure that at least 95% of the target volume received the prescribed dose. As shown in Figure 1.

Initially, no hippocampal protection strategy was applied during the planning process; thus, the natural dose exposure of the hippocampus could be observed in both systems. After optimization was completed, the target volume and hippocampal doses for each plan were analyzed in detail using dose-volume histograms (DVHs). Thus, the effect of GK and LINAC-based planning on hippocampal dose and target coverage rates was evaluated comparatively

Hippocampus Contouring and Dose Assessment

Hippocampal boundaries were determined by a single Radiation Oncologist using T1-weighted MR ratios according to the RTOG 0933 atlas. The PTV definition was created by adding a 1–2 mm isotropic margin to the GTV to minimize geometric uncertainties associated with the immobilization and image matching methods used. Although a GTV-based planning approach is preferred in many Gamma Knife applications, small safety margins can be used, especially in hypofractionated applications, while accounting for intrafraction motion and setup uncertainties. Stereotactic mask systems were used for immobilization in patients, and position verification was performed with image guidance before treatment. For each hippocampus, Dmax (the highest radiation dose reached at any point in the hippocampus volume), Dmean (the mean radiation dose to the whole hippocampal volume), V3Gy (the proportion of the hippocampal volume receiving 3 Gy), and V20Gy (the percentage of the hippocampus volume exposed to a dose of 20 Gray) were determined. The dose-volume constraints for the hippocampus and hippocampal protection region for SRS are shown in Table 2. Comparison of Dmax values in the hippocampus for Gamma Knife- and Linac-based

Table 2. Hippocampus and Hippocampal Protection Zone dose-volume constraints for SRS (15)

Hippocampus	D_{max} < 600 cGy
	$V_{3\,Gy}$ <%20
Hippocampal Protection Zone	D_{max} <2520 cGy
	V_{20Gy} <%20
	D_{max} <1200 cGy
	D_{ort} <3000 cGy

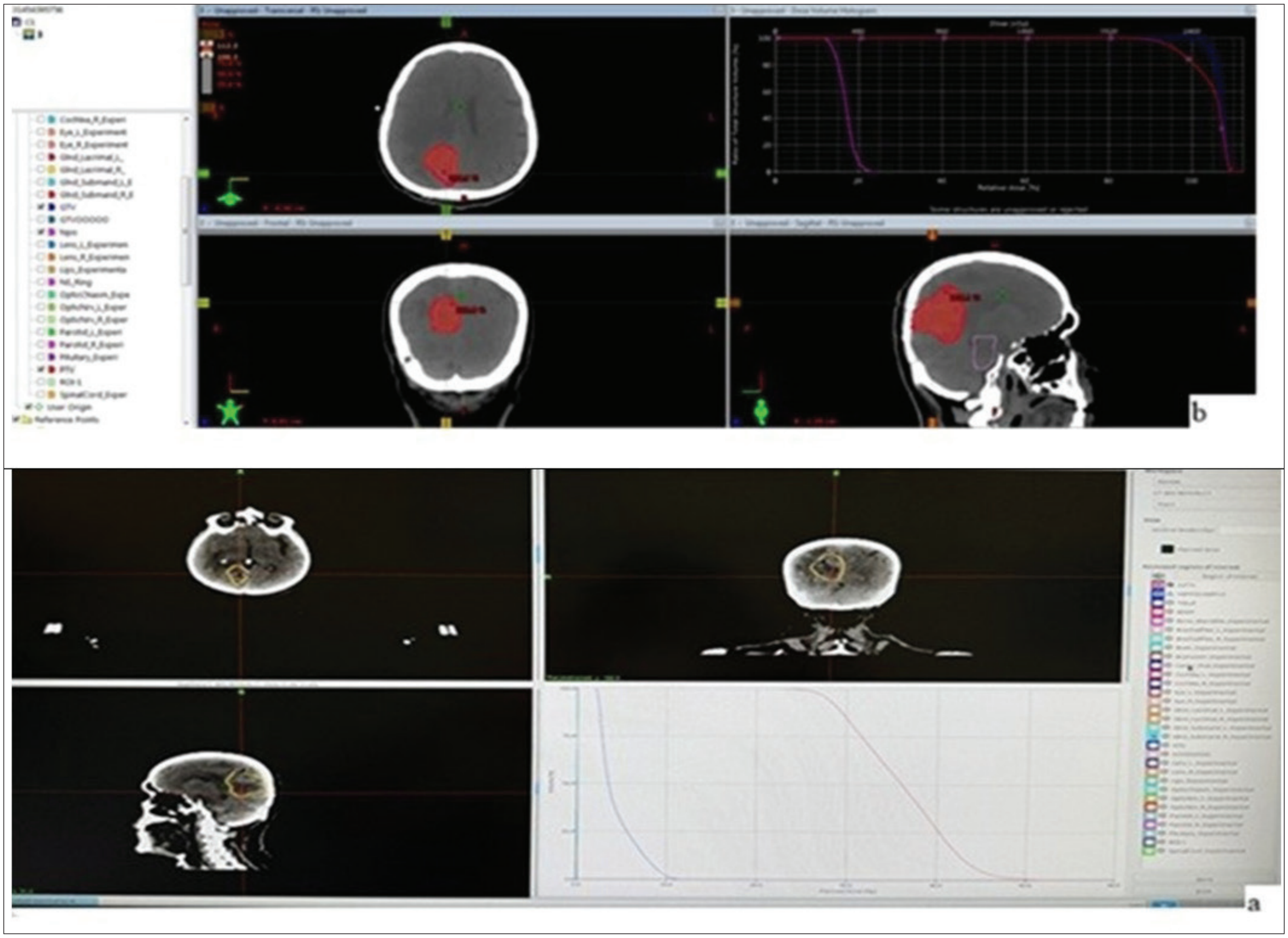

Figure 1. Gamma Knife (a) and Linac-Based (b)Radiosurgical Treatment Plans Dose- Volume Histograms

SRS is shown in Figure 2. These parameters were examined using data obtained from the dose-volume histogram (DVH). The Paddick Conformity Index (PCI), Gradient Index (PGI), and Homogeneity Index (HI) were also calculated to evaluate target coverage and dose falloff characteristics. A comparison of hippocampal doses in the planning of hypofractionated Gamma Knife and LINAC-based radiosurgery for patients with intracranial metastatic tumors is provided in Table 3.

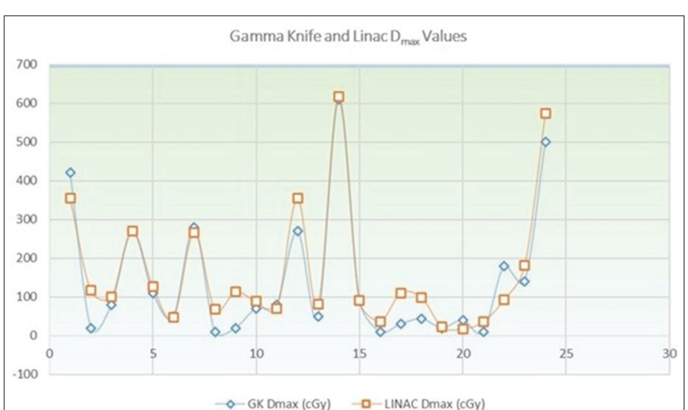

Figure 2. Comparison of D_{max} values in the hippocampus for Gamma Knife and Linac-based SRS

Paddick's conformity index

In stereotactic radiosurgery (SRS), achieving a highly conformal dose distribution is essential to reduce radiation exposure to surrounding normal tissues. To quantitatively assess the degree to which the high-dose region matches the target volume in both size and shape, Paddick introduced the Paddick Conformity Index (PCI) in 2000. This index assesses the relationship between the target volume (TV) and the prescription isodose volume (PIV) covering the target, thereby quantifying target coverage.

The PCI is formulated as (Eq. 1):

$$PCI = \frac{TV_{PIV}^2}{TV x PIV} \quad (1)$$

where TV_{PIV} represents the portion of the target volume covered by the prescription isodose volume. In an ideal plan, the CI equals 1 (8,9)

Table 3. Comparison of hippocampal doses in hypofractionated Gamma Knife and LINAC-based radiosurgery planning for patients with intracranial metastatic tumors

	Gamma Knife			Linac		
Patient No	D_{max} (cGy)	V_{3Gy}	V_{20Gy}	D_{max} (cGy)	V_{3Gy}	V_{20Gy}
1	422	35.3 %	0	355.2	33%	0
2	20	0	0	117.5	0	0
3	80	0	0	99.9	0	0
4	270	0	0	269.8	0	0
5	110	0	0	127.5	0	0
6	50	0	0	47.9	0	0
7	280	0	0	267.1	0	0
8	10	0	0	69.1	0	0
9	20	0	0	114.4	0	0
10	70	0	0	88.3	0	0
11	80	0	0	70.4	0	0
12	270	0	0	354.8	6.80%	0
13	50	0	0	80.9	0	0
14	610	27.2%	0	617.3	53.90%	0
15	90	0	0	90.7	0	0
16	10	0	0	36.9	0	0
17	30	0	0	110.4	0	0
18	43	24%	0	99.2	82%	0
19	20	0	0	23	0	0
20	40	0	0	18.2	0	0
21	10	0	0	36.3	0	0
22	180	0	0	93.6	0	0
23	140	0	0	181	0	0
24	500	65%	0	573	98%	0

Paddick's gradient index

While the conformity index is a valuable parameter for assessing how well a treatment plan conforms the dose to the target volume, dose fall-off outside the target is equally critical in stereotactic radiosurgery (SRS). The dose delivered to surrounding tissues is a key determinant of treatment-associated complications. In particular, the low-dose bath surrounding the planning target volume (PTV) is known to contribute significantly to normal tissue toxicity. Accordingly, assessing the steepness of the dose gradient outside the target volume is essential, especially in SRS plans characterized by very high dose gradients (10, 11).

The PGI is defined as (Eq. 2):

$$PGI = \frac{V_{50\%}}{V_{100\%}} \quad (2)$$

Paddick's Gradient Index (PGI) represents the ratio of the 50% isodose volume (V50%) to the prescription isodose volume (V100%).

Homogeneity Index (HI):

The Homogeneity Index (HI) characterizes dose homogeneity within the target, where values near unity reflect a more uniform dose distribution, whereas increasing deviation from 1 indicates greater dose heterogeneity(11).

The HI is defined as (Eq. 3):

$$HI = \frac{D_{max}}{D_P} \quad (3)$$

In this expression, Dmax refers to the peak dose within the target, whereas Dp denotes the prescription dose. An HI value approaching 1 is indicative of enhanced dose uniformity throughout the target volume(10).

Statistical Analysis

Dosimetry parameters were compared between GK and LINAC-based plans using matched statistical tests. All statistical analyses in our study were performed using the IBM SPSS Statistics software package (IBM Corporation, 1989, 2025). IBM SPSS Statistics for Windows, Version 31.0.0.0 (117), was used.

For statistical analysis, planning parameters were defined as descriptive statistics for dosimetric data (Dmax, PCI, PGI, and HI) and BOT (treatment time, in minutes) as Continuous variables were presented as mean ± standard deviation or median (minimum–maximum), as appropriate. Prior to comparisons within dependent groups, data distribution was assessed using numerical (Shapiro–Wilk test) and visual (histograms) methods. For normally distributed data, paired-sample t-tests were applied, whereas the Wilcoxon signed-rank test was used for non-normally distributed data. Statistical significance was defined as $p < 0.05$.

Comparative analysis of treatment plans demonstrated statistically significant differences between Gamma Knife and LINAC-based SRS for Dmax, PCI, and HI values ($p<0.05$). No statistically significant difference in PGI values was observed between the two modalities ($p>0.05$). Evaluation of treatment duration in terms of beam-on time (BOT) revealed a statistically significant difference ($p<0.05$). These results are presented in Tables 4 and 5.

Table 4. Hippocampal dose-volume constraints for Gamma Knife and LINAC treatment techniques. D_{max}, V3, V20

Planning Parameters	Gamma Knife	LINAC	p
D_{max} (cGy)	141.88 ± 34.1	164.26 ± 33.3	<0.05
V3	0	0	0
V20	0	0	0

Table 5. Planning parameters for Gamma Knife and LINAC treatment techniques. During treatment planning, the source dose rate was calculated to be roughly 2.66 Gy/min. Dmax, PCI – Paddick Conformity Index (Eq. 1); PGI – Paddick Gradient Index (Eq. 2); HI – Homogeneity Index (Eq. 3); BOT – Beam-on Time (minute).

Planning Parameters	GammaKnife	LINAC	p
PCI	0.89 ± 0.04	0.80±0.73	< 0.05
PGI	2.85 ± 0.21	5.32 ± 1.48	>0.05
HI	1.94 ± 0.16	1.17±0.28	< 0.05
BOT	14.24 ± 8.29	3.90±0.28	< 0.05

Main Points

- Gamma Knife (GK) plans generally provide lower hippocampal doses, particularly when the number of metastases is limited and the lesions are located farther from the hippocampus.
- LINAC-based FSRS plans tend to deliver higher hippocampal doses, but optimized planning and defining the hippocampus as an OAR can effectively reduce dose exposure.
- Dose–volume histogram (DVH) analysis revealed comparable hippocampal sparing between GK and LINAC systems, with low V20 values. A statistically significant difference was observed between the treatment plans in terms of hippocampal Dmax values (p = 0.002)
- Further research is needed to clarify hippocampal tolerance and neurocognitive dose–response relationships, as both platforms can achieve clinically acceptable doses with appropriate planning strategies

Results

Patient and Lesion Characteristics

The study cohort comprised 24 patients (12 females and 12 males; median age, 64 years; range, 38–75 years) with 24 solitary brain metastases. The most frequent primary tumor origins were lung (40%), breast (27%), and melanoma (13%). The median gross tumor volume (GTV) was 10.6 cm³ (range, 0.82–55.6 cm³). All patients underwent fractionated stereotactic radiosurgery (FRx-SRS) delivered in three fractions, with a median prescription dose of 27 Gy.

Hippocampus Dose Comparison

Dose–volume histogram (DVH) analysis showed that hippocampal doses were generally lower in GK plans than in LINAC-based SRS plans. Examining V3 (volume receiving 3 Gy within the hippocampus), there were 4 patients in the GK plans who received a dose exceeding 3 Gy to the hippocampus. In LINAC, 5 patients received a dose above 3 Gy to the hippocampus. Examining the V20 (volume receiving 20 Gy within the hippocampus) value, the volume receiving 20 Gy in the hippocampus is zero in both GK plans and the LINAC-based SRS. Similarly, the mean Dmax(cGy) values were 141.88 ± 37 Gy for GK and 164.26 ± 33.3 cGy for LINAC. Statistically, there is no significant difference in the Dmax value for the hippocampus between GK and Linac-based SRS planning (p = 0.002). Hippocampal dose–volume constraints for both Gamma Knife and LINAC treatment techniques are presented in Table 4.

Target Coverage and Conformity

Both Gamma Knife (GK) and LINAC-based radiosurgery treatment plans met institutional standards for acceptable target coverage. The mean Paddick conformity index (PCI) was 0.89 ± 0.04 for the GK plans and 0.80 ± 0.73 for the LINAC plans, with no statistically significant difference (p = 0.019). The gradient index (PGI), which reflects the dose falloff outside the target, was significantly lower in GK plans (2.85 ± 0.21) compared to LINAC plans (5.32 ± 1.48), with a statistically significant difference (p = 0.011). These findings suggest that steeper dose gradients are achieved with the Gamma Knife. The homogeneity index (HI) was 1.94 ± 0.16 for Gamma Knife plans and 1.17 ± 0.28 for LINAC-based plans, with no statistically significant difference between the two techniques (p = 0.010). Comparison of mean beam-on time (BOT) showed a significantly shorter treatment duration for LINAC-based SRS (3.90 ± 0.28 min) than for Gamma Knife (14.24 ± 8.29 min), with a statistically significant difference (p = 0.020). It should be noted, however, that Gamma Knife treatment time is influenced by source activity, which decreases over time due to cobalt decay, potentially affecting treatment duration. Planning parameters for Gamma Knife- and LINAC-based SRS are summarized in Table 5.

Discussion

ThThis study provides a comparative dosimetric analysis of hypofractionated stereotactic radiosurgery (FRx-SRS) delivered with Gamma Knife (GK) and LINAC-based systems for the treatment of brain metastases, with a particular focus on hippocampal dose exposure. The findings demonstrate that both platforms achieve comparable target coverage and conformity; however, GK offers a steeper dose gradient and consistently lower doses to the hippocampus. These results highlight important considerations for neurocognitive preservation during cranial radiotherapy.

Comparison With Previous Studies

The results of the present analysis are in agreement with earlier reports, which emphasize the superior dose-gradient characteristics of the Gamma Knife. Koide et al. (12) demonstrated that GK plans result in lower dose spillage to surrounding brain tissue while maintaining conformity comparable to LINAC-based plans in the treatment of multiple metastases. Similarly, Kondziolka et al. (13) attributed GK's enhanced dose fall-off to the use of multiple isocentric cobalt-60 beams and its inherently spherical beam geometry.

The present study extends these findings to the hypofractionated SRS setting, showing that even with multiple fractions, hippocampal dose metrics—Dmax, Dmean, and low-dose volumes—remain significantly lower with GK. This is particularly relevant to hippocampal avoidance strategies and efforts to mitigate neurocognitive decline. According to the RTOG 0933 protocol, maintaining hippocampal doses below Dmax (<16 Gy) and Dmean (<9 Gy) can reduce neurocognitive impairment during cranial radiotherapy (14). While SRS generally delivers hippocampal doses well below these thresholds, minimizing unnecessary exposure remains especially important in patients with a good prognosis, a long expected survival, or a potential need for future radiotherapy.

Clinical Implications

The ability of GK to achieve sharper dose gradients may translate into improved sparing of critical structures located near metastases, including the hippocampus, optic apparatus, and brainstem. This advantage is particularly relevant for patients enrolled in cognitive-preservation trials or for those with lesions adjacent to memory-related structures. On the other hand, LINAC platforms offer practical benefits such as shorter treatment times, workflow flexibility, and the integration of VMAT and IGRT techniques, making them advantageous in high-volume clinical environments. Thus, treatment modality selection should balance dosimetric precision, clinical workflow efficiency, and patient-specific factors.

Limitations

The present study is subject to certain limitations, most notably its retrospective nature and limited sample size, both of which may reduce the generalizability of the results. Only dosimetric parameters were evaluated, without correlation to post-treatment neurocognitive outcomes. Additionally, the analysis was based on simulated treatment plans, which may not fully reflect clinical implementation or patient-specific setup uncertainties. Future prospective studies incorporating neurocognitive testing and extended follow-up are required to better validate the clinical significance of hippocampal dose differences.

Conclusion

Both Gamma Knife and LINAC-based hypofractionated stereotactic radiosurgery (FRx-SRS) platforms provide highly conformal treatment for metastatic brain lesions and are associated with achieving clinically acceptable target coverage and plan quality. However, this study demonstrates that Gamma Knife offers a notable advantage in terms of hippocampal sparing and dose drop-off characteristics. The inherently steep dose gradients achievable with GK result in lower hippocampal Dmax, Dmean, and low-dose volumes, which may contribute to improved preservation of neurocognitive function—an increasingly important consideration as survival clinical outcomes in patients with metastatic disease are steadily improving.

LINAC systems, on the other hand, provide important logistical benefits, including shorter beam-on times, greater flexibility in treatment planning, and the ability to incorporate VMAT and IGRT workflows. These advantages make LINAC-based FRx-SRS a practical and efficient option in high-volume clinical settings. Therefore, the optimal modality should be selected based on the patient's anatomy, the closeness of lesions to critical structures, technological availability, and institutional workflow considerations.

As the role of hippocampal preservation becomes increasingly prominent in modern neuro-oncology, the clinical significance of even small differences in hippocampal dose may become more pronounced. Future prospective studies incorporating systematic neurocognitive assessment, long-term follow-up, and patient-reported outcomes are essential to better characterize the impact of hippocampal dose exposure on quality of life. Strengthening the evidence in this area will help refine treatment selection and support personalized stereotactic radiosurgery strategies for patients with brain metastases.

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Data Availability Statement: All relevant data are within the paper and they are available from the corresponding author on reasonable request.

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