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The Evaluation of Gamma Knife Indices for Treatment Planning (Single Session, Multi-Session, and Hypofractionation) for Gamma Knife Radiosurgery in Patients with Meningioma

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Abstract

Background Meningiomas are the most common benign intracranial tumors, making up about one-third of all primary brain tumors, some can cause issues due to difficult removal in sensitive or hard-to-reach areas. Gamma knife radiosurgery (GKR) is an effective treatment for meningioma.

Objective To assess better planned treatments, such as multisession and hypofractionation, as well as single session stereotactic radiosurgery.

Methods Fifty-two patients with meningiomas, diagnosed by neurosurgeons or oncologists, participated in a cross-sectional study at Saad Alwitry Hospital’s Gamma Knife Center. Gamma Knife therapy was administered by a specialist, with computed tomography (CT) and magnetic resonance imaging (MRI) used to evaluate the tumor characteristics. The dosimetry parameters used in this study are coverage, selectivity, gradient index (GI), and time (minutes). These parameters are obtained for each plan session.

Results There were significant differences in the mean value of selectivity between the three groups, with the highest value among the patients who received multi-session doses of GKR (Gy) than those who received single and hypo sessions of GKR (Gy). The results also revealed non-significant and slight differences in the mean values of the GI between patients who received multi, single, and hypo sessions. Patients who received multiple sessions required fewer mean values of GKR shot numbers. This study also found that patients who received hypo-session GKR required less time (minutes) for gamma knife radiation therapy. Ultimately, the results showed the differences in tumor size (cm^3) before and after GKR treatment according to doses given in the three sessions.

Conclusion Multisession GKR therapy offers a low-morbidity alternative that is secure, efficient, and well tolerated for these large lesions. The meningioma multisession GKR is successful in reducing the size of large tumors.

Keywords Gamma knife, stereotactic radiosurgery, coverage, selectivity, gradient index (GI), number of Shots (dose), tumor Reduction.

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List of abbreviations: ACE2 = Angiotensin-converting enzyme 2, BSA = Bovine serum albumin, *C* = Coverage, *C*I = Conformity index, GI = Gradient index, CS = Chitosan, COVID-19 = Corona virus disease 2019, CS = Chitosan, CS-NPs = Chitosan nanoparticles, ORF = Open reading frames, RBD = Receptor-binding domain, SARS-CoV-2 = Severe acute respiratory syndrome virus

Introduction

Meningioma typically attaches to the dura and develops from the arachnoid's meningothelial cells.

Meningioma is the most prevalent subtype of benign intracranial tumors. As they develop outside of the brain, they may cause symptoms. If they are located near the base of the skull, they could irritate cranial nerves. A meningioma can cause a number of symptoms, depending on the tumor's size and location [1]. Meningothelial cells of the arachnoid evolve into meningioma, which often adheres to the dura [2].

Since stereotactic radiosurgery reduces the likelihood of tumor recurrence in meningiomas that are still present without significantly boosting management risk, it has become one of the more popular alternatives for treating meningiomas. Stereotactic radiosurgery is more efficient for smaller tumor sizes [3].

The tumor volume is reduced through surgery, and tumors that have only undergone partial excise are managed through radiosurgery. The likelihood of future further radiosurgical treatment has significantly reduced the need for surgical radicality as well as, thus, the risk of likely postoperative complications [4].

The upgraded Leksell Gamma Knife (ICON) allows clinicians to employ a novel technique; Hypofractionation and multi-session are two ways to treat people with too many benign skull base tumors of different sizes or lesions that are too close to critical anatomy. Hypofractionation means that the needed tumor dose is given to the patient over a number of days, while multi-session means that the needed tumor dose is given to the patient all at once over a number of sessions. During multi-session stereotactic radiosurgery (SRS), high doses per fraction can be delivered to the tumor bed with quick dose falloff, sparing critical structures and minimizing radiation-related damage [5].

SRS is a non-invasive medical procedure that uses highly focused beams of radiation to treat tumors and other medical conditions in the brain. SRS delivers a high dose of radiation to the targeted area in a single session or in a small number of sessions. SRS is often used to treat small tumors or lesions that are difficult to remove through surgery or located in sensitive areas of the brain [6].

The required dose of radiosurgery is given in a single session, or, in the case of so-called multisession radiosurgery, a few fractions. To minimize exposure to healthy surrounding tissues, radio surgical treatments must have extensive target coverage (ablative therapy) and the sharpest dose gradient imaginable. To do this, the equipment must have high mechanical, geometric, and dosimetric precision as well as sub-millimeter patient positioning accuracy [7,8].

This study aimed to determine the most effective treatment plan for meningioma by assessing and selecting the most effective method among single-session, multi-session, and hypofractionated gamma knife radiosurgery (GKR) in patients with meningioma.

Methods

From September 2022 to March 2023, the Gamma Knife Center at Saad Alwitry Hospital for Neurosciences in Baghdad conducted a cross-sectional study on 52 patients diagnosed with meningiomas by an oncologist or a neurosurgeon. According to the type of tumor meningioma, the neurosurgeon prescribed dosages of 10–14 Gy for grade I meningiomas and 14–18 Gy for grade II and III meningiomas, respectively. Meningioma patients (of all grades) treated with hypofractionation in many sessions and GKR with integrated cone-beam imaging and online adaptive planning (ICON) in a single session. Philips has collected pictures from the Achieve 3 Tesla or 1.5 Tesla Magnetic Resonance Imaging (MRI) prototype [9]. Before and after 6 months of GKR, the group's results will be compared by using MRI of gamma knife pictures [10]. The optimal session was determined by estimating the impact of each session on tumor growth and treatment planning.

Only patients with meningioma were included in this study.

Statistical analysis

Analysis of data was carried out by using statistical package for social sciences, version 25 (SPSS-25). Data were presented in simple measures of percentage, mean, standard deviation, and range (minimum-maximum values). The significance of the difference of different means (quantitative data) was tested using students t-test for the difference between two independent means or the paired t-test for a difference of paired observations (or two dependent means). Scattering distribution curve used for correlation. Statistical significance was considered whenever the P value was equal to or less than 0.05.

Results

The diametric parameters used in this study are coverage, selectivity, gradient index (GI), and time (minute). These parameters are obtained for each form of plan session: hypofractionation group, single session group, and multisession group. The mean±standard deviation is shown in table (1).

Table 1. The evaluation parameters according to staging group

Parameters	Multi-session	Single-session	Hypo-session
Coverage	0.93±0.013	0.91±.006	0.89±0.009
Selectivity	0.92±0.019	0.74±.014	0.72±0.08
Gradient Index (GI)	2.7±0.052	2.69±.029	2.63±0.05
Number of Shots	2.79±0.052	10.19±.927	14.63±2.75
Time (Minutes)	35.81±2.56	57.88±22.72	27.61±4.56

Figure 1 shows the coverage parameter for each plan session and was found to be 0.93±0.013 in multi-session, 0.91±.006 in the single session, and 0.89±0.009 in hypo-session plans, respectively, with a P value of 0.02.

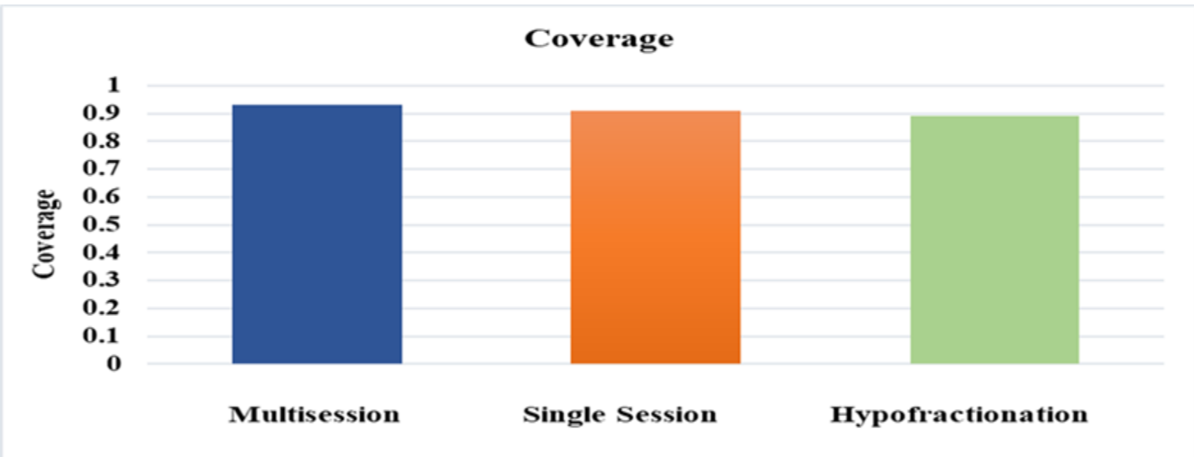

Figure 1. Comparison of coverage for sessions

The mean value of selectivity was significantly different between the three groups, as shown in figure (2). The patients who received multiple sessions of GKR (Gy) had the highest value, followed by those who received single sessions of GKR (Gy) and hypo sessions of GKR (Gy) (0.92±0.019, 0.74±.014, 0.72±0.08) respectively, with a P value of 0.03.

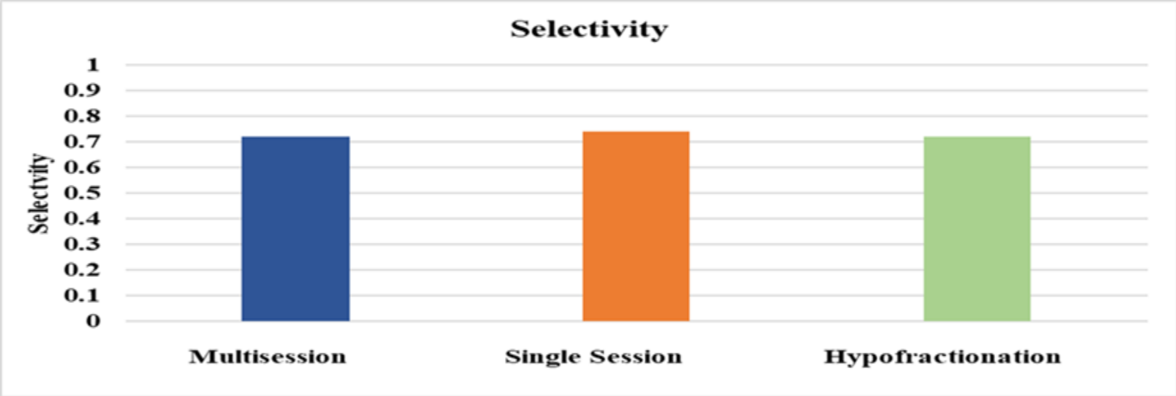

Figure 2. Comparison of selectivity

Also, there were small but not very important differences in the mean values of the GI between patients who got multiple, single, or hypo sessions of GKR (Gy) (2.7±0.052, 2.69±.029, and 2.63±0.05), the P value = 0.06 (Figure 3).

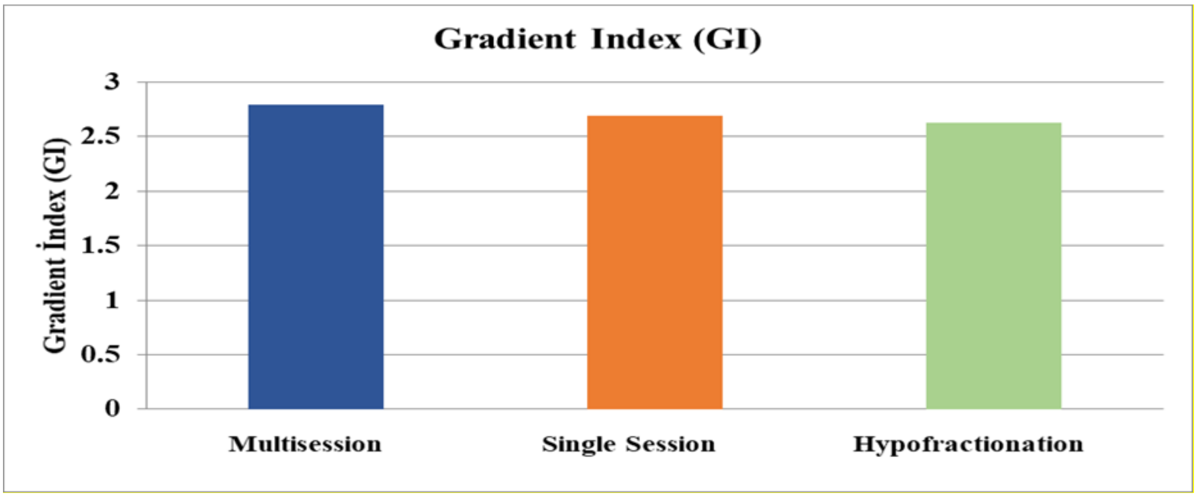

Figure 3. Comparison the gradient index

Although a lower mean shot number of GKR was required for the patients that received multi-session groups than those that received single and hypo session gamma knife radiation therapy (2.79±0.052, 10.19±.927, 14.63±2.75), respectively, the P value was 0.08 (Figure 4).
The results also recorded that those patients who received hypo session GKR received less time (minutes) for giving gamma knife

radiation therapy compared to those who received multi- and single-session GKR respectively, with a P value of 0.55 as shown in figure (5).

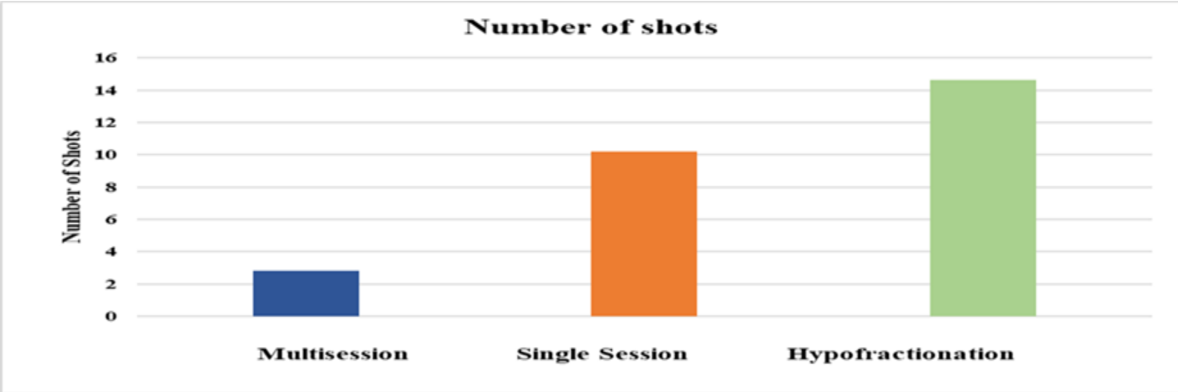

Figure 4. Comparison the number of shots

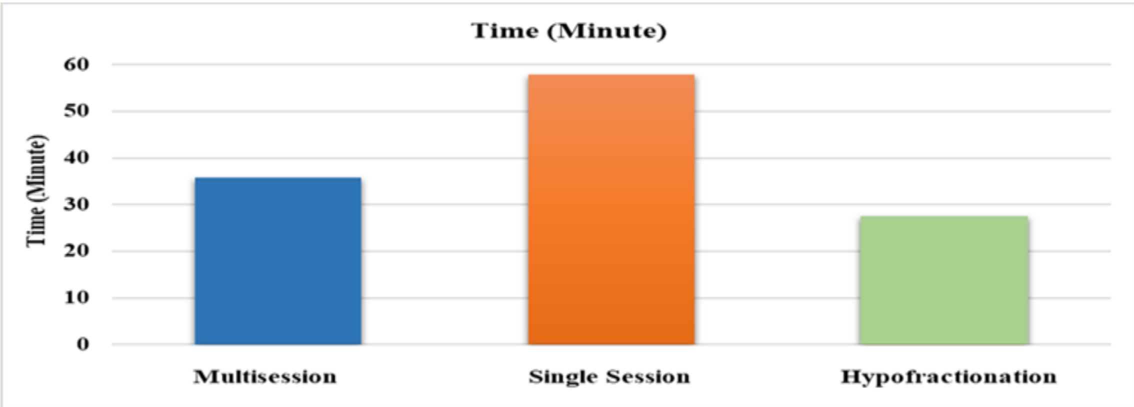

Figure 5. Comparison the time (minutes)

Table 2 illustrates that the patients received a variety of doses, and the results showed that multi-session doses were more effective in reducing tumor size than single and hypo-session dosages.

Table 2. Tumor size reduction

Dose	% of tumor reduction (M±SD)		Hypo-session
	Multi-session	Single session	
10 Gy	74.14	28.68	-
12 Gy	67.21	28.41	-
13 Gy	61.84	52.97	-
14 Gy	45.16	1.54	2.92
15 Gy	76.08	70.97	95.29
16 Gy	-	58.82	73.28
18 Gy	-	-	60.02

Discussion

A comparative analysis was conducted among three groups of meningioma patients who underwent different treatment approaches: multisession, single session, and hypofractionation. The dosimetry parameters assessed included coverage, selectivity, GI, and treatment time (in minutes).

The coverage parameter assessed the extent to which the prescribed dose in each treatment group encompassed the target volume. On the other hand, selectivity assessed the treatment's ability to spare surrounding healthy tissues while delivering the desired dose to the tumor. The GI was used as a measure of the rate at which the radiation dose fell off from the target volume, indicating the sharpness of the dose fall-off. Finally, the treatment time was recorded in minutes to assess the duration of each treatment approach. These dosimetry parameters were used to comprehensively compare the three different treatment groups in terms of their ability to achieve adequate coverage of the target volume, spare healthy tissues, achieve a sharp dose fall-off, and minimize treatment time.

The results showed that the multisession technique had the ability to cover the tumor significantly more than those treatments with single sessions, followed by hypofractionation sessions.

The findings revealed notable variations in the selectivity of treatment outcomes among three groups, with the highest selectivity observed in patients who underwent multiple sessions of GKR at higher doses (in Gy) compared to those who received single-session or hypo fractionated GKR. The results also showed that the GI, which is a measure of dose falloff, did not differ significantly among patients who received multiple, single, and hypo fractionated GKR sessions. These results suggest that the total dose given as well as the dose fractionation scheme may affect the selectivity of GKR treatment outcomes. However, the different dose regimens may not have a big effect on the GI. Many primary tumors, such as meningiomas and metastatic brain malignancies, are treated with either single-fraction radiosurgery (SRS) or hypo fractionated (2-5 fraction) cranial radiosurgery (fSRS) [11]. The three techniques used in this study are single session, multi-session, and hypofractionation [12,13].

The dose of radiation administered for meningioma patients varied depending on the treatment approach. For multi-session gamma knife treatments, the dose ranged from 10 to 15 Gy, while for single-session gamma knife treatments, it ranged from 10 to 16 Gy. However, for patients who received the hypofractionation technique, the dose ranged from 14 to 18 Gy. The impact of radiation on tissue is quantified by considering the amount of radiation absorbed per unit mass and the volume of tissue that is irradiated. Mayneord [14] proposed the concept of "integral dose" (ID) as a means to estimate the total energy absorbed by tissue from radiation. ID is calculated as the product of mean dose and target volume, expressed in millijoules (mJ) ([ID] = mean dose x target volume), and it can also be defined as the area under a differential dose volume histogram. Gamma knife stereotactic radiosurgery (GKSRS) treatments are known for their steep dose falloff, which is facilitated in part by allowing for a significant dose hotspot (often around 100% of the prescribed dose) at the center of the dose distribution [15].

The absorbed dose (D) and the mass of the irradiated tissue (dm) are combined to determine the ID. The ID is a measure of the total energy absorbed by the tissue due to radiation exposure. Notably, the volume of irradiated tissue influences the ID, with larger volumes absorbing more energy compared to smaller volumes, even when exposed to the same absorbed dose [16]. Gamma radiation irradiates the patients, absorbing the dose into the brain organ and causing necrosis. Symptomatic necrosis can happen when there is direct brain damage or necrosis inside the target that sets off an inflammatory cascade. This can cause a mass effect and/or surrounding edema, compression, and even herniation of normal brain tissue. Vascular endothelial damage is the hypothesized cause of necrosis. Edema may also develop in the absence of necrosis. Edema and/or necrosis symptoms include headache, nausea, vomiting, ataxia, seizure, and focal site-dependent functional impairments (16,17).

The results of this study revealed that patients who received multi-session gamma knife treatment had larger tumor volumes for meningiomas compared to those treated with the hypofractionation technique. Conversely, patients who underwent single-session gamma knife treatment had smaller tumor volumes.

Henzel and colleagues (18) observed a significant mean regression of 16.6% in the first 6 months post-SRS and identified a comparable trend in regression, with the most rapid response in the first 6 months. In contrast, Astner et al. (19) did not observe volume reduction until 11 months posttreatment, and they only noted a mean regression of 27%. Notably, the cohort primarily consisted of meningiomas treated with fractionated stereotactic radiotherapy and six tumors treated with radiosurgery, resulting in a median volume reduction of 44%.

Current findings agreed with those of Harrison et al., who found that certain tumors had non-uniform responses to SRS. Cancers that eventually shrank by 9 percentage points (6 percentage points total) were more common than tumors that eventually shrank by 35 percentage points but still advanced (2.4 percent overall). Transient expansion before regression may be perplexing, although a partial therapeutic response before advancement may fit an anticipated response pattern (20,21).

This study findings may be attributed to a transient increase in tumor volume, which could occur as the tumor center responds to the targeted injury inflicted by SRS. Notably, these changes in tumor volume may vary depending on the length of time elapsed after the SRS procedure. Further investigation and analysis are warranted to better understand the underlying mechanisms and temporal dynamics of this observed phenomenon (22,23).

The "shot" refers to the gamma radiation beam used in SRS for patient treatment. The number of shots required varied depending on the treatment approach. Patients who received the hypofractionation technique required a higher number of shots compared to those treated with a single-session gamma knife, followed by patients treated with a multi-session gamma knife. Single-fraction therapy of small lesions is successful for tumor management and normal tissue sparing, but for bigger tumors, striking a balance between tumor control and radiation-induced damage may be a significant difficulty. The Radiation Therapy Oncology Group (RTOG) study showed that tumor diameters over 2-3 cm restrict the capacity to safely administer a sufficient dosage in a single fraction to big tumors. In larger tumors and those close to key structures, fractionated GKRS (usually 2–5 sessions) may offer a better balance of tumor reduction and normal tissue damage compared to single-fraction GKRS (24).

In conclusions, this study revealed that multisession GKR is significant in the reduction of meningioma tumor size. This finding may provide valuable insights into the dosimetric aspects of the different treatment approaches for meningioma patients, aiding in the optimization of treatment planning and decision-making in clinical practice. Further details of the dosimetry parameters and their implications in the context of meningioma treatment can be explored in the subsequent sections.

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Author contribution
Ibrahim: Contributed to the treatment plan for patients under the supervision of supervisors, collected the data and wrote the paper. Dr. Ahmed: Checked the treatment plan, conceived and designed the analysis. Dr. Hassan: Gived the specified radiation dose and supervising the treatment plan.

Conflict of interest
Authors declare there is no conflict of interest.

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