Gamma knife surgery of superficially located meningioma

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Object. The authors analyzed tumor control rates and complications in patients with superficially located meningiomas after gamma knife surgery (GKS).

Methods. Between 1998 and 2003, GKS was performed in 23 patients with 26 lesions in whom follow-up imaging for 1 year or more was available. The male/female ratio was 1:22. The mean age was 59 years. The median tumor volume was 4.7 cm³, and the mean margin dose was 16 Gy at the 50% isodose line. Peritumoral edema was revealed on magnetic resonance (MR) imaging in four patients before GKS. Magnetic resonance imaging and clinical examinations were performed every 6 months after GKS. The mean follow-up duration was 32 months.

The tumor shrank in eight cases, was stable in 17, and enlarged in one; thus 25 (95%) of 26 tumors were controlled. A peritumoral high signal on T₂-weighted MR images was found in eight lesions and preexisting edema was aggravated in three lesions after GKS. Ten of these 11 patients complained of severe headache, and three patients experienced neurological deficits at the same time after a mean latency of 3 months; however, high signal was not demonstrated on imaging before 6 months on average. Steroid agents, when required, gave relief to all patients. The complication rate was 43% (10 of 23 cases). High signal disappeared in nine patients and decreased in the remaining two. High signal was associated with a high integral dose and a large tumor volume. Tumor shrinkage at the last follow-up examination was more prominent in the patients with symptomatic high signal (p = 0.03).

Conclusions. There was a good tumor control rate with a high complication rate. Longer follow up of more patients is needed. Adjusting the dose–volume relationship should be considered to reduce complications.

Key Words • meningioma • gamma knife surgery • edema • superficial • peritumoral

Clinical Material and Methods

Patient Population

Between January 1998 and March 2003 GKS was performed in 28 patients with 31 superficially located meningiomas. Twenty-six lesions in 23 patients with follow-up neuroimaging of 1 year or more form the basis of this study. The mean clinical and imaging follow-up period was 33 months (range 12–75 months). The distribution of tumor sites was falx eight, parasagittal six, tentorium five, and convexity seven. Twenty-two tumors were above the tentorium. The male/female ratio was 1:22. The mean patient age was 59 years (range 43–73 years). Nineteen patients were symptomatic (six with headache, three with mild hemiparesis). Gamma knife surgery was the primary treatment in 21 patients. The reason for this in seven cases was the lesion’s location adjacent to an eloquent area of the brain and in one patient the medical condition was poor. The remaining 13 patients receiving GKS as the primary treatment for their asymptomatic lesions did so at their own request. Two patients were treated for postoperative residual tumors. Gamma knife surgery was performed with the Leksell
Gamma Knife model B (Elekta Instrument AB, Stockholm, Sweden). Gadolinium-enhanced T1-weighted and/or T2-weighted MR images were obtained in all patients with a slice thickness of 1 to 1.5 mm. Magnetic resonance images were digitized and transferred to the treatment planning system (Leksell GammaPlan; Elekta Instrument AB) through a picture archiving and communication system.

The mean tumor volume was 4.7 cm³ (range 0.6–17 cm³), and the mean margin dose was 16 Gy (range 12–20 Gy) at the 50% isodose line. At the time of GKS, peritumoral edema was visible on the MR imaging in four patients. Neurological examinations and MR imaging were performed every 6 months for 2 years after GKS. If there was no progression, an MR image was obtained every year thereafter. Whenever any symptom that could be associated with tumor occurred, a new MR image was obtained to assess the status of the disease.

The authors measured the volume of high signal by using Osiris software (version 4.18; developed by the digital imaging unit of the University of Geneva in 1994), which allows the measurement of three-dimensional volume on the basis of MR images. 9,13 The edema index was defined as the ratio of the volume of high signal to the tumor volume. Tumor control was defined as regression, no change, or growth of less than 25% of the initial volume. The authors analyzed correlations between high signal and tumor volume, location, margin dose, integral dose to the tumor, and tumor shrinkage.

**Statistical Analysis**

The Kaplan–Meier method with the log-rank test were used to compare the two groups in univariate analyses of nonordered categorical variables. The Cox proportional hazard model was used in analyses of continuous variables. The Cox proportional hazard model with the backward stepwise method was used for multivariate analyses. All statistical analyses were performed with commercially available software (SPSS version 10.0; SPSS Inc., Chicago, IL).

**Results**

Tumor control was achieved in 25 (96%) of 26 tumors. The volume was decreased in eight tumors and stable in 17. In the one remaining case, GKS was repeated for local recurrence. During follow up after GKS, 10 patients (43%) complained of severe headache, and three patients had hemiparesis in addition to the headache. Peritumoral high signal was demonstrated in seven patients with newly developed post-GKS symptoms. The mean time to the development of symptoms was 3 months after GKS (range 1–12 months), and the mean duration of symptoms was 9 months (range 2–24 months). Five patients were treated with steroid agents, and the other patients were managed with analgesic agents only. Headache and hemiparesis were resolved in all 10 patients after the medication.
Gamma knife surgery of superficial meningiomas

![Graph of dose-volume relationships for superficially located meningiomas.](image)

The peritumoral high signal occurred after a mean interval of 6 months (range 2–11 months). On average, high signal reached a maximum at 14 months after GKS. It disappeared in nine patients and its mean duration was 11 months (range 5–23 months). In the remaining two patients high signal, although still present, was much decreased on the most recent follow-up MR image. The relationship of complications to high signal was significant ($p < 0.001$). A typical case of a parasagittal meningioma that showed high signal is illustrated in Fig. 1.

The mean value of the maximum edema index was 16.6 for parasagittal meningiomas, 2.5 for falk meningiomas, and 1.5 for convexity meningiomas; however, there was no statistically significant correlation between tumor location and edema index ($p = 0.34$). There was no difference in the amount of edema between the groups receiving steroids and those who did not ($p = 0.81$). The high signal occurred in three parasagittal meningiomas, three falk tumors, and five convexity lesions. Tumor location was not related to the occurrence of high signal.

Tumor volume was significantly larger in the high signal group than in the non–high signal group ($p = 0.03$). In a univariate analysis, a high integral dose to the tumor and large tumor volume were significantly related to the occurrence of high signal ($p = 0.02$ and $p = 0.04$, respectively). The tumor margin dose did not have a relationship with the development of high signal. In tumors larger than 4.2 cm³ high signal occurred more frequently ($p = 0.02$). No statistically significant risk factor was found in a multivariate analysis. In a graph of the dose–volume relationships in our cases, the patients with high signal were distributed close to or above the known 3% risk line (Fig. 2).² Interestingly, tumor shrinkage seen at the most recent follow up was more prominent in the high signal group. The mean tumor volume shrinkage was 15% in the high signal group, and no volume change was observed in the non–high signal group ($p = 0.03$, Student t-test).

**Discussion**

Gamma knife surgery is a fairly frequently used treatment option in meningiomas. The majority of cases so treated occur at the skull base where GKS has shown comparable tumor control and complication rates to craniotomy; however, GKS has not been commonly performed for superficial meningiomas because of considerable complication rates due to post-GKS peritumoral edema.³,⁴,⁵,⁶,⁷,⁸ Total tumor removal by craniotomy is recommended in patients with superficially located meningiomas because these tumors are usually not difficult to resect. Sometimes observation is another option for patients with asymptomatic or incidental tumors, because such lesions have been reported to show only minimal growth during long-term follow up.⁹ Another approach is needed in some cases; for example, postoperative morbidity is not negligible when the tumor is located near an eloquent region of the brain. Patients sometimes refuse invasive procedures. Moreover, some patients, because of anxiety, will not accept an observation-alone strategy and want to undergo a noninvasive treatment.

We performed GKS in patients with superficially located meningiomas and adapted the dose–volume guideline of Flickinger, et al.² The tumor control rate was satisfactory (96%) but a considerable rate of complications was observed (43%) as in previous reports.³,⁴,⁶,⁷,¹²,¹⁴,¹⁷ The duration and severity of the symptoms were not negligible even though all patients recovered after steroid or other medication. High signal was observed in all patients who had post-GKS complications and so analysis of the cause and evolution of the high signal is important. Based on univariate analyses the present study indicates that the integral dose and the tumor volume are factors of significance in the development of high signal, although these relationships did not show up in multivariate analysis. This would suggest that a reduction in prescription dose should be considered because this would perforce reduce the integral dose. The tumor control rate must also be considered before such a reduction in the margin dose is approved. In this context, there are reports of good results with a lower margin dose than was used in this study for GKS with skull base meningiomas. Lee and coworkers¹⁴ suggested 13 Gy as a useful margin dose for cavernous sinus meningiomas. Nakaya, et al.¹⁵ and Iwai, et al.,⁴ applied low-dose radiosurgery to meningiomas, with a mean margin dose of only 10 Gy. The tumor control rate was 100% at 12 months and at 30 months of follow up. Because the control rates in these series are satisfactory there seems to be justification for reducing the margin dose in superficial meningiomas too; there is no reason to believe that the anatomical location of a meningioma has a significant effect on its cellular behavior and response to radiation treatments.

Ganz, et al.⁵ suggested that the margin dose was an important factor in the development of edema and 18 Gy or more should be avoided. Chang, et al.¹¹ reported an edema rate of 24% and a symptomatic edema rate of 10%. In a multivariate analysis, they suggested that tumor location was the only significant risk factor for edema. In their series, convexity and parasagittal meningiomas were associated more frequently (> 30%) with edema after GKS. Preexisting edema, occlusion of a venous sinus, and patient age were not significant.¹ Singh, et al.¹⁵ reported that the edema rate was 22% for non–skull base meningiomas. They also suggested that the margin dose and tumor volume were not correlated with the occurrence of edema after GKS. The only significant factor was tumor location. Because parasagittal meningiomas were associated with edema.
ma more frequently, they thought that the effect on the venous sinus of parasagittal meningioma was important for developing post-GKS edema. In our series, parasagittal meningiomas showed more remarkable edema than others without statistical significance. Taking these results into consideration, there seems to be a tendency for parasagittal meningiomas to be associated more frequently with post-GKS peritumoral edema. Further study with more accumulation of cases and longer follow-up data are necessary. In our study, the integral dose and the tumor volume were the statistically significant factors in the univariate analysis in the development of high signal.

In summary, many authors have monitored tumor location, margin dose, tumor volume, and integral dose to the tumor as possible risk factors; however, the risk factors for high signal are not yet elucidated. Considering the facts that margin dose, target volume, and integral dose are closely related to each other, one of these three together with tumor location seems to be the risk factor for the development of high signal after GKS in superficially located meningiomas.

Conclusions

Gamma knife surgery of superficially located meningioma can achieve a good tumor control rate but is associated with a high complication rate for the volumes and margin doses used in this series. A larger number of patients, consistent dosimetry, and long-term follow-up data are needed to clarify the risk factors for high signal. In the short term, reduction of the margin dose below the levels used in this study needs to be considered.

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References


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