Master of Medicine

Efficacy and Tolerability of Radiosurgery in the Treatment of Benign Meningioma:

Dose Comparison Study from a Single-Center Analysis

The Graduate School

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지난 2년간 직장 생활을 병행하며 많은 분들의 배려와 이해로 석사 과정을 진행해 왔습니다. 그리고 오늘, 학위 논문을 제출함으로 모든 석사과정을 마무리하게 되며 혼자라면 절대 해내지 못했을 그 과정에 도움 주신 분들께 감사의 인사를 드립니다.

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그리고 귀중한 시간을 할애하시어 데이터 수집에 도움 주신 이왕춘 선생님께도 이 자리를 빌려 감사인사 드립니다. 바쁜 업무 중에 저의 짐을 나누어 주시기 쉽지 않으셨을 텐데, 흔쾌히 함께 해 주신 점에 대해 깊이 감사드립니다.

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Abstract

Efficacy and Tolerability of Radiosurgery in the Treatment of Benign Meningioma: Dose Comparison Study from a Single-Center Analysis

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OBJECTIVE: Meningioma is a mostly benign brain tumor, constituting about a third of all brain tumors. It's categorized into three grades by the WHO. The primary treatment is surgical removal, but stereotactic radiosurgery (SRS) is increasingly used, especially for low-grade, difficult-to-access, or recurrent tumors. SRS delivers targeted radiation, showing high efficacy in tumor control and neurological function preservation. Despite its efficacy, optimal radiation doses and long-term effects are still uncertain, and treatment approaches continue to evolve, with recent trends favoring lower radiation doses.

METHODS: In this study, 162 patients with WHO grade I benign meningiomas

were treated with single-session SRS using the TrueBeam system from 2014 to 2022. Patients undergoing repeated or fractionated SRS were excluded. Treatment effectiveness was assessed using radiologic image scans, focusing on local control rate, progression-free survival, and radiation-induced toxicity. Patients were divided into two groups based on their radiation dose (above or below 14 Gy) for further analysis. Statistical analysis was conducted using SPSS, following STROBE guidelines and with IRB approval.

RESULT: Between March 2014 and December 2022, 162 patients with 190 meningiomas were treated with SRS at our center. After excluding some cases, 147 patients with 164 lesions were analyzed. The patients' average age was 61 years, predominantly women (76.2%). Most were asymptomatic, while others had various symptoms. Diagnoses were mainly via Magnetic Resonance Imaging, with some histopathologic confirmations.

The lesions were almost equally split between skull base and non-skull base locations. The median follow-up was 42 months. The average target volume for SRS was 4.49 cm^3, with a median dose of 14 Gy. Clinical progression was observed in 8 patients (5.4%), with high progression-free survival rates at 1, 2, and 5 years. Treatment outcomes included partial responses and stable disease, with a 95.1% crude local control rate.

Radiation-induced adverse events occurred in 27.2% of patients, varying in severity. Peritumoral edema post-SRS was noted in 12.8% of lesions, with a higher incidence in the group receiving higher radiation doses. Overall, the study highlighted the effectiveness and safety profile of SRS in meningioma treatment, with considerations for optimal radiation dosing.

CONCLUSION: This study found that a radiation dose of less than 14 Gy effectively controls the tumor without significantly impacting the local control rate and results in fewer side effects, making it a preferable dose for future treatments.

Key words: Meningioma, Radiosurgery, Dose, Toxicity

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Introduction

Meningioma, a primary intracranial tumor originating from the meninges enveloping the brain and spinal cord, predominantly manifests as a benign neoplasm, with only a minority exhibiting malignant characteristics [1, 2]. Currently, it constitutes 40.8% of all primary intracranial neoplasms [3]. The World Health Organization (WHO) classifies meningioma into three grades based on their characteristics, enabling the prediction of their behavior, including natural growth tendencies and likelihood of recurrence post-treatment [4]. Although surgical resection remains the primary modality for addressing symptomatic or proliferating meningioma, stereotactic radiosurgery (SRS) has emerged as a significant adjuvant or alternative intervention for low-grade meningioma. This is particularly relevant for tumors positioned in close proximity to critical anatomical structures, recurrent lesions, or in cases where resection or general anesthesia poses a high risk to patients [5, 6].

SRS precisely administers a high dose of radiation to the tumor, effectively minimizing radiation exposure to adjacent normal tissues. Numerous studies have substantiated the efficacy of SRS in achieving robust tumor control and preserving neurological function over both short and long-term durations [7-14]. In a comprehensive systematic review conducted by Marchetti et al., encompassing findings from the International Stereotactic Radiosurgery Society, single-fraction SRS with a prescribed dose of 12-15Gy for meningioma exhibited

notable efficacy. Results revealed a 10-year local control rate (LCR) ranging from 71% to 100% and a progression-free survival (PFS) rate spanning from 55% to 97% [9]. Additional investigations corroborate these findings, demonstrating an LCR of 87-100%, particularly when the administered dose falls within the range of 12 to 16Gy. Notably, in WHO grade I meningioma, a 10-year LCR exceeding 90% was consistently observed [8, 15].

While SRS has found extensive utility in the treatment of meningioma, there persists a degree of uncertainty regarding the optimal radiation dosage, the enduring implications on lesion control, and the potential for radiation-induced complications. A universally accepted guideline for dose selection is conspicuously absent, compelling practitioners to rely on an amalgamation of empirical data and institutional experiences [15]. The imperative to continually refine our comprehension of the most judicious radiation dosing for meningioma is underscored, necessitating a delicate equilibrium between effective tumor control and the mitigation of treatment-related adverse effects.

In our institution, our treatment paradigm has undergone a transformative evolution. In earlier years, we administered a comparatively elevated dose exceeding 14Gy to meningioma patients undergoing SRS. However, guided by accrued experience and an expanding body of evidence, a deliberate shift in strategy transpired, leading to a reduction in the mean prescribed dose to below 14Gy in recent years. This investigation scrutinizes the comprehensive clinical

outcomes and associated toxicities of radiosurgery for meningioma. Through a comparative analysis between two cohorts subjected to distinct radiation doses, the study delves into parameters such as LCR and radiation-induced peritumoral edema (PTE). The overarching objective is to distill the most contemporary insights into the optimal radiation dose, thereby contributing valuable perspectives for informed clinical decision-making.

Material and Methods

Patient and tumor characteristics

In this retrospective study, a comprehensive examination was conducted on the medical records and radiology reports of patients subjected to SRS for benign meningioma. Diagnosis establishment involved histopathologic findings through open resection or the identification of characteristic imaging features consistent with benign meningioma, validated by a consensus between neurosurgeons and neuro-radiologists based on magnetic resonance imaging (MRI) observations. From March 2014 to December 2022, a total of 162 patients with meningiomas were treated using TrueBeam radiosurgery at our institution. The inclusion criteria comprised patients diagnosed with benign meningioma who underwent single-session SRS, either as a primary intervention or as an adjuvant measure. To minimize

selection bias, individuals undergoing fractionated radiosurgery or repeated radiosurgery for identical lesions were excluded. Furthermore, patients lost to follow-up were omitted from the analysis due to the unavailability of treatment outcome data.

Stereotactic radiosurgery and follow-up examination

For treatment planning, pre-treatment high-resolution T1-weighted MRI with a slice thickness of 1 mm and gadolinium enhancement, was acquired. Additionally, a contrast-enhanced computed tomography (CT) scan, with a slice thickness of 1.5 mm, was conducted with the patient immobilized in a thermoplastic mask and utilizing a compatible fiducial localizer. Integration of MR and CT images was achieved, with subsequent delineation of the target and all organs at risk performed on the MR images, utilizing iPlan RT Image version 4.1 and iPlan RT Dose version 4.5 planning software (Brainlab, Feldkirchen, Germany). Typically, lesions were subjected to the 85-90% isodose line. Single isocenter treatment plans employing several static beams or dynamic conformal arcs with three to five gantry positions were executed for all patients. The determination of the total dose was contingent upon factors such as target pathology, lesion size, previous treatments, and proximity to critical structures. Administered via a Varian TrueBeam STx linear accelerator (Varian Medical Systems, Palo Alto, CA), the prescribed dose was delivered to each patient in a single fraction. After treatment, a clinical examination and imaging follow-up were conducted at the 6-month mark after radiosurgery,

followed by subsequent annual assessments.

Radio surgical and evaluation parameters

The investigated variables encompassed age, gender, meningioma location, prior resection history, histologic subtypes, initial target volume, and various irradiation parameters, including prescription dose, conformity index (CI), and coverage. Primary outcome measures consisted of LCR, PFS, and radiation-induced toxicity for all enrolled patients. A secondary analysis compared LCR and PTE between two groups Stratified into two groups based on their prescription dose: over 14 Gy (Group 1) and less than 14 Gy (Group 2). Clinical progression incorporated both local progressions, defined as an uncontrolled or recurrent lesion, and distant progression, marked by the identification of a new lesion during follow-up. LCR was categorized following the Response Assessment in Neuro-Oncology Working Group (RANO) criteria (16): 1) complete response (CR), signifying the total disappearance of the target lesion, 2) partial response (PR), indicating a reduction of the sum of the maximal perpendicular diameters by 50% or more relative to baseline, 3) minor response (MR), denoting a decrease between 25% and 50%, encompassing 25%, 4) stable disease (SD), signifying cases that do not fit other classifications, such as less than 25% decrease but less than 25% increase in area relative to nadir, 5) progressive disease (PD), encompassing an increasing lesion size over 25%. Radiation-induced toxicity was evaluated and categorized according to the Common

Terminology Criteria for Adverse Events (CTCAE) version 5.0 (17).

This study adhered to the guidelines stipulated in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement. All data acquisition and analysis procedures in this study received approval from the Institutional Review Board (IRB number: #2023-10-016), with the necessity for written informed consent being waived.

Statistical Analysis

The entire statistical analysis was conducted using SPSS version 20 (IBM Corp., Armonk, New York, USA). Estimates of LCR, PFS, and radiation-induced toxicity were computed from the date of initial treatment employing the Kaplan-Meier method to assess primary outcome measures. The log-rank test was employed for significant comparisons of LCR and PTE between the two groups in the secondary analysis. Continuous variables underwent analysis using the t-test, while categorical variables were subjected to examination through the chi-square and Fisher's exact tests. A p-value of <0.05 was considered indicative of statistical significance.

Results

Demographics

From March 2014 to December 2022, a total of 162 patients underwent SRS for 190 meningiomas at our institution. Subsequent to exclusions, which accounted for 15 patients with 26 lesions—comprising 8 meningiomas in 8 patients subjected to fractionated SRS, 7 meningiomas in 7 patients lost to follow-up, and 11 meningiomas treated repeatedly—this study enrolled 147 patients with 164 treated lesions as Figure 1 referred.

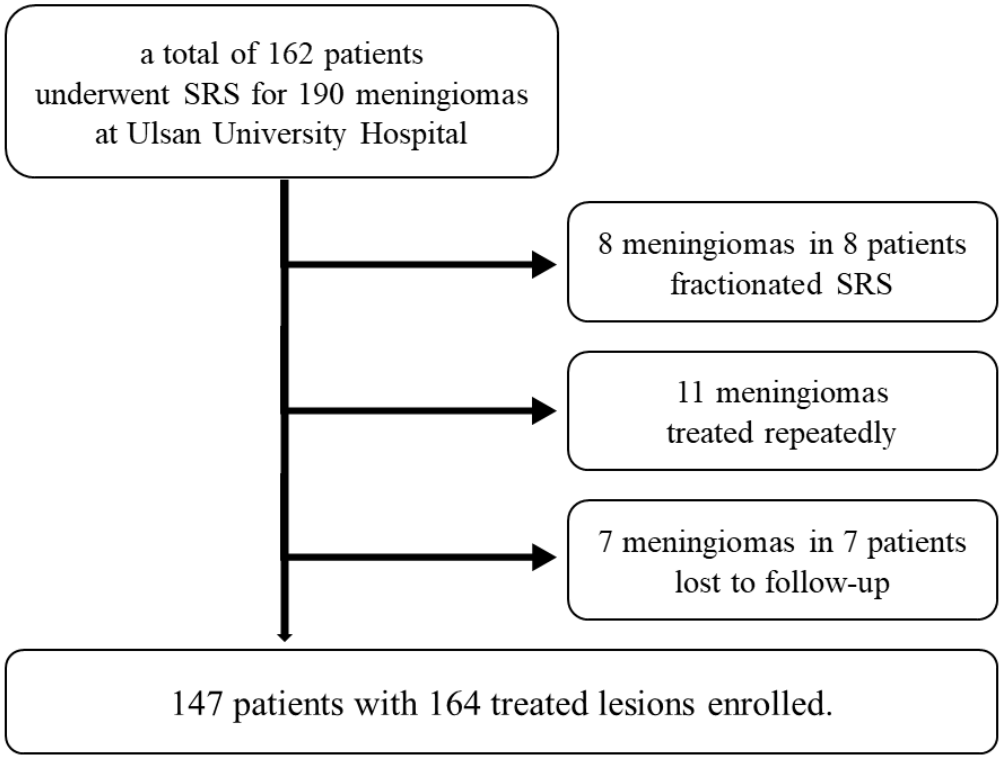

Fig 1. Flow chart for inclusion and exclusion criteria.

The mean age of the cohort was 61 years (range, 37-79 years), with a composition of 35 men (23.8%) and 112 women (76.2%). The majority of patients (55.1%) were asymptomatic, while the remainder presented with diverse symptoms including headache, dizziness, visual disturbances, nausea, motor weakness, hearing decline, facial pain, facial palsy, tremor, and seizures. Objective neurological manifestations were observed in 13 patients (8.8%), encompassing hemiparesis, dysesthesia, visual impairment, and various cranial nerve deficits. Diagnostic modalities comprised MRI for 122 patients, while 25 patients (17%) with a history of open resection underwent histopathologic confirmation. Lesion distribution included 81 skull base meningiomas (49.4%) and 83 non-skull base meningiomas (50.6%). The median follow-up duration was 42 months (range, 6-116 months). Table 1 presents a detailed overview of the clinical characteristics of the patient cohort.

Table 1. Clinical characteristics of the patients with meningioma

Characteristics	Number (n=147)
Sex (M/F)	35/112
Mean age in years (range)	61 (37-79)
Clinical presentation	
Asymptomatic	81
Headache	26
Dizziness	18
Visual symptoms	4
Nausea	1
Motor weakness	3
Hearing decline, loss	2
Facial pain, numbness	4
Facial palsy	2
Tremor	3
Seizure	1
Others	2
Neurologic manifestation	
Nonspecific	134
Hemiparesis	4
Dysesthesia	2
Visual decline	1
6^{th} nerve palsy	2
7^{th} nerve palsy	2
8^{th} nerve dysfunction	2

Continued

Pathology	
Meningothelial	14
Angiomatous	2
Fibroblastic	1
Microcystic	1
Transitional	4
Mixed	3
No pathological diagnosis	122

Clinical and radio surgical outcome

The average target volume for single-session SRS was 4.49 cm^3, ranging from 0.33 to 13.9 cm^3, with a median dose of 14 Gy (range: 12-16 Gy). The mean coverage was 99.32% (range: 90-100%), and the mean CI was 1.80 (range: 1-4.62). Dose parameters exhibited a maximum dose of 16.3 Gy (range: 14.2-23.6 Gy), a minimum dose of 12.3 Gy (range: 5.8-15.2 Gy), and a mean dose of 15.5 Gy (range: 12.8-19.2 Gy). No significant differences were observed in target volume, lesion location distribution, and treatment parameters between the two groups, except for the radiation dose, as detailed in Table 2.

Table 2. Treatment parameters according to the subgroup

	Group 1	Group 2	P value
Number of lesions	61	103	
Lesion location (skull base/non-skull base)	31/30	50/53	0.778
Target volume (㎤, mean±SD)	1.75 ± 1.62	1.90 ± 2.24	0.628
Coverage (%, mean±SD)	99.48 ± 0.69	99.43 ± 0.61	0.653
Conformity index (mean±SD)	1.76 ± 0.40	1.72 ± 0.51	0.630
Prescription dose (Gy, mean, range)	15 (14-16)	13 (12-13.5)	<0.001
Maximum dose (Gy, mean, range)	17.3 (16.0-20.4)	15.8 (14.2-23.6)	<0.001
Minimum dose (Gy, mean, range)	13.5 (7.5-15.2)	11.5 (5.8-14.4)	<0.001
Mean dose (Gy, mean, range)	16.4 (15.3-19.0)	14.9 (12.8-19.2)	<0.001

Clinical progression, involving both recurrent and new lesions, occurred in 8 patients (5.4%). Notably, the 1-year, 2-year, and 5-year PFS rates were 99.3%, 96.3%, and 91.9%, respectively, as illustrated in the Kaplan-Meier curve presented in Figure 2. Among the 8 patients with recurrent meningioma, 3 underwent open resection, 4 received repeat SRS, and one, who underwent repeat SRS for meningothelial meningioma, exhibited malignant progression to atypical meningioma, ultimately requiring resection. Additionally, one patient experienced repeat SRS for a newly developed meningioma at another site.

The overall crude LCR for the entire study cohort was 95.1%. Although CR was not observed, PR was noted in 10 cases (6.1%), MR in 12 cases (7.3%), and SD in 134 cases (81.7%). Only 8 lesions (4.9%) displayed signs of local progression, necessitating additional SRS or resection, as summarized in Table 3. LCR over different time intervals was estimated at 99.4% at 1-year, 96.8% at 2-year, 94.0% at 5-year follow-up. When comparing LCR between the two groups (Group 1 and Group 2), with 4 cases of PD in each group, no statistically significant difference was observed ($p=0.423$). The specific LCRs for each group at different time points were as follows: 1-year LCR (Group 1: 93.4% vs. Group 2: 96.1%), 2-year LCR (Group 1: 94.6% vs. Group 2: 96.7%), and 5-year LCR (Group 1: 94.6% vs. Group 2: 91.3%), as illustrated in the Kaplan-Meier curve presented in Figure 3.

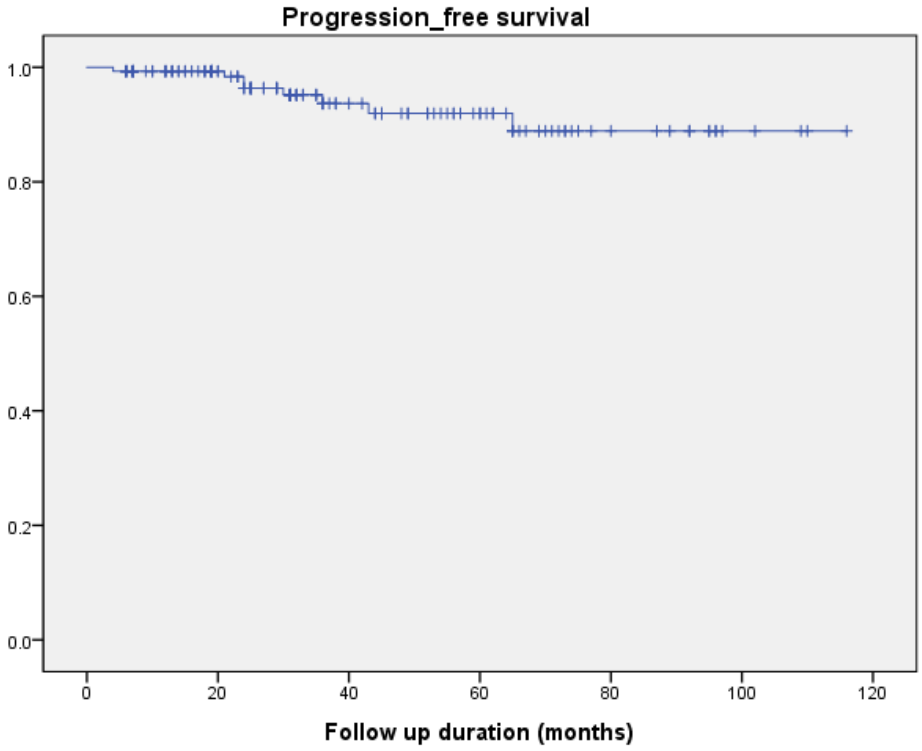

Fig 2. Kaplan-Meier curve showing overall progression-free survival.

Table 3. Radio surgical outcome and radiation induced edema

Outcomes	Total 164 lesions
Mean follow up duration (months)	42 (range, 6-116)
Overall tumor control rate	156/164 (95.1%)
Complete response	0
Partial response	10 (6.1%)
Minimal response	12 (7.3%)
Stable	134 (81.7%)
Progression	8 (4.9%)
Radiation induced peritumoral edema	21 (12.8%)
CTCAE 1-2	15 (9.1%)
CTCAE 3-4	6 (3.7%)

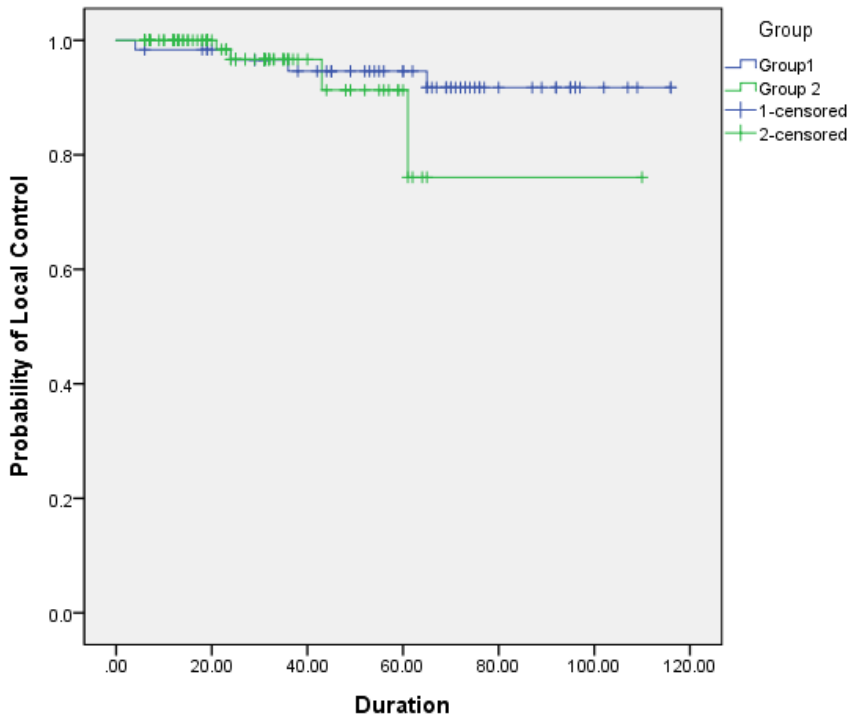

Fig 3. Probability of local control rate of stereotactic radiosurgery for meningioma based on prescription dose (Group 1 vs Group 2).

Radiation induced toxicity

Collectively, radiation-induced adverse events, categorized according to the CTCAE, were observed in 40 out of 147 patients (27.2%). This encompassed 30 patients with CTCAE Grade 1 (20.4%), 3 with Grade 2 (2.0%), 6 with Grade 3 (4.1%), and 1 with Grade 4 (0.7%) toxicity.

During the acute phase (within 3 weeks post-SRS), symptoms such as nausea, lethargy, and headache were reported in 15 cases with Grade 1 toxicity. Additionally, three patients with Grade 2 toxicity experienced facial numbness and pain three months post-SRS, which were effectively managed with medication. One patient with Grade 3 toxicity presented with new-onset generalized seizures, necessitating additional antiseizure medication.

Notably, no instances of clinical or radiological radiation necrosis were identified post-SRS. Radiation-induced PTE directly attributable to SRS was observed in 21 out of 164 lesions (12.8%), manifesting around 6 months post-treatment. Referred to Figure 4, Axial contrast-enhanced T1 weighted and T2 weighted magnetic resonance imaging scans at the time of radiosurgery (A, D), 6 months later (B, E), and 3 years later (C, F) demonstrating peritumoral edema around the treated meningioma which was managed with high dose steroid. Meningioma and peritumoral edema were stabilized 3 years after radiosurgery. Radiosurgery was performed using a tumor margin dose of 15 Gy.

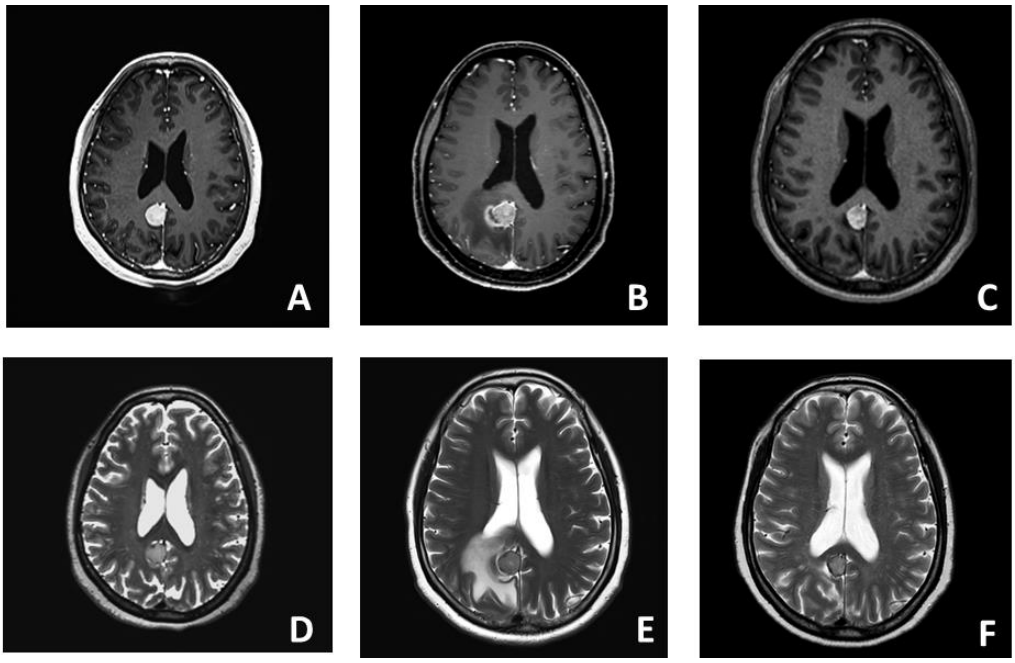

Figure 4. The case of peritumoral edema around the treated meningioma with radio surgery.

Among these cases like this, 15 lesions (9.1%) were classified as CTCAE Grade 1-2, and 6 lesions (3.7%) as CTCAE Grade 3-4. Mild edema which was asymptomatic and required no active intervention was observed in 15 patients. Mild, asymptomatic edema requiring no active intervention was observed in 15 patients. In cases of symptomatic PTE (CTCAE 3), five patients were managed with oral steroids (three cases) and intravenous steroids (two cases). Notably, one case necessitated open resection due to uncontrolled seizures associated with abnormal pachymeningeal thickening around the tumor and PTE (CTCAE 4). A comparison of PTE incidence between the two groups revealed a higher frequency in Group 1 (12 lesions, 19.7%) than in Group 2 (9 lesions, 8.7%), demonstrating statistical significance (p=0.042). Furthermore, severe edema (CTCAE grade 3-4) was more prevalent in Group 1 (6.6%) compared to Group 2 (1.9%).

Discussions

The primary objective in the management of benign meningioma is typically oriented toward attaining sustained, long-term control, achievable through surgical intervention or radiosurgery. Specifically, within the domain of SRS, the administered radiation dose emerges as a pivotal determinant in accomplishing effective local control. Commonly reported SRS doses range from 12 to 18 Gy, meticulously tailored to account for the tumor's size and its proximity to critical anatomical structures [15, 18, 19]. Numerous studies have endeavored to ascertain the optimal radiation dose for low-grade meningiomas; however, the majority of these investigations are retrospective in nature, emanating from single-center studies characterized by heterogeneous patient cohorts. A limited number of studies have conducted direct comparisons of distinct radiation doses

Ganz et al. identified an escalated risk of treatment failure in cases where tumor edge doses fell below 10 Gy, in contrast to the group receiving doses exceeding 12 Gy, thereby proposing 12 Gy as a minimum threshold for efficacious SRS in meningioma treatment [20]. Conversely, Kondziolka et al. demonstrated no discernible advantage in tumor control with marginal doses surpassing 15 Gy compared to doses below this threshold [21]. Similarly, Stafford et al. found no statistically significant discrepancy in LCR for benign meningioma at the 5-year mark when contrasting doses below and above 16 Gy, suggesting that higher doses may not uniformly

confer additional benefits [22]. In a long-term retrospective study, Lippitz et al. reported elevated recurrence rates in patients receiving doses of 13.4Gy or less, highlighting the intricate balance required in determining an optimal dose that balances efficacy and safety [23]. Pollock et al. corroborated these findings, reporting a 10-year LCR of 99.4% with a mean tumor margin dose of 15.8Gy in an updated study [24]. Collectively, these studies underscore the imperative of a personalized approach in radiation therapy, factoring in both the minimum effective dose and potential risks associated with higher doses. However, these insights, predominantly derived from single-center investigations, do not establish a definitive dosing guideline. Consequently, reliance on recommendations from authoritative bodies such as the Radiation and Oncology Advisory Committee on Radiation Oncology Practice (ESTRO-ACROP) and the National Comprehensive Cancer Network (NCCN) is advocated, suggesting a dose range of 12 to 16Gy [25, 26].

At our institution, adherence to the recommended radiation dose for SRS in the treatment of low-grade meningiomas has been a consistent practice. However, periods of dose reduction have been implemented, affording the opportunity to compare two distinct cohorts subjected to varying radiation doses. One cohort received doses of 14Gy or higher (Group 1), while the other received doses less than 14Gy (Group 2). In our study, where the overall LCR was 99.4% at 1 year, 96.8% at 2 years, and 94.0% at 5 years, subgroup analysis yielded no statistically

significant difference in LCR between the two groups (p=0.423). This outcome suggests comparable efficacy across different radiation doses.

While patients diagnosed with benign meningiomas generally exhibit a favorable long-term prognosis, it is imperative to deliberate on the potential toxicity and delayed effects associated with the treatment itself. In SRS, radiation-induced toxicity in meningiomas can manifest diverse symptoms as headache, nausea, fatigue, seizure, focal neurologic change, or, in severe cases, radiation necrosis. The occurrence and nature of these effects are contingent upon variables such as tumor size and location [5]. The pathogenesis underlying adverse radiation effects on the central nervous system is thought to entail a combination of vascular structure damage, inflammatory responses, and direct cellular compartment damage [27]. In our study, instances of radiation-induced toxicity were observed in 40 out of a total of 147 patients (27.2%), assessed using the CTCAE. This observed frequency exceeds the overall rate of 8.1% (range: 2.5-28.2) reported in previous meta-analyses [5, 13, 28]. This discrepancy may be attributed to heterogeneity in the definition of radiation-induced toxicity and variations in evaluation tools employed. In our study, even mild clinical symptoms were scrutinized through the CTCAE following SRS, with more clinically symptomatic events (CTCAE grade 3-4) accounting for only 4.8% (7 out of 147 patients), a figure comparable to findings from previous investigations

In addition, the emergence of new-onset or exacerbation of PTE constitutes objective imaging findings considered pivotal in determining treatment outcomes. PTE is frequently implicated in clinical deterioration post-SRS, often necessitating supplementary interventions such as steroid administration or open surgery. Previous investigations have reported the incidence of PTE in patients undergoing SRS for meningiomas to range from 15% to 28% [29-34]. Factors such as a larger targeted tumor volume, hemispheric tumor location, pre-existing PTE prior to SRS, higher marginal dose, or maximum dose have been associated with an elevated risk of PTE [29, 32, 35]. Pertaining to dose prescription, Kollova et al. observed a significant association between a marginal dose exceeding 16Gy and post-SRS PTE [32]. Similarly, Flickinger et al. reported a higher frequency of post-SRS complications in cases with a median marginal dose of 17Gy compared to 14Gy [36]. The relative edema indices reached its maximum value at 11 months after SRS and subsequently declined, with symptom resolution occurring within 24 months in the majority of patients [30, 31, 35, 37]. In the present study, PTE was observed in 21 out of 164 total lesions (12.8%), with the majority manifesting six months post-treatment. Fifteen lesions were graded as Grade 1-2, while six lesions were graded as Grade 3-4. Upon comparing the overall incidence of PTE between the two groups, a disparity was noted, with rates of 19.7% in Group 1 and 8.7% in Group 2. Furthermore, Grade 3-4 severe edema was more prevalent in Group 1, exhibiting statistical significance.

Collectively, these observations imply that the prescription of radiation doses exceeding 14Gy in Stereotactic Radiosurgery (SRS) treatment for benign meningioma yields no substantial advantages in terms of tumor control, while significantly amplifying the incidence of radiation-induced side effects. Consequently, based on the conclusions drawn from this study, consideration may be given to radiation doses below 14Gy in the context of SRS treatment for patients diagnosed with benign meningioma.

Limitation

This study is basically limited by its design of single center study, small sample size, and retrospective nature. Also, most of included patients underwent SRS for radiographic presumed benign meningiomas, which possibly include some higher-grade tumor, leading some negative effects on the study outcome. Additionally, the patients in Group 2 (radiation dose less than 14Gy) were treated relatively recently, the mean follow-up duration was shorter than Group 1, which limits comparisons to long-term follow-up. However, the significance of this study is that it considered only dose and tried to exclude various confounding factors. For a safer and more effective treatment of benign meningiomas, structured large prospective studies with long-term follow-up are needed in the future.

Conclusion

SRS is highly effective treatment option for benign meningioma to compliment open surgery. Radiation dose is an important factor that determines the outcome of the SRS. While higher radiation doses are generally linked to better tumor control, they also elevate the risk of complications, necessitating the balance between LCR and complication rate. In this study, a radiation dose of less than 14Gy did not make a significant difference in the LCR, but it has fewer toxicity rate, so it is a dose worth considering in future treatments.

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국문 요약

양성 뇌수막종은 기존의 외과적 치료가 원칙이었으나, 기술의 발전과 함께 무증상의 저등급 뇌수막종 및 접근이 어렵거나 재발한 경우에 정위적 방사선수술이 효과적인 치료 방법으로 그 가치를 인정받고 있다. 정위적 방사선수술은 고선량 방사선으로, 종양을 정확하게 표적화 하여 주변 조직 손상을 최소화하여 종양 성장을 제어함과 동시에 신경 기능을 보존하는 데 효과적인 것으로 입증되었다.

적절한 방사선량의 선택이 방사선 치료의 효과와 합병증을 결정하는 중요한 요소임에도 불구하고 대규모 전향적 연구 부족으로, 선량 선택에 대해 보편적으로 인정되는 지침이 없어 현재까지 경험적 데이터와 기관의 프로토콜에 따라 치료해 왔다. 기존의 연구는 12-16Gy 사이의 이질적인 환자 집단 사이에서 각각의 치료기관별로 시행한 후향적 연구에 따라 진행되었으며 두 군을 비교하는 연구는 더욱 제한적이었다. 본 연구는 저등급 뇌수막종에 대한 정위적 방사선수술의 치료 방사선량의 최적 값을 확인하기 위해 14Gy 이상과 14Gy 미만의 두 군으로 나누어 비교하였다.

본 연구는 2014년부터 2022년까지 영상의학적으로 저등급으로 판독되거나, 병리적 진단을 통해 WHO 1등급으로 확인된 양성 수막종 환자가 트루빔 시스템을 사

용하여 단일 세션 정위적 방사선수술을 시행한 162명을 대상으로 하였다. 이전에 방사선 치료를 받은 이력이 있거나 반복 또는 분할 정위적 방사선수술을 받은 환자는 제외하였다. 치료 효과는 국소 조절률, 무진행 생존율, 방사선 유발 독성에 중점을 두고 MRI 및 CT 소견으로 평가하였다. 처방한 방사선 선량이 14Gy 이상의 환자를 그룹 1, 14Gy미만의 환자를 그룹 2로 환자를 나누었으며, 두 군의 차이에 대한 통계적 분석은 SPSS(version 20)를 사용하였다. 본 연구는 STROBE 가이드라인에 따라 작성되었고 IRB 승인(번호 #2023-10-016)을 받아 진행되었다.

2014년부터 2022년까지 단일기간에서 정위적 방사선수술을 받은 190개 뇌수막종을 가진 162명의 환자 중 반복 또는 분할 방사선수술을 받거나 추적 관찰 중 사망한 환자를 제외하고, 164개의 병변을 가진 147명의 환자를 대상으로 분석하였다. 환자는 대부분 여성(76.2%)으로 평균연령이 61세이고, 다양한 임상증상을 보였으며, 신경학적 증상은 8.8%에서 보였다. 종양의 평균 목표 용적은 4.49cm^3였고, 처방한 방사선량의 중앙값이 14Gy인 단일 세션으로 방사선수술을 시행하였다. 국소 조절률, 무진행 생존율, 방사선 유발 독성에 초점을 맞추어 두 군을 비교 분석하였다. 전체 환자의 5.4%에서 재발 및 새로운 병변을 포함한 병의 진행이 관찰되었다. 1년, 2년, 5년 무진행 생존율은 각각 99.3%, 96.3%, 91.9%이었고, 국소 조절률 추정치는 1년 99.4%, 2년 96.8%, 5년 94.0%였다. 방사선량에 따른 두 그룹(그룹1 대 그룹2) 간 국소 조절률에서 1년(93.4% 대 96.1%), 2년(94.6% 대 96.7%),

5년(94.6% 대 91.3%) 모두 유의한 차이가 없었다(p=0.423). 방사선 유발 독성은 27.2%의 환자에게서 관찰되었으며, 대부분은 경미한 증상이었다. 병변의 12.8%에서 정위적 방사선수술과 관련된 종양 주변부 뇌부종이 발생했으며, 처방 방사선 선량이 높은 그룹1에서 저등급 뇌부종과 고등급 뇌부종의 발생이 그룹2에 비해 모두 의미 있게 높았다(p=0.042).

본 연구 결과는 저등급 뇌수막종의 정위적 방사선수술에서 14Gy 미만의 방사선 선량이 14Gy이상과 비교하여 국소 조절률에서 차이가 없으면서 방사선 유발 독성이 적어 향후 치료에 바람직한 선량이라는 것을 시사하고 있다.

중심 단어: 뇌수막종, 방사선 수술, 방사선량, 독성