

Evaluation of gamma knife radiosurgery in the treatment of oligodendrogliomas and mixed oligodendroastrocytomas

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Object. Radiosurgery is commonly used for the treatment of patients with glioma. The goal of this study was to evaluate the safety and efficacy of radiosurgery in the management of patients with oligodendrogliomas (ODGs) or mixed oligoastrocytomas (OGAs).

Methods. A retrospective chart review of patients treated between May 1990 and January 2000 identified 18 patients (21 tumors) with either an ODG (10) or a mixed OGA (11) who had undergone radiosurgery. The median patient age was 43 years (range 23–67 years). Sixteen patients had undergone one or more tumor resections before radiosurgery; in two patients biopsy sampling alone had been performed. Tumor grades at the most recent operation were Grade 1 (one), Grade 2 (one), Grade 3 (12), and Grade 4 (seven patients). Seventeen patients had undergone prior radiotherapy; 11 were treated with chemotherapy before radiosurgery, and one had undergone a prior linear accelerator–based radiosurgery treatment. The median tumor volume was 8.2 cm³ (range 1.9–47.7 cm³); the median margin dose was 15 Gy (range 12–20 Gy); and the median maximum dose was 32 Gy (range 24–50 Gy).

In this heterogeneous group, 12 patients died whereas six remain alive. Survival after radiosurgery was 78%, 61%, and 44% at 12, 24, and 48 months, respectively. Factors associated with an improved survival rate included younger age and smaller tumors.

Conclusions. For patients with oligoastroglial tumors that have failed to respond to conventional therapies, radiosurgery may provide some survival benefit. Further study is needed to determine which subpopulation of these patients will have the best chances of enhanced survival from this treatment.

KEY WORDS • brain tumor • oligodendroglioma • oligodendroastrocytoma • stereotaxy • gamma knife

OLIGODENDROGLIOMAS and OGAs are intracranial glial tumors that arise from either pure oligodendroglial elements or as a combination of oligodendroglial and astrocytic components. Oligodendroglioma represent between 5 and 18% of all intracranial gliomas^{10,11} whereas OGAs have a similar reported incidence of 1.8 to 19%.⁸ Although ODGs and OGAs typically have a better prognosis than their astrocytic counterparts,^{3,12} their management still presents certain clinical challenges, especially in recurrent lesions. Whereas surgical resection, radiation therapy, and chemotherapy all have a role in the treatment of ODGs and OGAs,^{1,5,6,13} the role of stereotactic radiosurgery has not been defined for these types of tumors.

At our center, we have performed radiosurgery for a select group of patients with recurrent ODG and OGA in whom standard treatments have failed over the past decade. To define better what role radiosurgery has in the clinical management of patients with ODGs and OGAs,

we retrospectively reviewed our experience with 18 patients.

Clinical Material and Methods

Between May 1990 and January 2000, 18 patients underwent radiosurgery at our center for either an ODG or an OGA. We reviewed all available clinical and imaging information. Tumor characteristics were derived from neuroimaging studies and included site, size, and volume. All pathological data, including outside specimens, were reviewed and graded by our neuropathologists who used a four-tiered grading system.⁸ Briefly, Grades 1 and 2 correlate to World Health Organization Grade II, whereas Grades 3 and 4 are Grade III in the World Health Organization classification. This grading system is controversial and not universally accepted.²

The 18 patients included nine men and nine women. The median patient age was 43 years (range 23–67 years). Overall, 21 tumors were treated. Sixteen patients (89%) had undergone one or more tumor resections prior to radiosurgery. Two patients underwent biopsy sampling alone. Tumor locations included frontal lobe (10), parietal

Abbreviations used in this paper: MR = magnetic resonance; ODG = oligodendroglioma; OGA = oligoastrocytoma.

TABLE 1

Summary of pathological grades in 18 patients with 21 tumors

Tumor Grade	No. of Tumors
ODG	
Grade 1	1
Grade 2	0
Grade 3	7
Grade 4	2
OGA	
Grade 1	0
Grade 2	1
Grade 3	5
Grade 4	5

lobe (six), temporal lobe (one), occipital lobe (none), corpus callosum (two), and intraventricular (one case). Ten lesions were ODGs and 11 were OGAs. The tumor grades are outlined in Table 1. Seventeen patients had undergone radiotherapy previously (median dose 54.9 Gy). Eleven patients had received prior chemotherapy; nine (50%) had received a regimen of procarbazine, lomustine, and vincristine. One patient had undergone prior linear accelerator-based radiosurgery.

Radiosurgery was performed using the Leksell gamma knife (Elekta Instruments, Norcross, GA). Magnetic resonance imaging was used for dose planning in all cases. The median tumor volume was 8.2 cm³ (range 1.9–47.7 cm³); the median tumor margin dose was 15 Gy (range 12–20 Gy); and the median maximum dose was 32 Gy (range 24–50 Gy).

All patients underwent a minimal follow up of at least 24 months or until death. Survival times were calculated from the date of radiosurgery by using the Kaplan–Meier method.⁷ Comparison of survival curves was performed using the log-rank test. Multivariate analysis was performed using a Cox proportional hazards model.

Results

At the time of data collection, six patients (33%) remained alive whereas 12 (66%) had died. The median survival period for patients who died was 15 months (range 2–71 months). The six remaining patients had a median survival period of 44 months after radiosurgery (range 24–101 months). Actuarial survival for the entire group was 78%, 61%, and 44% at 12, 24, and 48 months after radiosurgery, respectively (Fig. 1 upper). Stratification by pathological lesion type showed that ODG patients tended to have an improved survival (median survival 28 months) during the first 30 months compared with those with mixed tumors (median survival 8 months) as illustrated in Fig. 1 lower. The study, however, did not have enough power to detect a statistical difference between these two groups. Using a Cox proportional hazards model, we found that patient age at treatment and tumor size at treatment were statistically significant continuous variables. Younger patients (risk ratio = 1.10, 95% confidence interval 1.02–1.19, $p = 0.01$) and those with smaller tumors (risk ratio = 1.05, 95% confidence interval 1.01–1.10, $p = 0.03$) fared better in our cohort.

No complications were noted after radiosurgery. Additional treatments after radiosurgery included repeated resection (two) and chemotherapy (four).

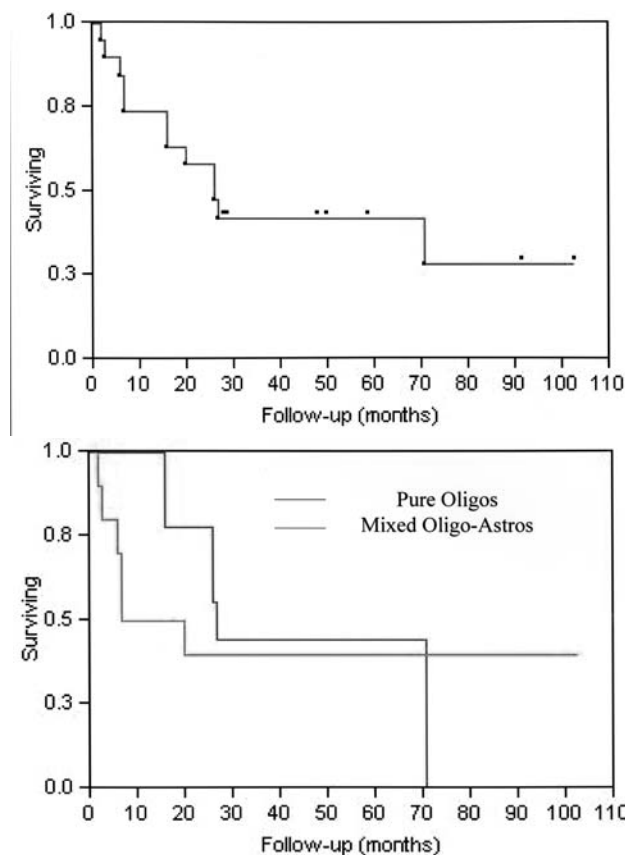


FIG. 1. Graphs. Upper: Actuarial survival for 18 patients (21 tumors) with recurrent ODGs (10) and OGAs (11). Lower: Actuarial survival by tumor type. Patients with ODGs had better 30-month survival than patients with mixed OGAs.

Illustrative Cases

Case 1

This 23-year-old woman presented 6 years after undergoing complete resection of a Grade 1 left occipital ODG. She did not undergo external-beam radiotherapy or chemotherapy. Follow-up neuroimaging revealed a tumor recurrence (Fig. 2). Because the patient was asymptomatic and the lesion was small, she did not undergo a repeated biopsy sampling. The tumor was treated with a margin dose of 20 Gy and a maximum dose of 50 Gy. The tumor volume was 1.9 cm³. Two years after radiosurgery, the patient remains well and no tumor is visible on follow-up MR imaging.

Case 2

This 33-year-old woman developed seizures; examination of a stereotaxy-assisted biopsy sample showed a right parietal Grade 3 ODG (Fig. 3). Based on this diagnosis, the patient underwent external-beam radiotherapy (54 Gy/30 fractions) and procarbazine, lomustine, and vincristine chemotherapy. Four years later, the tumor progressed and a subtotal tumor resection was performed. Twenty-one months later, the patient developed a second recurrence and underwent radiosurgery. The tumor volume was 2.3 cm³; the tumor margin dose was 15 Gy; and

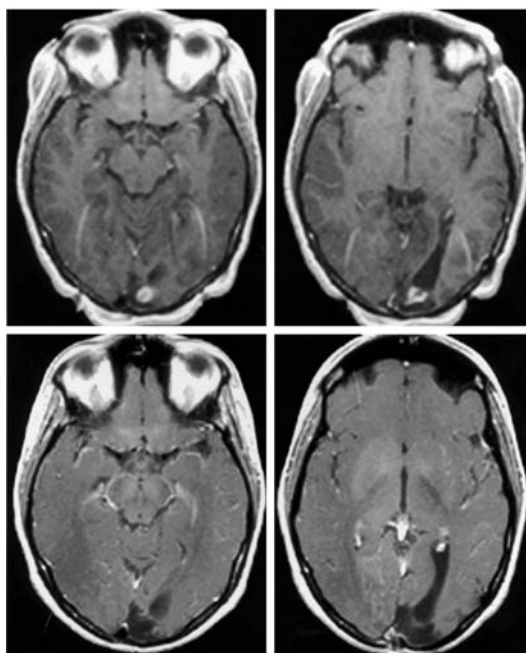


FIG. 2. Axial T₁-weighted postgadolinium MR images obtained in a 23-year-old woman with a recurrent left occipital ODG. The tumor was Grade 1 6 years earlier, but another biopsy was not obtained prior to radiosurgery. *Upper*: Images acquired at the time of radiosurgery. *Lower*: Images obtained 24 months after radiosurgery demonstrating no visible tumor.

the maximum dose was 25 Gy. Five months after radiosurgery, the enhancing lesion increased in size. The patient died 13 months after radiosurgery.

Discussion

We reviewed our experience of a small cohort of patients with recurrent ODGs or OGAs who were managed with radiosurgery over a 10-year period. Overall, our patients had the typical demographic features associated with these diagnoses in terms of age, presentation, and tumor location.^{4,9} Moreover, they represented a group of patients in whom traditional treatments had failed. Eighty-nine percent had undergone resection, 94% had prior radiotherapy, and 61% had prior chemotherapy. Thus, our finding of a median survival of 26 months is encouraging based on the patient population. Moreover, no patient experienced complications related to radiosurgery. In subgroup analysis, patients with pure ODGs survived longer, and this finding is in agreement with earlier reports showing that patients with mixed tumors have a worse prognosis and their clinical courses behave more like those of astrocytomas.¹² Favorable prognostic factors for our patients included younger age and smaller tumor volumes. Based on our experience, we believe that radiosurgery may be a helpful adjunct in the management of selected patients with ODGs or OGAs.

Several important points must be remembered when interpreting these results. First, the number of patients is small and they were treated over a relatively long period. Moreover, the data were gathered retrospectively and thus our findings are susceptible to the defects of that method.

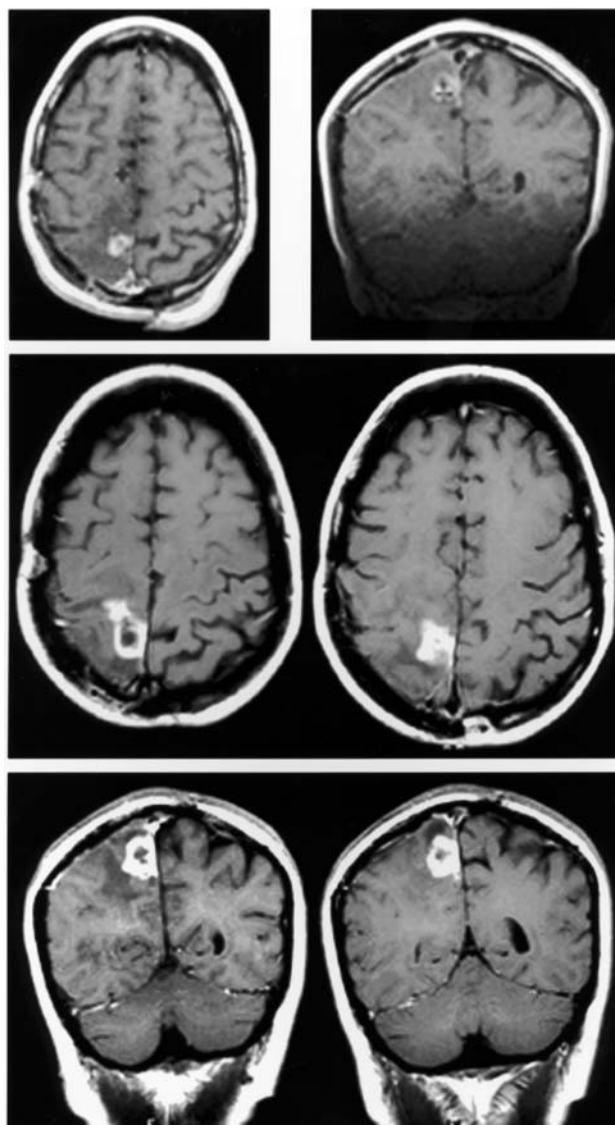


FIG. 3. Axial and coronal T₁-weighted postgadolinium MR images obtained in a 33-year-old woman with a recurrent right parietal Grade 3 ODG. *Upper*: Images acquired at the time of radiosurgery. *Center and Lower*: Axial and coronal images obtained 5 months after radiosurgery revealing enlargement of the enhancing tumor. The patient died 8 months later.

Second, the population was quite heterogeneous in regard to age, tumor size, and prior treatments. Third, certain selection biases undoubtedly influenced our results with patients more likely to survive being considered good candidates for radiosurgery. As a result, our findings may not apply to the general population of patients with ODGs and OGAs. With regard to other available treatments for patients in whom conventional treatments have failed, however, radiosurgery compares favorably and is associated with a low treatment associated morbidity. For example, in a recent study of 30 patients with recurrent anaplastic ODGs treated with temozolomide the authors reported that less than one third of the patients exhibited a response after using this agent.¹⁴ Median survival was 13 months, compared with 26 months in our series. Future studies are

needed to refine our knowledge of radiosurgery compared with other salvage therapies.

Conclusions

Despite improvements in the care of patients with ODGs and mixed OGAs, tumor recurrences after conventional care are not uncommon and are difficult to successfully manage. For patients with recurrent oligoastroglial tumors, radiosurgery appears to provide some survival benefit at low risk to the patient. Further study is needed to determine which subpopulation of these patients will benefit most from radiosurgery.

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