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A Novel Perspective to Gamma-Knife Radiosurgery for Solitary Meningiomas: Adaptability of Fast Imaging Employing Steady-State Acquisition/Constructive Interference in Steady-State Magnetic Resonance Imaging

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ABSTRACT

AIM: To compare T1-weighted contrast-enhanced (T1+C) with fast imaging employing steady-state acquisition (FIESTA) magnetic resonance imaging (MRI) sequences to protect healthy brain tissue during meningioma treatment with Gamma-Knife radiosurgery (GKRS).

MATERIAL and METHODS: After reviewing the data of 54 patients with solitary meningioma who underwent GKRS between January 2020 and June 2022, demographic characteristics were noted, tumor volumes on T1+C and FIESTA MRI sequences were measured, and sequences were compared. The patients were then divided into two groups according to the presence of invasion to intracranial venous sinuses (groups 1 and 2, respectively). SPSS 11.5 software was used for data analysis, with the level of significance set at 0.05.

RESULTS: While no significant age and tumor size differences were observed between groups 1 and 2, sinus invasion was significantly higher among males. Tumor volumes measured in both groups were significantly smaller on FIESTA sequences than on T1+C sequences.

CONCLUSION: The T1+C sequence has been the primary imaging method because of meningiomas' high contrast enhancement feature. However, the T1+C sequence during GKRS planning is an effective imaging method in treating meningiomas; FIESTA sequences can more precisely delineate the tumor border. In this study, we consider that using the FIESTA/CISS sequence MRI for planning meningioma therapy with Gamma-Knife can reduce target volume and prevent irradiation of healthy brain tissue.

KEYWORDS: FIESTA/CISS, Meningioma, Gamma-Knife radiosurgery, Magnetic resonance imaging, Image-guided neurosurgery, Radiosurgery, MRI sequences

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INTRODUCTION

Meningiomas are the most common benign intracranial tumors in adults, constituting around 34% of all brain tumors (41). Although surgical resection is the first-line treatment in managing extensive tumors, stereotactic radiosurgery (SRS) can be a safe and effective alternative, especially for small meningiomas and those adjacent to critical neurovascular structures (19).

The Gamma-Knife radiosurgery (GKRS) is a unique, non-invasive, stereotactic radiotherapy method that utilizes precisely targeted gamma radiation beams to deliver concentrated doses of radiation to intracranial lesions such as metastases, schwannomas, arteriovenous malformations, meningiomas, and, less frequently, glial tumors, as well as for specific pathologies like trigeminal neuralgia, essential tremor, and obsessive-compulsive disease while sparing surrounding healthy tissue (42).

Magnetic resonance imaging (MRI) is indispensable in GKRS planning for the treatment of all aforementioned pathologies. T1-enhanced (T1+C) sequences are preferred for evaluating lesions. Generally, gadolinium-based contrast agents shorten the T1 relaxation time and make meningiomas appear hyperintense in the T1 series (10). Nowadays, more than 500 million doses of gadolinium have been used for MRI despite its well-known toxic side effects, such as nephrotoxicity and problems with muscle contraction and nerve conduction (11, 14). One of the contrast-free techniques is fast imaging employing steady-state acquisition (FIESTA) with high-resolution T2-weighted MRI sequences, which has a high signal-to-noise ratio that provides well-contrasted images (6).

This study aimed to evaluate the efficiency of FIESTA and T1-enhanced (T1+C) MRI sequences during GKRS planning for meningiomas.

MATERIAL and METHODS

The written informed consent was taken for each participant in this study. The Ethical Institutional Review Board of Pamukkale University reviewed and approved this study protocol (E-60116787-020-258960). It was conducted in line with the requirements of the Declaration of Helsinki.

MRI images from 102 patients with meningiomas who had undergone GKRS (Leksell Gamma-Knife® Perfexion™) between January 2020 and June 2022 at Pamukkale University were reviewed. GKRS planning was conducted using T1+C MRI sequences as suggested. Furthermore, FIESTA MRI examinations were performed using the specified parameters (repetition time/echo time, 6,7/2,8 msec; FA 60°; matrix, 320X256; section thickness, 2 mm; intersection gap, 0 mm; field of view, 240X240 mm). Patients who had previously undergone surgery or received other treatments, such as radiotherapy, were excluded from the study, as their inclusion could compromise the evaluation of the assessed MRI images. Therefore, we retrospectively reviewed the data of 54 patients with solitary meningioma who underwent first-time GKRS. The patients were divided into two groups: Group 1 consisted of those with meningiomas with venous sinus invasion (Sindou Type I–VI) (35), whereas Group 2 consisted of those without invasion. The reason for dividing groups according to their sinus invasion is that the dural sinus's high and homogenous contrast enhancement may reveal similar to adjacent meningioma and exaggerate the target volume. Therefore, we decided to investigate the meningiomas with sinus invasion separately. In addition, the demographic data, tumor volumes (in T1+C and FIESTA MRI sequences), and anatomical locations of the tumors were examined, as shown in Figures 1 and 2.

Statistical Analysis

SPSS 11.5 software was used for data analysis. Quantitative variables were presented as mean ± standard deviation and median (minimum-maximum), whereas qualitative variables were presented as the number of patients (percentage). Differences in the categories of qualitative variables and the two categories of quantitative variables were determined using the Student t-test for normality distributed data and the Mann-Whitney U test for non-normally distributed data. The Wilcoxon signed-rank test was used to determine differences in the two dependent quantitative variables (before-after), given that the assumptions of a normal distribution were not satisfied. The level of significance was set at 0.05 ($p<0.05$).

RESULTS

Patient demographic data (i.e., age and gender) and tumor volume results on each sequence are summarized in Table I. A median dose of 14 Gy (12–18 Gy) was prescribed to that isodose-line covering 97–100% of the target volume. The mean age of the patients was 58.72 ± 13.35 (range 35–89) years and 57.48 ± 12.31 (38–92) years in group 1 (n=29) and group 2 (n=25), respectively. No significant difference in patient age was observed between the two groups. Males accounted for 10.3% (n=3) and 40% (n=10) of the patients in groups 1 and 2, respectively. Sinus invasion was more common in males than females ($p=0.011$). Tumor volume measurements on both T1+C and FIESTA sequences revealed higher tumor volume in group 2 than in group 1, albeit insignificant ($p>0.05$). Nevertheless, tumor volume measurements in both groups were smaller on FIESTA sequences than on T1+C sequences ($p<0.01$; Table II).

DISCUSSION

To the best of our knowledge, this has been the first study published on the potential benefit of the FIESTA MRI sequence during GKRS planning for treating solitary meningiomas. Meningiomas, the most common benign intracranial tumors, are generally asymptomatic when smaller than 2 cm (24). Around 2.5% of meningiomas are incidentally detected during MRI studies performed on adult patients (4). Treatment approaches have been controversial, especially for incidental meningiomas (7,15,25,43). Generally, surgery is not preferred in cases with asymptomatic or mild symptoms (e.g., headache), especially in tumors <3 cm. Among patients in which meningiomas were incidentally detected, 24–57% showed progression during follow-up without any intervention (15,25,31). Sughrue

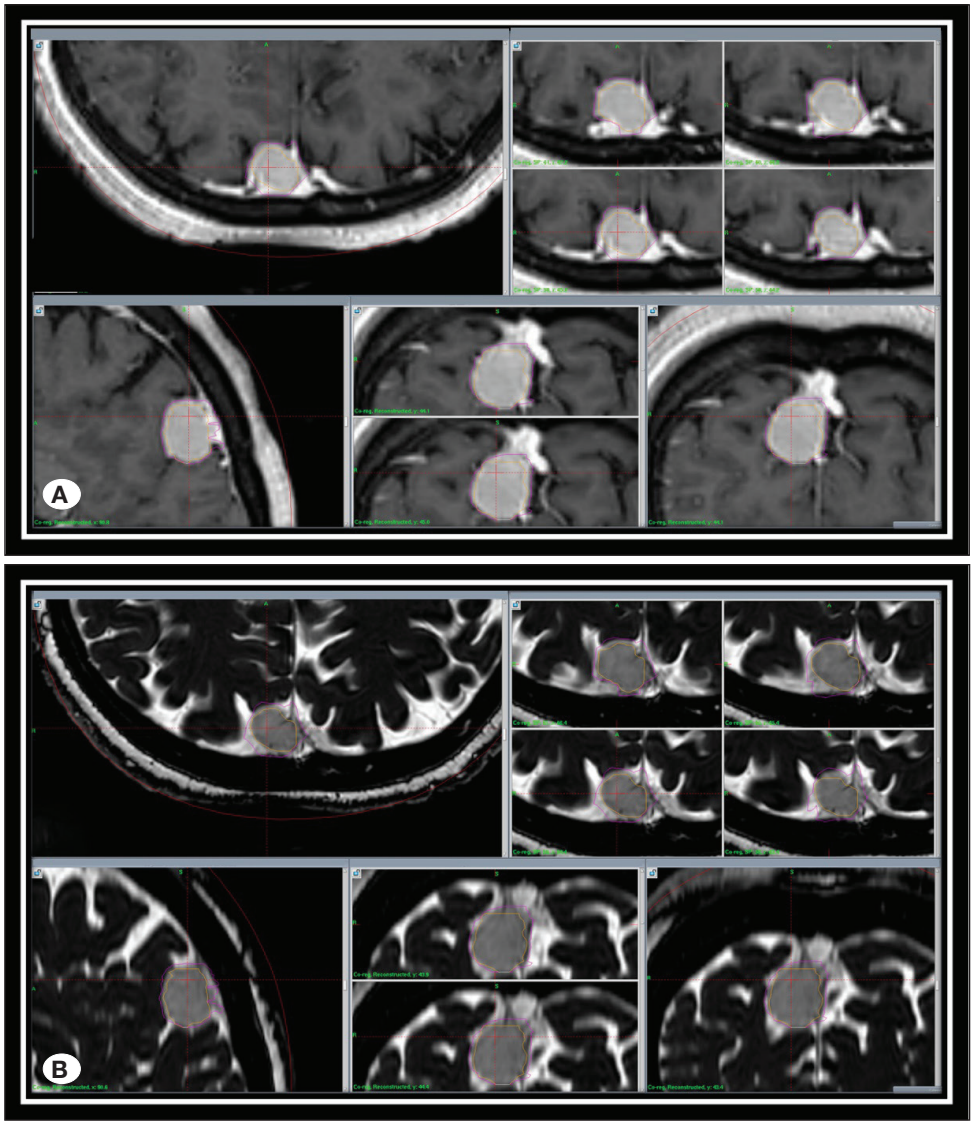

Figure 1: A) The purple line represents the right parasagittal meningioma border determined by T1 contrast-enhanced MRI for GKRS. **B)** The yellow line represents the right parasagittal meningioma border in the same section of the same tumor on FIESTA sequence MRI.

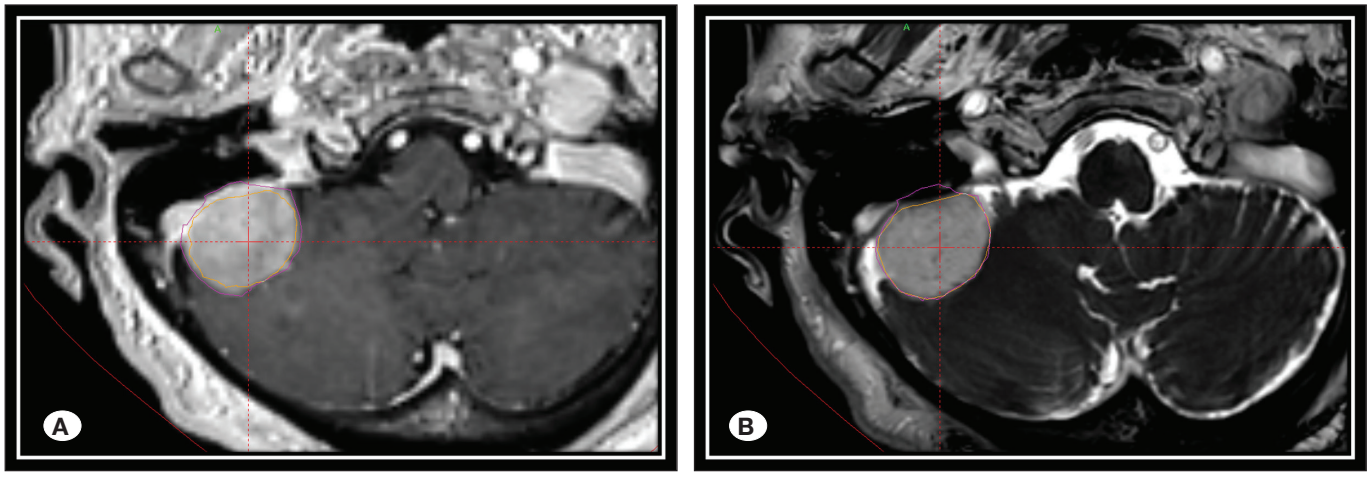

Figure 2: A) The purple line represents the right cerebellar meningioma border determined by T1 contrast-enhanced MRI for GKRS. **B)** The yellow line represents the border of the right cerebellar meningioma in the same section of the same tumor on FIESTA sequence MRI.

Table I: Comparison of Variables Between the Groups

Variables		Group 1	Group 2	p-value
Age	Mean ± SD	58.72 ± 13.35	57.48 ± 12.31	0.596
	Median (Min–Max)	58.00 (35.00–89.00)	56.00 (38.00–92.00)	
Gender; n (%)	Male	3 (10.3)	10 (40.0)	**0.011**
	Female	26 (89.7)	15 (60.0)	
T1+C Volume (cm^3)	Mean ± SD	3.22 ± 2.92	4.39 ± 3.41	0.143
	Median (Min–Max)	2.32 (0.34–11.99)	3.30 (0.61-12.93)	
FIESTA Volume (cm^3)	Mean ± SD	2.36 ± 2.41	3.36 ± 3.04	0.125
	Median (Min–Max)	1.60 (0.16–10.46)	2.21 (0.47–11.80)	

SD: *Standard deviation,* ***Min:*** *Minimum,* ***max:*** *maximum.*

Table II: Comparison of within-Group T1-Enhanced and FIESTA Sequences

Group	T1+C Volume (cm^3)		FIESTA Volume (cm^3)		
	Mean ± SD	Median (Min–Max)	Mean ± SD	Median (Min–Max)	p-value
1	3.22 ± 2.92	2.32 (0.34–11.99)	2.36 ± 2.41	1.60 (0.16–10.46)	**<0.001**
2	4.39 ± 3.41	3.30 (0.61–12.93)	3.36 ± 3.04	2.21 (0.47–11.80)	**<0.001**

SD: *Standard deviation;* ***Min:*** *Minimum;* ***max:*** *Maximum.*

et al., who examined the natural history of meningiomas, indicated that these lesions would likely become symptomatic when growth exceeds 10% per year. Peritumoral hyperintensity occurs on the T2 sequence during follow-up. In contrast, they stated that tumors <2 cm and with a yearly growth of <10% have a close to 0% probability of being symptomatic (37). In such cases, GKRS is frequently employed as the treatment method (28,31), especially in critical areas such as the skull base (12,23). GKRS has been considered a safe treatment approach for meningiomas in areas wherein surgical intervention carries high risk, providing low morbidity and 5-year progression-free survival of over 90% (3,29,31).

GKRS usually involves using single or multiple isocenters with different beam diameters to obtain a treatment plan that fits the 3D volume of the target. Although the basic principle of GKRS is to irradiate the target through high-dose gamma rays, evidence has shown that surrounding tissues are also affected by this radiation (3). In addition, studies have revealed that GKRS can cause lethal toxicity by inducing radiation necrosis, with an incidence of 5–24% (32). Moreover, peritumoral edema may develop or increase by 7–38% after GKRS (20,27,33,34). Pre-existing peritumoral edema raised brain parenchyma–meningioma contact surface, parasagittal and parafalcine locations, tumor size, and high-grade pathology have been identified as factors for increasing the incidence of edema in such cases (5,9,17,20,27,33,34,39).

Several studies suggest that different radiological examinations could be used in the differential diagnosis and follow-up of cranial lesions (8,13,16,30,36,38,40). While planning GKRS, understanding the association with the dural sinuses is essential. Exaggerated tumor volume delineation due to misinterpretation of the dural sinus as a lesion might lead to excessive irradiation of normal tissues. We examined FIESTA MRI sequences to distinguish between the dural sinuses and meningiomas and trace the tumor borders in our study. Given that T1-enhanced MRI may show meningiomas and dural sinuses in almost the same signal intensity, we speculate that the tumor volume might appear larger than it should be. In the present study, comparing T1-enhanced and FIESTA sequences in the same tumor revealed that the determined tumor was significantly smaller on FIESTA sequences. Furthermore, we observed that all meningioma volumes were significantly more diminutive on the FIESTA series than on the T1-enhanced series ($p<0.05$).

Several studies have been published regarding FIESTA MRI sequences in tumor imaging and follow-up. In 2009, Özgen et al. used only follow-up imaging of vestibular schwannomas to inspect the accuracy of constructive interference in steady-state (CISS) sequence. Notably, they reported 100% sensitivity, specificity, and accuracy in detecting the progression of the CISS sequence (26). Abele et al., who used CISS and coronal T2-weighted MRI sequences to see small (≤10 mm) internal auditory canal lesions, found a 100% sensitivity for tumor detection (1). In 2021, Arya et al. demonstrated that 3D FIESTA MRI sequences showed 100% sensitivity and specificity in assessing the cerebellopontine angle (CPA) tumor borders and cranial nerve involvement (2). Moreover, Lang et al., who compared CISS and T1-weighted MRI sequences for imaging pituitary adenomas in Cushing's patients, suggested

that adding CISS sequences improves lesion detection (22).

Nonetheless, recent studies have been published on the risks of gadolinium and its deposition in tissues (10,18). Some authors have attempted to find different tumor imaging methods using deep learning architecture (21). As is well known, contrast agents should not be recommended for patients with renal dysfunction. In fact, since 2014, research on this subject has continued to increase, considering that gadolinium can accumulate piles up in the tissues of patients with normal kidney function (18). Reports have shown that increased hyperintense signals during repetitive T1+C examinations of brain tissue, especially in the basal nuclei, were correlated with gadolinium deposition from previous administrations. In addition, pathological investigations have revealed that residual gadolinium accumulates in extracranial tissues, such as the liver, skin, and bone tissues, apart from brain tissue (18). Therefore, using FIESTA instead of T1+C sequences in the future might help avoid tissue deposition and contrast agent toxicity.

Some limitations of the current study are worth noting. First, this was a retrospective study with a limited sample size. The applicability of FIESTA MRI to different tumor pathologies constitutes another limitation of our research. Moreover, we failed to evaluate the treatment efficiency of GKRS planning using only the FIESTA sequence in clinical practice. The other restriction is we only focused on volumetric analysis, not on location; however, potential tissue damage after GKRS also depends on proximity to adjacent neuronal structures (such as the optic nerve, cochlea, brainstem, etc.). Therefore, more prospective studies are needed to better understand the efficiency of this sequence's exclusive use.

CONCLUSION

Based on the studies mentioned herein, applying the FIESTA sequence in the planning of GKRS to treat meningiomas is a unique approach and, this is the first study in the literature. Furthermore, the present study revealed that FIESTA sequences yielded smaller volume measures than T1+C sequences in the same tumor. This new perspective in GKRS planning for treating meningiomas may limit excessive irradiation of normal brain tissue and contrast agent deposition. Nonetheless, future studies with larger sample sizes will help clarify the benefit of FIESTA sequences in meningiomas.

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Declarations

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Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: Authors declare no conflict of interest.

AUTHORSHIP CONTRIBUTION

Study conception and design: UAD, EE, ES
Data collection: RA, FY, BA
Analysis and interpretation of results: BB
Draft manuscript preparation: UAD, EE
Critical revision of the article: MEC
Other (study supervision, fundings, materials, etc...): FA, SC
All authors (UAD, EE, FY, RA, BA, SC, BB, ES, FA, MEC) reviewed the results and approved the final version of the manuscript.

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