Gamma knife surgery for atypical meningiomas

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Object. Complete resection is the optimal treatment for atypical meningiomas (AMs) but its feasibility depends on the tumor site. The object of this study was to assess the effect of gamma knife surgery (GKS) on AM.

Methods. In 15 patients 21 AMs were treated by GKS. Four patients had residual lesions and 10 patients had recurrent tumors after one or more microsurgical interventions. Three patients were treated twice with GKS because of tumor tissue outside the treatment volume, either at the margin or at a distant location. The median clinical and neuroimaging follow-up period was 35 months (range 21–67 months).

Ten tumors shrank 6 to 12 months after GKS, 10 remained stable, and one grew. Between 18 and 36 months after GKS, four patients had a distant recurrence, and two had a margin recurrence. In one of these cases, an additional local recurrence was demonstrated 1 year later, and the patient underwent standard radiotherapy. No patient suffered persistent adverse effects after radiosurgery.

Conclusions. After early tumor shrinkage, high recurrence rates were demonstrated both at the treatment margin and at distant locations in cases treated for AM. There was only one recurrence within the GKS radiation field. For small- and medium-sized AMs GKS may be a safe adjunct to other treatment modalities.

Keywords • gamma knife surgery • atypical meningioma • radiosurgery
pathological entity to an atypical histology defined at the time of reoperation; in one at reoperation for a recurrent tumor at the margin after GKS.

Fourteen patients harbored one tumor, one patient two tumors, and three patients were treated twice with GKS, two for a margin and one for three distant recurrences. Therefore, a total of 21 tumors were treated in 15 patients. A median of one (range one–two) GKS procedures was performed per patient. All repeated radiosurgery procedures were for recurrent tumor. Tumor locations are presented in Table 1.

There were nine women and six men whose median age at the time of radiosurgery was 51 years (range 30–75 years). In 12 patients the Karnofsky Performance Scale score was greater than or equal to 80. Four patients had residual disease, and 10 recurrent tumors after one or more previous operations (median two; range one–four). One patient underwent EBRT after microsurgery and before GKS.

Radiosurgery was performed using a Leksell Gamma Knife model B (Elekta Instrument AB, Stockholm, Sweden). Multishot-dose plans were created to construct a radiation field conformal with the often irregularly shaped tumors. Treatment planning was performed using Leksell Gamma Plan (Elekta Instrument AB). Standard techniques for GKS planning were used. Prescription doses were based on tumor volume, location, and previous irradiation. Because WHO Grade II tumors are associated with a higher rate of recurrence (29–40%) than WHO Grade I tumors (7–20%), we tried to prescribe higher radiation doses than those for benign meningiomas in the hope of achieving better tumor control in cases involving more aggressive AMs; however one patient had previously undergone EBRT and others will probably undergo EBRT for recurrent post-GKS tumor. Therefore the prescription dose was limited to 18 Gy to reduce the incidence of symptomatic radiation-induced necrosis. Depending on tumor volume and adjacent radiosensitive structures, a margin dose of 18 Gy could be administered in only 12 tumors. The other AMs were treated with prescription doses between 14 and 16 Gy. Thus, the median prescription dose was 16 Gy (range 14–18 Gy); the median maximum dose was 32 Gy (range 28–36 Gy); and the median target volume was 5 cm³ (range 0.4–13 cm³).

The median neuroimaging and clinical follow-up period was 35 months (range 21–67 months). Patients were instructed to undergo MR imaging every 6 months after radiosurgery. Follow-up MR images were compared with images obtained the day of radiosurgery. In each case, the tumor diameters in the x, y, and z planes were determined, and the MR images were reviewed for evidence of adverse radiation-related effects. Tumor sizes were classified as unchanged, decreased, or increased. Tumor growth adjacent to the irradiated tumor and outside the prescription isodose volume was defined as a margin recurrence. Tumors developing in noncontiguous sites were considered distant recurrences. The performance status of each patient was described as unchanged, improved, or worse on the basis of the patient's current performance status compared with that at the time of radiosurgery.

Results

At 6-month follow up, 11 patients remained clinically stable without change in neurological signs or symptoms. Three patients improved clinically, with two suffering fewer headaches; one patient was free from epileptic seizures without medication. Smaller tumors in these patients were demonstrated on follow-up MR images. The patient who had previously undergone postoperative EBRT exhibited tumor progression 6 months after radiosurgery; he underwent two additional resections and died 39 months after GKS. No new specimen could be obtained to examine the histological grade of the meningioma again.

Thus one tumor had increased, 10 were unchanged, and 10 had decreased. Shrinkage of AM at 6 to 12 months after treatment is shown in Fig. 1.

Between 18 and 36 months after GKS four patients had
Radiosurgery for atypical meningiomas

![Coronal contrast-enhanced MR images](image)

**Fig. 2.** Coronal contrast-enhanced MR images obtained in a patient with recurrent AM at the falx after three previous resections of a parasagittal AM. A: Postoperative recurrent falcine tumor. B: Six months after GKS the AM has decreased in size. C: Tumor control 1 year after GKS. D: Two consecutive coronal contrast-enhanced slices of the only in-field recurrence 2.3 years after GKS.

Developed a distant and two a tumor margin recurrence. All distant recurrences developed in the region of the surgical approach or resection. In one of the patients with distant recurrent tumor treated with a prescription dose of 15 Gy, an additional local (in-field) recurrence was demonstrated 2.3 years after GKS as shown in Fig. 2 and underwent EBRT for both tumors (54 Gy); however, the AMs continued to grow and both had to be resected. All but one patient with recurrent tumor were treated with prescription doses less than 18 Gy.

Three patients underwent repeated GKS, two for margin and one for three distant recurrences. In the last two patients distant recurrent AMs had to be resected because their volumes were already too large for radiosurgery. One of these tumors recurred again after 4 months. None of these patients with residual postoperative tumor treated with GKS showed an in-field or marginal tumor growth or return. Recurrent AMs were only found in patients with smaller tumor soon after GKS.

No persistent adverse effects occurred. One patient presented with a peritumoral edema with hemiparesis and focal epileptic seizures 3 months after GKS. The edema and clinical deterioration resolved completely during 6 months. This patient had exhibited the same symptoms after each of two previous tumor resections.

**Discussion**

**Recurrence Rates in the Literature**

In the new WHO classification of tumors of the nervous system, the histopathological criteria of WHO Grade II AMs are now precisely defined. It divides meningiomas into three categories, each with different recurrence rates. Prior to this it was difficult to classify meningiomas into aggressive varieties. Several studies used the scoring system of Jäskeläinen, et al., to classify these tumors. Others have used different classification systems. They examined the clinical course of atypical and malignant meningiomas after complete or partial surgery, possibly with additional adjuvant EBRT. In a series by Jäskeläinen and coworkers, the authors reported a 5-year recurrence rate for AMs of 38%. Maier, et al., described recurrence rates of 34% in contrast to classic meningiomas with a rate of 6.9%. Palma, et al., reported that patients with AM had significantly better outcomes in terms of cumulative survival, recurrence-free survival, and median time to recurrence during a long-term follow-up period than did patients with malignant meningiomas; however, when they considered only cases involving incomplete resection the survival curve of AMs was not significantly better than that of malignant meningiomas. They and other authors found that only radical extirpation and histological grade were related to survival.

**Stereotactic Radiosurgery**

Because gross-total resection is not always possible, we used adjuvant GKS for residual or recurrent AM in our study. Our preliminary results indicate no recurrence of residual tumor treated with GKS. Harris, et al., found that “early GKS” (treatment was given soon after craniotomy in the absence of neuroimaging-documented disease progression) was a significant predictor of better progression-free survival. They advocated radiosurgery as an up-front boost to EBRT to improve outcomes. In their study and the report of Ojemann, et al., for malignant meningiomas, it was found that greater tumor volumes influenced the progression-free survival negatively. We only irradiated AM with a volume up to 13 cm³ and a median volume of 5 cm³. No persistent adverse effects occurred. Thus, residual small-and medium-sized AM should be treated soon after resection with GKS. The role of EBRT after GKS of residual tumors must still be discussed because few studies with small patient populations have been published.

Between 18 and 36 months after GKS of recurrent AM six of 15 patients (40%) had distant or marginal recurrent tumors; in one case there was an additional in-field recurrence after 2.3 years. All recurrent AMs had at first become smaller. Thus, after early tumor shrinkage high recurrence rates were associated with margin or distant locations despite the use of GKS. The lower in-field recurrence rate of tumors compared the incidence cited in the literature could be due to our higher prescription doses of 18 Gy, or the short follow-up period of 21 to 67 months. Limitations of the current study include the small patient population and a relatively short median follow-up time of 33 months. The only patient with a local relapse was treated with a prescription dose of 15 Gy.

In contrast to benign meningiomas 10 of 21 tumors significantly decreased 6 to 12 months after radiosurgery, and only these tumors recurred, probably because of the “proliferative potential” of AMs. Even tumors treated with a pre-
scription dose of 14 Gy shrink.

Because two recurrent AMs had already grown too large for radiosurgery during a 6-month follow-up period, perhaps AM that decrease should be examined every 3 months.

**Adjuvant Radiotherapy**

Recurrent tumors were located marginal to or distant from the region of surgical approach or resection in our study. Therefore, after complete resection and adjuvant fractionated EBRT should be considered. Based on review of the literature no conclusions regarding therapeutic benefits can be drawn because of the small number of patients undergoing fractionated EBRT.12 Although Milosevic, et al.,14 reported improved local control for atypical and malignant meningiomas when radiation doses were over 50 Gy, in other studies1 the numbers were not large enough to draw any conclusions with regard to radiation dose and treatment outcome. Hug, et al.,8 also described that most reports are based on only small populations, retrospectively reviewed data, and data often collected over several decades, thereby pre-dating in part modern imaging and treatment techniques. We found that the definition of histological "malignancy" varies greatly throughout the literature. In the majority of reports, radiotherapy is recommended for all malignant meningiomas regardless of whether resection was total or subtotal. It is important to balance the risks of aggressive treatment (with possible complications such as radiation necrosis) with the risks of conservative treatment (with suboptimal tumor control and poor clinical outcomes).8 We propose early GKS for incompletely resected residual AMs. For gross totally resected tumors, fractionated EBRT should be considered. If focal recurrences develop after resection or margin or distant recurrent AM develop after radiosurgery, GKS is an alternative to repeated microsurgery.

**Conclusions**

Patients with AMs continue to exhibit high recurrence rates despite aggressive treatment including surgery, EBRT, and radiosurgery. After GKS, early tumor shrinkage occurred. Tumor recurrence was essentially outside the GKS radiation field. Preliminary results indicate that GKS may have a place as an adjunct to treatment for residual or recurrent small- and medium-sized AMs.

**References**


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