Relative roles of microsurgery and stereotactic radiosurgery for the treatment of patients with cranial meningiomas: a single-surgeon 4-year integrated experience with both modalities

MARK E. LINSKEY, M.D., STEPHEN A. DAVIS, R.N., AND VANEERAT RATANATHARATHORN, M.D., M.B.A.

Departments of Neurological Surgery and Radiation Oncology, University of Arkansas for Medical Sciences, Little Rock, Arkansas

Object. The authors sought to assess the respective roles of microsurgery and gamma knife surgery (GKS) in the treatment of patients with meningiomas.

Methods. The authors culled from a 4-year prospective database data on 74 cases of meningiomas. Thirty-eight were treated with GKS and 35 with microsurgery. Simpson Grade 1 or 2 resection was achieved in 86.1% of patients who underwent microsurgery. Patients who underwent GKS received a mean margin dose of 16.4 Gy (range 14–20 Gy). The mean tumor coverage was 94.7%, and the mean conformity index was 1.76. Significant differences between the two treatment groups (GKS compared with microsurgery) included age (mean 60 compared with 50.7 years), volume (mean 7.85 cm³ compared with 44.4 cm³), treatment history (55.3% compared with 14.3%), and tumor location ( cavernous sinus/petroclival, 14 compared with three). The median follow up was 21.5 months (range 1.5–50 months). In patients with benign meningiomas GKS tumor control was 96.8% with one recurrence at the margin. The recurrence rate was zero of 27 for Simpson Grade 1 or 2 resection and three of four for higher grades in those patients who underwent microsurgery. There was no procedure-related mortality or permanent major neurological morbidity. The mean Karnofsky Performance Scale score was maintained for both forms of treatment. Symptoms improved in 48.4% of patients undergoing microsurgery and 16.7% of those who underwent GKS. Transient and permanent cranial nerve morbidity was 7.9 compared with 2.9%, and 5.3 compared with 8.5% for GKS and microsurgery, respectively. In a patient satisfaction survey 93.1% of microsurgery patients and 91.2% of GKS patients were highly satisfied.

Conclusions. Both GKS and microsurgery serve important roles in the overall management of patients with meningiomas. Both are safe and effective and provide high degrees of satisfaction when used for differentially selected patients.

Key Words • gamma knife surgery • skull base surgery • stereotaxy • meningioma • microsurgery • skull base surgery • stereotaxy

Microsurgery and GKS are complementary for managing patients with cranial meningiomas yet are often presented as competitive, with most series reporting and championing the results of one homogeneous treatment approach. Few data exist with which a direct comparison of the outcomes achievable with both modalities can be made at a single institution, let alone in the hands of a single surgeon. Predictions of probable higher patient satisfaction rates for patients undergoing GKS based on the less invasive nature of the treatment modality are commonly unsupported by patient satisfaction data, and when available are usually not accompanied by the corresponding satisfaction data for microsurgery performed at the same institution or by the same surgeon(s).

A retrospective analysis was made of prospectively acquired data in a treatment database that included a consecutive series of patients with meningioma treated by a single surgeon over a 4-year period by using both microsurgery and GKS as part of a consistently applied comprehensive multimodality approach. While the two modalities have been studied head-to-head to compare tumor control efficacy, this is the first study to evaluate directly the differential clinical outcomes of the two modalities for patients with meningiomas, as well as the degree of patient satisfaction for each approach when the patients are counseled and both treatments are administered by the same practitioner.

Clinical Material and Methods

Patient Population

From February 1998 through January 2003, a total of 91 patients with dural-based homogeneously enhancing mass lesions with a “dural tail” were referred for evaluation. Seven (7.7%) had a known history of primary cancer or hemangiopericytoma and were excluded from the study. All other men older than 50 years of age and all other women...
referred with dural-based masses, who were to be followed clinically with serial neuroimaging or treated without a tissue diagnosis, were evaluated with serum prostate-specific antigen and mammograms, respectively, to limit the likelihood of missing dural-based metastases. No additional cases were identified for exclusion. Of the resulting 83 patients with neuroimaging evidence of probable meningiomas who were referred for evaluation during this 4-year period, three (3.6%) turned out to have tumors other than meningiomas on subsequent resection (one hemangioma, two sarcomas) and were also excluded from study. Of the remaining 81, one patient with an optic nerve sheath meningioma and preserved functional vision was treated with GKS and, 16 (20%) are currently being followed clinically with serial neuroimaging.

The remaining 64 patients who were treated with microsurgical resection, GKS, or stereotactic biopsy form the subject of this report. Ultimately, 74 operations were performed in these 64 patients (35 microsurgery, 38 GKS, one stereotactic biopsy). Five patients (7.8%) underwent planned staged microsurgery followed by GKS: three with both stages performed by the senior author (M.E.L.), and two with only the second GKS performed by the senior author. Of the nine patients in this series who underwent multiple surgical interventions, three had two separate tumors treated (one patient: two microsurgical resections; two patients: two GKS in the same session), three underwent staged microsurgery/GKS as described previously, one had three separate tumors treated with GKS in the same session, one had repeated GKS for a margin recurrence, and one had GKS followed by two resections for multiple local recurrences of a malignant meningioma.

Microsurgery, GKS, fractionated radiotherapy, and systemic chemotherapy or antihormonal treatments were discussed as alternatives with all patients harboring meningiomas less than or equal to 3 cm in average diameter. Patients with larger lesions were not considered candidates for GKS. Resection was our recommended strategy for young, relatively healthy patients with tumors in locations in which there was a high likelihood of achieving complete resection with acceptable risks of procedure-related morbidity, as well as all patients with tumors too large for GKS who could reasonably be predicted to tolerate the stress of the procedure and a general anesthetic. Gamma knife surgery was our recommended procedure for patients with tumors of appropriate size with the following findings: a tumor either 2-mm distance from the optic pathways or closer if there was no remaining functional vision; elderly or medically infirm patients; tumors arising from surgically inaccessible locations; and patients who preferred GKS to microsurgery after thorough discussion.

All patients with atypical or malignant meningiomas who had already received fractionated radiotherapy were recommended for this treatment in addition to their microsurgery and/or GKS.

The average patient age was 57.2 years (median 60, range 4 months–85 years, SD 16.9 years). The female/male ratio was 2.05:1. Nine patients (14.1%) presented with multiple meningiomas. Only one patient had neurofibromatosis Type 2. Of the 69 tumors (excluding three staged procedures and three reoperations on the same tumor) 61 (88.4%) were benign, one was radiation associated (1.4%), five (7.2%) were atypical, and two (2.9%) were malignant.

In the 38 cases of GKS, tissue pathology samples were available for 20 (52.6%) of 38. For the purpose of this study the 18 cases treated without prior tissue diagnosis were included in the “benign” category for analysis purposes.

Serial neuroimaging evidence of tumor growth was present prior to treatment in 24 (63.2%) of 38. Only eight tumors were treated with GKS without a prior tissue diagnosis or prior evidence of tumor growth on serial neuroimaging. In five cases this was due to the existing proximity to radiation sensitive structures (optic apparatus, ventral brainstem) where additional growth in that direction would have potentially eliminated the patient from consideration for GKS. In two cases proceeding rather than observing was a matter of patient choice. In one case we were requested to proceed by the patient’s psychiatrist because of decompensation of baseline schizophrenia resulting from attempts to deal with the presence of an untreated small brain tumor and the refusal to have open surgery.

Prior resection had been performed in 23 tumors (31.1%) in this series (three microsurgical operations in two patients performed as resections, 20 GKS procedures performed as second procedures). All microsurgery patients with benign tumors underwent operation for the first time. One patient with a benign meningioma who underwent GKS had a history of failed fractionated radiotherapy for their tumor. One 23-year-old patient who underwent staged microsurgery and GKS had a history of craniospinal fractionated radiotherapy for childhood medulloblastoma. One patient who underwent GKS and then two resections for a malignant meningioma had a history of fractionated radiotherapy as well as 1 year of systemic chemotherapy. One patient with a benign meningioma who underwent GKS had a history of failed fractionated radiotherapy as well as 1 year of treatment with the chemotherapeutic agent RU-486 for the tumor.

Microsurgery was performed using the approaches outlined in Table 1. Preoperative embolization with polyvinyl alcohol was performed in one case. Specialized skull base microsurgical techniques/approaches were performed in 16 cases (45.7%). Intraoperative neuronavigation with image guidance and frameless stereotactic techniques (eight patients) or intraoperative ultrasound (seven patients) was performed in 15 cases (42.9%).

Gamma knife stereotactic radiosurgery was performed using a Leksell model B gamma unit (Elekta AB, Stock-
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Follow-up MR imaging consisted of standard slice acquisition diagnostic techniques and were performed either at our institution or an institution closer to the patient’s home with hard copy films sent with the patient to their follow-up appointments. All images were measured using either the software package within our institutional PACS system or caliper measurements compared against the internal measurement scale on hard copy outside films.

Our measurement strategy proceeded in the following manner based on previous work published by the senior author.51 The maximum diameter of the lesion on any axial section was first identified. This line could course in any direction and was labeled “Diameter A.” A perpendicular line defining the maximum orthogonal diameter relative to Diameter A in the same plane was then defined as “Diameter B.” A final maximum orthogonal diameter in the rostral–caudal plane labeled “Diameter C” was measured on either the coronal or sagittal section containing the maximal rostral–caudal dimension. The average maximal 3D tumor diameter “D” was calculated from the formula: $D = (A + B + C)/3$. Measurements of “A,” “B,” and “C” were made at similar positions for each follow-up neuroimage for a given tumor and the average maximal 3D tumor diameters “D” were compared over the course of follow up. Technical measurement error was estimated to be $\pm 1$ mm. For the purpose of this study, we considered tumor size to have significantly changed if the change in the average maximal 3D tumor diameters (“D”) was greater than 2 mm (twice the calculated measurement error for D) over the time interval in question. Volumes for microsurgical cases were calculated using the formula $V = 4/3\pi(D/2)^3$. Volumes for GKS cases were obtained from the dose–volume histogram based on summed serial 1-mm region of interest tracings.

**Statistical Analysis**

All postoperative complications and changes in neurological symptoms, examination findings, and medication requirements were recorded. Differences in parametric statistics between patient groups were compared using analysis of variance of the mean. Differences in nonparametric statistics were calculated using chi-square analysis with appropriate degrees of freedom. Durability of tumor control over time was analyzed using life table analysis.

**Results**

Several significant differences between the two treatment groups reflected preoperative selection criteria as shown in Table 2 and Fig. 1. Microsurgery patients in general tended

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GKS</th>
<th>Surgery</th>
<th>Surgery of Tumor ≤ 3 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>38</td>
<td>35</td>
<td>18</td>
</tr>
<tr>
<td>mean age in yrs (range)</td>
<td>60 (23–85)</td>
<td>50 (4 mos–79 yrs)</td>
<td>43.85 (4 mos–75 yrs)</td>
</tr>
<tr>
<td>atypical (%)</td>
<td>73% (18.4)</td>
<td>53% (14.3)</td>
<td>—</td>
</tr>
<tr>
<td>F/M ratio</td>
<td>2.17</td>
<td>1.69</td>
<td>—</td>
</tr>
<tr>
<td>prior treatment (%)</td>
<td>21/38 (55.3)*</td>
<td>3/35 (14.3)*</td>
<td>—</td>
</tr>
<tr>
<td>mean KPS score (range)</td>
<td>84.76* (60–100)</td>
<td>87.42 (60–100)</td>
<td>91.11* (80–100)</td>
</tr>
<tr>
<td>mean vol in ml (range)</td>
<td>7.8* (0.49–39.6)</td>
<td>44.4* (0.53–179.6)</td>
<td>—</td>
</tr>
</tbody>
</table>

* Statistically significant difference.
to be younger and have larger tumors, whereas those undergoing GKS were significantly more likely to have a history of treatment attempts on their tumor. The mean age of the microsurgery group was 50.7 years (range 4 months–79 years) compared with 60 years (range 23–85 years) for the GKS group (p = 0.0223). This difference became even more striking if the microsurgery analysis was limited to the 18 tumors less than 3 cm in diameter that could have been subjected to either microsurgery or radiosurgery (mean 43.85 years, range 4 months–75 years). The mean tumor volume of the microsurgery group was 44.4 cm$^3$ (range 0.52–179.6 cm$^3$) compared with 7.85 cm$^3$ (range 0.49–39.6 cm$^3$) for the GKS group (p = 0.0078). In the GKS group, 21 (55.3%) of 38 patients had a history of failed treatment compared with three (14.3%) of 35 in the microsurgery group (p < 0.0001).

Another area in which the two groups differed was in the anatomical point of origin for the tumors. As demonstrated in Fig. 1, certain tumor locations were more likely to be treated with either GKS or microsurgery. Tumors arising from the convexity, sphenoid ridge without cavernous sinus involvement, and the posterior fossa were far more likely to undergo resection. In contradistinction, cavernous sinus and petroclival tumors as well as tumors involving the torcular herophili were far more likely to undergo GKS.

The mean KPS score of the GKS group was 85 (range 60–100) compared with 87 (range 60–100) for the microsurgery group. Although the functional status of patients in both overall groups was similar, the mean KPS score of microsurgery patients who could have undergone either microsurgery or GKS (tumors < 3 cm in diameter) was 91 (range 80–100), which was significant (p = 0.0321). The two groups did not differ significantly in the percentage of tumors that were histologically atypical or malignant (six [15.8%] of 38 for GKS compared with five [14.3%] of 35 for microsurgery). They also did not differ in terms of female/male ratio.

The extent of resection achieved by microsurgery is presented in Table 3. The single Grade 5 resection was a stereotactic biopsy performed in an elderly woman who was admitted febrile to the intensive care unit with a new-onset seizure and evolving myocardial ischemia. She had a small ring-enhancing lesion with surrounding edema near the surface of her left parietal lobe. A meningioma with spontaneous intratumoral infarction was diagnosed based on biopsy sampling to rule out abscess or metastasis. Three of the four patients in whom a Grade 3 or 4 resection was performed were to undergo planned staged microsurgery followed by GKS. As a result, in the remaining 32 cases complete resection was attempted and Grade 1 or 2 resection was achieved in 96.9% of cases. As expected, Grade 1 resection was more likely to be achieved if the tumor was not located in the skull base (78.9 compared with 62.5%).

For the GKS group, the median margin prescription dose was 16 Gy (mean 16.4 Gy, range 14–20 Gy, SD 1.48 Gy). The median prescription isodose was 50% (range 42.5–60%). The median number of isocenters used per tumor was 18 (mean 15.9, range one–36, SD 8.12). Customized beam blocking of select isocenters was per-

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**TABLE 3**

<table>
<thead>
<tr>
<th>Simpson Grade</th>
<th>No. of Tumors (%)</th>
<th>Skel Base</th>
<th>Non-Skel Base</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/16 (62.5)</td>
<td>15/19 (78.9)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>4/16 (25)</td>
<td>2/19 (10.5%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>2/19 (10.5%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>2/16 (12.5)*</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
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</tbody>
</table>

*Three of the four Grade 3 or 4 resections were part of an intentionally planned microsurgery/GKS staged approach.
formed in 15 (39.5%) of 38 cases. The median percentage of the tumor volume included within the prescription dose was 98% (mean 94.7%, SD 7.9%, range 85–100%). The median conformity index (dose prescription volume/tumor volume) was 1.63 (range 0.941–4.74).

Neuroimaging follow up was available for review in all patients (median 2 years, range 1 day–5 years). Three patients were eventually lost to clinical and neuroimaging follow up. One patient in whom two tumors were treated with GKS was lost after the 6-month follow-up MR imaging study and clinical evaluation. Two patients who underwent microsurgery were lost to follow up after 1.5 months and 2 months, respectively. The remaining 61 (95.3%) of 64 patients had updated follow up through the end of the study period (median 2.5 years, range 3 months–5 years).

In patients with benign tumors, all 28 with Grade 1 or 2 resections remained free of recurrent tumor (Fig. 2). Two of the three patients who underwent staged microsurgery followed by GKS demonstrated tumor progression over the 9 to 12 months between their two planned stages of treatment (Fig. 3). The overall tumor recurrence/progression rate for the microsurgery benign tumor group was two (6.7%) of 30. Only one patient with a presumed benign tumor treated with GKS developed recurrence over the study period (96.8% tumor control). The recurrence occurred 2 years after GKS to treat a cribriform plate meningioma that had recurred after initial resection elsewhere. It was subsequently controlled with repeated GKS. Seventeen (53.1%) of the 32 benign GKS tumors remained stable in size over the study period, whereas 13 (40.6%) of 32 demonstrated modest shrinkage (Fig. 4). Life tables of tumor control rates for both modalities are presented in Fig. 5.

Results for atypical or malignant meningiomas were not encouraging in either group. Tumors recurred relatively quickly after two of five resections for malignant meningioma at 13 months and 6 months postoperatively. Both recurrences were in the same patient after serial operations. Tumors recurred or progressed in two of six patients with atypical or malignant meningioma treated with GKS. The first progression developed 13 months after GKS in the patient described previously who went on to have two additional cranietomies. The second occurred 6 months after GKS in the prior resection bed outside the GKS treatment volume in a patient with a malignant meningioma who underwent planned staged microsurgery followed by GKS for the portion within his posterior sagittal sinus. Of the remaining four atypical/malignant tumors, three remain stable, and one has decreased in volume over the study period. Both patients with malignant meningioma underwent fractionated radiotherapy in addition to their microsurgery.

Fig. 2. Neuroimaging demonstrating a giant right atrium and occipital horn lateral ventricular, heavily calcified, meningioma in a 43-year-old man who presented with a complete homonymous hemianopsia and a new-onset seizure disorder. The tumor was removed in a single stage through an occipital interhemispheric prefrontal cortisotomy approach. A: Preoperative axial bone window computerized tomography scan. B: Preoperative noncontrast T1-weighted MR image. C: Preoperative contrast-enhanced T1-weighted axial MR image. D: One-year postoperative contrast-enhanced T1-weighted axial MR image.

Fig. 3. Neuroimaging in a 53-year-old woman who presented with mild numbness and diplopia from a fourth nerve palsy. Her petroclival meningioma was treated in a planned staged microsurgery/GKS approach. A: Preoperative contrast-enhanced T1-weighted axial MR image revealing a large petroclival meningioma. B: Twenty-four-hour postoperative contrast-enhanced T1-weighted axial MR image after the stage-one resection via a presigmoid, retrolabyrinthine, subtentorial, transtentorial petrosal approach. C: Nine-month postoperative contrast-enhanced T1-weighted axial MR image revealing return of the brainstem to the anatomical position and subtle interval growth of the tumor posteriorly out of Meckel cave and the posterior cavernous sinus. D: Stage-two GKS treatment plan demonstrating the 50% (yellow), 40%, and 20% (both green) isodose lines.
and/or GKS either before or after their index procedure. Three of five patients with atypical meningioma underwent fractionated radiotherapy in addition to their microsurgery and/or GKS either before or after their index procedure. One microsurgery and one GKS patient with atypical meningioma were counseled to have additional fractionated radiotherapy and declined it but without adverse sequelae to date.

There were four deaths during the study period. The patient with the malignant meningioma described previously resisted all therapies and eventually died. Three patients died of other unrelated causes.

Functional KPS scores improved as a result of treatment in both groups, but the magnitude of improvement was greater in the microsurgical group (Fig. 6). The average KPS score improved from 87 to 92 in the microsurgery group and 84 to 86 in the GKS group. Neither increase in KPS score was statistically significant.

Changes in baseline neurological symptoms after microsurgery or GKS are outlined in Table 4. The chances of improving baseline neurological symptoms were greater with microsurgery than with GKS (48.4 compared with 16.7%, \( p < 0.0001 \)). The most common symptoms, which improved with microsurgery, were: symptoms from mass effect on surrounding brain, including cerebellar imbalance/dizziness, cognitive or memory deficits, pronator drift, astereognosis, sensory extinction, and behavioral or emotional lability. The second most common symptoms relieved were due to relief of mass effect on cranial nerves including the eighth, fifth, seventh, and second.

Additional improvements included resolution of headaches, resolution of seizures, relief of torticollis in a 4-month-old child with a dorsal foramen magnum tumor, and additional miscellaneous signs and symptoms. In contradistinction, the most common symptom that improved after GKS was relief of mass effect on the optic apparatus (optic nerve/chiasm/tract) leading to improved vision and visual fields. The second most common was relief of headache and relief of symptoms from mass effect on the cerebellum.

There was no difference in the chance of experiencing worsening of baseline neurological symptoms between the two groups (15.2% microsurgery compared with 13.9%...
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GKS; however, types of symptoms that usually worsened differed between the two groups. Three of the five cases in which symptoms worsened with microsurgery were cavernous sinus cranial neuropathies (third once, fourth once, and fifth twice), whereas the other two cases involved new frontal lobe symptoms in a patient with a malignant meningioma invading the frontal lobe bilaterally and a case of subtle memory disturbance in a patient who had an anterior falx meningioma and a third ventricular colloid cyst removed in the same sitting via an interhemispheric–transcallosal approach. Two of the five GKS cases involved mildly worsened visual field deficits resulting from treatment of parasellar tumors. One patient with a parasagittal meningioma developed transient hemiparesis and seizures from temporary reactive edema. One patient developed mild worsening of baseline hemiparesis from recurrent growth of their atypical petroclival meningioma. A second patient with a petroclival tumor developed mild conductive hearing loss from serious otitis related to eustachian tube dysfunction.

There was no procedure-related or 30-day mortality or major permanent neurological morbidity in either group. Temporary neurological complications and other complications encountered in both groups are listed in Table 5. No patient undergoing GKS for a parasellar region meningioma developed any new hormonal deficits on serial endocrinological testing. Of the 26 surgical patients who completed follow up over the study period, all responded to the patient satisfaction survey (giving a 92.9% overall response rate). Of the 32 GKS patients who were not lost to follow up over the study period all responded to the patient satisfaction survey (giving a 91.4% overall response rate). The results of the survey for both groups are presented in Table 6.

Of the two dissatisfied patients who underwent microsurgery, one was a 39-year-old woman with an anterior falx atypical meningioma and a third ventricular colloid cyst that were removed in the same sitting via an interhemispheric–transcallosal approach. She not happy with the subtle subjective memory problems that persisted. The second was a 43-year-old moderately cognitively impaired woman with extreme macrocephaly from compensated congenital communicating hydrocephalus. She always wished to have GKS instead of microsurgery for a small asymptomatic enlarging parasagittal meningioma but we were unable to successfully construct the Leksell model G stereotactic frame (Elekta) around her head, requiring us to resort to microsurgery, which was performed with Grade 1 resection and no complications.

Of the three dissatisfied patients who underwent GKS, one was a 59-year-old woman with repeated recurrences of an atypical petroclival meningioma, which progressed despite GKS and 18 months of neuroimaging stability. The second was a 72-year-old man with a parasagittal meningioma, who developed transient hemiparesis and seizures resulting from temporary reactive edema beginning 3 months after GKS. The third was an 85-year-old woman with a 14.4 cm³ cerebellopontine angle meningioma. Gamma knife surgery controlled her tumor but she was dissatisfied that it did not improve her preexisting baseline dizziness despite clear preoperative counseling that GKS was not likely to improve her dizziness.

Discussion

The results of this study suggest that in experienced hands, microsurgery is no more likely than GKS to worsen patients’ symptoms, despite its more invasive nature. In fact, although GKS is more likely to stabilize preoperative symptoms rather than improve them, microsurgery is more likely to improve patient symptoms because of its greater ability to relieve symptomatic mass effect physically and

![Fig. 6. Bar graph demonstrating the change in mean KPS scores from preoperative evaluation (red) to most recent follow-up evaluation (blue) for both the microsurgery and GKS groups.](image)

**TABLE 4**
Long-term symptom outcome in patients undergoing microsurgery or GKS

<table>
<thead>
<tr>
<th>Treatment Modality</th>
<th>Symptoms Improved</th>
<th>Symptoms Unchanged</th>
<th>Symptoms Worsened</th>
</tr>
</thead>
</table>
| microsurgery       | relief of CNS mass effect 4  
relief of cranial nerve mass effect (VIII, V, VII, II) 5  
headache relief 2  
other (e.g. relief of seizure, torticollis, etc) 4  
improvement in visual acuity or visual field 4  
headache relief 3  
from relief of cerebellar mass effect 2 | 15 worsened cranial nerve function (III, IV, V) 3  
cognitive worsening 1  
subtle subjective memory complaints 1 | |
| GKS                |                   | 24 subtly worsened visual field 2  
increased hemiparesis from tumor growth 1  
hemiparesis & seizure 1  
worsened hearing (serous otitis) 1 | |

* Microsurgery and stereotactic radiosurgery carried equal risk of worsening baseline preoperative symptoms; however, microsurgery was significantly more likely to improve as opposed to stabilize preoperative symptoms: p < 0.0001. Abbreviation: CNS = central nervous system.
These findings are similar to the results reported by Pollock and colleagues. The likelihood of Grade 1 or 2 resection is achieved microsurgery if Simpson Grade 1 or 2 resection is achieved. There is a trend toward slightly improved control for microsurgery, but the difference in 5-year tumor control for microsurgery and GKS; however, there is a trend toward slightly improved control for microsurgery, with patient-acceptable levels of morbidity will depend on the individual surgeon’s training and experience, particularly since specialized skull base techniques are commonly required for meningiomas (46% in this study). Just as a quick procedure, it is by no means a randomized or controlled clinical trial. It is difficult to compare the results obtained with microsurgery or GKS by a single surgeon over a specified time period in a consecutive series of patients has been performed; however, it is by no means a randomized or controlled clinical trial. There are significant differences between the patients in the two treatment groups, and these differences must be taken into account as potential sources of bias when interpreting the results observed. The younger age in the microsurgery group would likely bias the results toward lower perioperative complication rates and better clinical symptom outcomes than if patients were of a similar mean age as those in the GKS group. The same can be said for the higher KPS scores for the subset of the microsurgery group harboring tumors of a size that could have been treated with either microsurgery or GKS. The presence of larger tumors in the microsurgery group predisposed this group to have a greater chance of relapsing mass effect symptoms than if all the tumors were small enough to undergo either microsurgery or GKS. Gamma knife surgery also relieved symptomatic mass effect; however, this effect was less common and was not predictable preoperatively. Conversely, the fact that GKS does not have the ability to enlarge are equivalent clinical end points (tumor control). Universal agreement on this point among surgeons is likely to prove problematic. The fact that GKS does not have microsurgery’s potential to “cure” a patient with a benign tumor—in terms of permanently eliminating the neoplasm from their body—may turn out to be an academic point of more interest to surgeons than to many patients.

This is the first study in which a direct prospective comparison of the results obtained with microsurgery or GKS by a single surgeon over a specified time period in a consecutive series of patients has been performed; however, it is by no means a randomized or controlled clinical trial. There are significant differences between the patients in the two treatment groups, and these differences must be taken into account as potential sources of bias when interpreting the results observed. The younger age in the microsurgery group would likely bias the results toward lower perioperative complication rates and better clinical symptom outcomes than if patients were of a similar mean age as those in the GKS group. The same can be said for the higher KPS scores for the subset of the microsurgery group harboring tumors of a size that could have been treated with either microsurgery or GKS. The presence of larger tumors in the microsurgery group predisposed this group to have a greater chance of relieving mass effect symptoms than if all the tumors were small enough to undergo either microsurgery or GKS. Gamma knife surgery also relieved symptomatic mass effect; however, this effect was less common and was not predictable preoperatively. Conversely, the fact that the average age of the microsurgery patients harbored tumors too large for GKS (some of them giant tumors) and that this microsurgery subset was similar in age and KPS score to the

### TABLE 5

<table>
<thead>
<tr>
<th>Procedure-related morbidity in 73 patients with cranial meningiomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microsurgery (35 patients)</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>mortality</td>
</tr>
<tr>
<td>major permanent neurological morbidity</td>
</tr>
<tr>
<td>epidural abscess (reexplored, resolved)*</td>
</tr>
<tr>
<td>asymptomatic resection cavity hematoma (reexplored)†</td>
</tr>
<tr>
<td>deep venous thrombosis (1 pulmonary embolus)</td>
</tr>
<tr>
<td>bilateral temporal lobe HSV encephalitis 2 wks postop‡</td>
</tr>
<tr>
<td>temporary frontalis nerve paresis</td>
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<tr>
<td>persistent pericranial scalp numbness</td>
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</tbody>
</table>

* Patient with a malignant meningioma, a history of four cromatotomies with an acrylic cranioplasty in place, who had previously been treated with both GKS and fractionated radiotherapy and who was also receiving chemotherapy at the time of the operation.
† Giant meningioma removed with ultrasonic aspirator leading to a transient period of disseminated intravascular coagulation confirmed by laboratory analysis. Hematoma found on routine postoperative imaging.
‡ Bi- temporal hemorrhagic encephalitis with HSV origin confirmed by cerebrospinal fluid PCR.
§ Foramen magnum tumor unchanged in size after treatment at the time of asymptomatic syrinx formation.
|| Both cases occurred with parasagittal tumors and hemiparesis and seizures resolved with resolution of the T2 MR signal changes in the surrounding brain.
** Both superficial convexity tumors.
†† Cavernous sinus tumors.

### TABLE 6

<table>
<thead>
<tr>
<th>Patient Satisfaction Survey*</th>
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<td>Microsurgery</td>
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<td>Were you satisfied &amp; would you recommend the same procedure to family &amp; friends in similar circumstances?</td>
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<td>again in similar circumstances?</td>
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</table>

* Of the 26 surgical patients who did not die (four patients) and were not lost to follow-up over the study period (two patients), 100% responded to our patient satisfaction survey (92.9% overall response rate). Of the 32 GKS patients who did not die (two patients) and were not lost to follow up over the study period (one patient), 100% responded to our patient satisfaction survey (91.4% overall response rate). See text for details regarding the five dissatisfied patients.

G. E. Linskey, S. A. Davis, and V. Ratanatharathorn

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GKS group would bias the microsurgery results to overestimate the perioperative complication rates and potentially underestimate clinical symptom outcomes. The higher percentage of patients with a history of failed treatment in the GKS group suggests that this group may reflect selection pressures for more aggressive (recurring) or rapidly growing (early recurrence detection), which may influence their observed control rate negatively compared with microsurgery. Finally, it is well established that for microsurgery, tumors involving the basal dura and dural sinuses are more likely to recur, mostly likely reflecting the greater difficulty of achieving a Simpson Grade 1 resection in these locations. Our results confirmed these findings with only a 62.5% Grade 1 resection rate for skull base tumors compared with a 78.9% rate for non–skull base tumors. The fact that our case selection relatively underrepresented cavernous sinus, petroclival, torcular herophili, and posterior two-thirds sagittal sinus tumors in the microsurgery group would tend to bias the results towards underestimating our actuarial microsurgical recurrence rate. The differences in the microsurgery and GKS groups in this study directly reflect criteria used in our multimodality treatment algorithm outlined in the Clinical Material and Methods section.

Microsurgery Management

Microsurgery is the proven gold standard for managing patients with meningiomas. The technical challenge posed by meningiomas has been an integral part of the history and development of cranial neurosurgery. Since 1957, we have known that the chance of tumor recurrence is directly related to the extent of original tumor resection quantified by the Simpson grade. If follow up is purely clinical, a minimum of 20 years is necessary to detect the majority of recurrences. With modern neuroimaging techniques, the majority of recurrences will be identified with a minimum of 10 years of follow up. Simply using annual computerized tomography scanning as a follow-up screening measure will reduce the average time to detecting recurrence to 2.9 years compared with an average of 5.7 years for first recurrence. As a result, we have been reluctant to lower our dose prescription to meningiomas with GKS as others have done. We continue to use a median dose of 16 Gy to treat the tumor margin (range 14–20 Gy). Because the primary driving force for lowering dose is the desire to limit dose toxicity to surrounding structures, maintaining a higher tumor margin dose requires exquisite attention to the conformity details of 3D dose planning. Our accentuated use of multiisocenter planning and selective beam blocking patterns reflects this effort and has led to GKS morbidity rates no higher than those reported with lower doses, while maintaining a presumably more optimal tumor dose.

Staged Microsurgery and Stereotactic Radiosurgery

We are not the first group to advocate or practice a planned, staged, microsurgery followed by GKS for selected patients with meningioma when indicated. We believe that this approach makes the most sense for patients with tumors too large for GKS who have cavernous sinus, torcular herophili, or posterior two-thirds sagittal sinus involvement and tumors too close to the optic nerve, chiasm, or tract for safe GKS. In these situations, we advocate microsurgical cytoreduction of that portion of the tumor that can be reached with minimal morbidity as well as creation of adequate margins of space between the residual tumor surface and the differentially radiosensitive surrounding structures. The optimal timing of the two stages...
remains a matter for debate. Delay between stages of 12 to 18 months will allow for maximum recovery of any partial cranial neuropathy that occurs as a result of first-stage microsurgery before exposing the recovering nerve(s) to an additional pathological stress with GKS. Delay, however, increases the likelihood of interval tumor growth, which can undo advantages achieved in the first stage and may lead to loss of safety space achieved with the first stage because previously compressed and displaced normal surrounding tissue returns to its natural position. In two of our purposefully planned staged procedures, tumor growth was detected on MR imaging 9 months after microsurgery and the original schedule of a 12-month interval was accelerated by 3 months to respond to the changing situation. If a delay between stages is contemplated, we recommend regular neuroimaging at 3-month intervals to pick up and react to any unexpected circumstances.

**Fractionated Radiotherapy**

Fractionated radiotherapy has a long history of empirical efficacy in the treatment of patients with meningiomas. In the past it has been predominantly used for patients with inoperable tumors, recurrent or residual tumors, patients too ill for surgery, and patients with atypical or malignant meningiomas. Fractionated radiotherapy can now be delivered with standard port and wedge techniques, 3D conformal techniques, IMRT, or stereotactic radiotherapy. It can be delivered with conventional fractionation prescriptions, or with a two to five fraction (hypofractionation) technique. Fractionated radiotherapy clearly reduces the recurrence rate of subtotally resected meningiomas compared with subtotal resection alone.

The concerns for not favoring fractionated radiotherapy as a primary treatment modality for benign meningiomas fall into three categories. The first concern relates to the greater exposure of normal surrounding brain to radiation than when more highly conformal GKS is performed in a patient with a benign disease and a potentially normal life span. Concerns surround long-term cognitive effects (especially with exposure of bilateral mesolimbic system structures) as well as the risk of pituitary hormonal deficiencies in patients with tumors close to the parasellar region. The second concern is a consequence of the theoretical biological disadvantages of fractionation strategies as opposed to using a high single-fraction dose for treating meningiomas. Brain tissue is not embedded or distributed throughout the substance of the meningioma. As a result, there should not be normal central nervous system tissue within a properly planned GKS target volume to benefit from fractionation as a central nervous system sparing strategy. Furthermore, as a late-responding target tissue with a low proliferative index, and an α/β ratio similar to surrounding brain, a high single dose is more likely to have the desired biological effect on the meningioma tissue than multiple lower doses. The exception to this scenario is the optic nerve sheath meningioma when the tumor surrounds the radiosensitive optic nerve. In this situation we favor a fractionated approach, preferably with an IMRT technique (see **Clinical Material and Methods**). The third concern involves the risk of secondary malignancy over the course of the lifespan of a patient with a benign tumor. Although GKS also carries a risk of secondary malignancy, theoretically this risk should be lower given the greater restriction in the volume of exposure and the fewer number of individual radiation exposures involved.

Anaplastic or malignant meningiomas will likely have a higher α/β ratio and certainly have a higher proliferative index. We currently recommend fractionated radiotherapy for all patients with anaplastic or malignant meningiomas, even if their tumor has been resected and/or have had a residual or recurrence already treated with GKS. We also recommend fractionated radiotherapy for optic nerve sheath tumors, benign tumors too close to the optic apparatus for safe GKS where microsurgery cannot be performed to improve the situation, and for tumors too large for GKS when they are unable to undergo safe cytoreductive microsurgery.

**Conclusions**

Both microsurgery and GKS are safe and effective and provide equivalent degrees of patient satisfaction when used for differentially selected patients.

In our series, Simpson Grade 1 or 2 resection was achieved in 86.1%, but tumors with cavernous sinus, torcular, or posterior two-thirds sagittal sinus involvement were underrepresented because of a tendency to preferentially treat these patients with GKS. There were no procedure-related deaths or permanent major neurological morbidity, and the mean KPS score was maintained in both groups. Both modalities carried a similar risk of worsening patient symptoms. Microsurgery provided a greater chance of improving (as opposed to stabilizing) patient symptoms than GKS, predominantly through more rapid and effective relief of symptomatic tumor mass effect; however, much of this difference may be attributable to selection criteria.

Both GKS and microsurgery serve important and predominantly complementary roles in the overall management of patients with meningiomas. Both techniques should be available for patients with meningiomas.

**References**


M. E. Linskey, S. A. Davis, and V. Ratanarathorn
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*Address reprint requests to:* Mark E. Linskey, M.D., Department of Neurological Surgery, University of California Irvine Medical Center, Building 3, Room 313, Rt 81, 101 The City Drive South, Orange, California 92668-3298. email: mlinskey@uci.edu.

M. E. Linskey, S. A. Davis, and V. Ratanatharathorn