Long-term outcomes after meningioma radiosurgery: physician and patient perspectives

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Object. Stereotactic radiosurgery is a primary or adjuvant management approach used to treat patients with intracranial meningiomas. The goal of radiosurgery is long-term prevention of tumor growth, maintenance of the patient’s neurological function, and prevention of new neurological deficits. The object of this study is to report longer-term patient outcomes.

Methods. The authors evaluated 99 consecutive patients who underwent radiosurgery for meningioma between 1987 and 1992. Evaluation was performed using serial imaging tests, clinical evaluations, and a patient survey that was administered between 5 and 10 years after radiosurgery. Four patients underwent two radiosurgery procedures for separate meningiomas. The average tumor margin dose was 16 Gy and the median tumor volume was 4.7 ml (range 0.24–24 ml). Fifty-seven patients (57%) had undergone prior resection, of which 12 procedures were considered “total.” Five patients received fractionated radiation therapy before radiosurgery. Eighty-nine patients (89%) had skull base tumors.

The clinical tumor control rate (no resection required) was 93%. Sixty-one (63%) of 97 tumors became smaller, 31 (32%) remained unchanged in size, and five (5%) were enlarged. Resection was performed in seven patients (7%), six of whom had undergone prior resection. New neurological deficits developed in five patients (5%) 3 to 31 months after radiosurgery. Twenty-seven (42%) of 65 responding patients were employed at the time of radiosurgery and 74% of these remained so. Radiosurgery was believed to have been “successful” by 67 of 70 patients who completed an outcomes questionnaire 5 to 10 years later. At least one complication was described by nine patients (14%) and in four patients the complications resolved.

Conclusions. Five to 10 years after radiosurgery, 96% of surveyed patients believed that radiosurgery provided a satisfactory outcome for their meningioma. Overall, 93% of patients required no other tumor surgery. Incidences of morbidity in this early experience were usually transitory and relatively mild. Radiosurgery provided long-term tumor control associated with high rates of neurological function preservation and patient satisfaction.

KEY WORDS • meningioma • radiosurgery • skull base • microsurgery • radiation therapy

Clinical Material and Methods

Patient Population

Ninety-nine consecutive patients underwent stereotactic radiosurgery for treatment of an intracranial meningioma at the University of Pittsburgh between 1987 and 1992. Four patients underwent radiosurgery twice for separate tumors. The characteristics of the patients are listed in Table 1. The majority of tumors were located in the cranial base (89%; Table 2). Prior resection had been performed in 57 patients (57%). Sixteen patients had undergone two tumor resections, three patients three resections, two patients four resections, and one patient had undergone five resections. The most common deficit before radiosurgery was cranial neuropathy. Patients with pathological evidence of malignant meningioma were excluded from this analysis.

Radiosurgical Technique

All patients underwent stereotactic radiosurgery performed using the gamma knife (Elekta Instruments, At-
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TABLE 1
Characteristics in 99 patients before meningioma radiosurgery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (yrs)</td>
<td></td>
</tr>
<tr>
<td>median</td>
<td>62</td>
</tr>
<tr>
<td>range</td>
<td>12–84</td>
</tr>
<tr>
<td>gender</td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>68 (69%)</td>
</tr>
<tr>
<td>male</td>
<td>31 (31%)</td>
</tr>
<tr>
<td>prior subtotal tumor resection</td>
<td>45 (45%)</td>
</tr>
<tr>
<td>prior gross-total resection</td>
<td>12 (12%)</td>
</tr>
<tr>
<td>prior fractionated radiation therapy</td>
<td>5 (5%)</td>
</tr>
</tbody>
</table>

TABLE 2
Locations of meningiomas in brain observed at radiosurgery in 99 patients

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>cavernous sinus</td>
<td>30</td>
</tr>
<tr>
<td>petrous apex</td>
<td>22</td>
</tr>
<tr>
<td>tentorium</td>
<td>8</td>
</tr>
<tr>
<td>cerebello pontine angle</td>
<td>6</td>
</tr>
<tr>
<td>foramen magnum</td>
<td>4</td>
</tr>
<tr>
<td>sphenoid ridge</td>
<td>4</td>
</tr>
<tr>
<td>falx</td>
<td>4</td>
</tr>
<tr>
<td>tuberculum sellae</td>
<td>4</td>
</tr>
<tr>
<td>clivus</td>
<td>3</td>
</tr>
<tr>
<td>intraventricular</td>
<td>3</td>
</tr>
<tr>
<td>parasagittal</td>
<td>3</td>
</tr>
<tr>
<td>confluence of falx &amp; tentorium</td>
<td>3</td>
</tr>
<tr>
<td>planum sphenoidale</td>
<td>2</td>
</tr>
<tr>
<td>jugular foramen</td>
<td>1</td>
</tr>
<tr>
<td>torcular herophili</td>
<td>1</td>
</tr>
<tr>
<td>anterior clinoid</td>
<td>1</td>
</tr>
</tbody>
</table>

Lanta, GA). Radiosurgery was performed after local anesthesia had been induced in the patient; the anesthesia was supplemented by mild intravenous sedation when necessary. Between 1987 and 1991, radiosurgery was performed with the aid of computerized tomography (CT) scanning (Fig. 1). Patients treated in 1991 and 1992 underwent radiosurgery aided by magnetic resonance (MR) imaging. A prospective comparison study confirmed the accuracy of MR imaging–based stereotactic targeting.12 Multiple irradiation isocenters were used to construct a radiosurgical plan that fit the often irregular tumor margins.7 The 50% isodose line was used to cover the tumor margin in 77 patients (78%). Image-integrated dose planning was performed using a computer workstation. The median dose delivered to the tumor margin in this series was 16 Gy (range 9–25 Gy). The median maximum tumor dose was 32 Gy (range 18–50 Gy). The lowest dose administered was for a child with a radiation-induced meningioma of the sella. Specific dose selection was based on several factors including tumor volume, surgical history, irradiation history, neurological status, tumor location, and patient preference. After radiosurgery, all patients received a single 40-mg dose of intravenous methylprednisolone and were discharged from the hospital the next morning.

Follow-Up Evaluations

Serial imaging studies (MR imaging, or CT scanning when MR imaging was contraindicated) were requested every 6 months for the first 2 years, annually for the next 2 years, and biennially thereafter. Patients who lived far from Pittsburgh (approximately 50% of those patients reported here) underwent imaging at their home site and were evaluated by their referring physician. Regional patients returned to our center for evaluation. Each patient underwent a detailed examination that included cranial nerve testing and evaluation of central and peripheral nervous system function. Contrast-enhanced imaging studies were used to define the tumor response and to identify any peritumoral imaging changes. Before and after radiosurgery, each tumor was measured in three separate dimensions by using calipers according to a protocol previously reported.16 Using this caliper method, a significant imaging change was defined as a difference of ± 2 mm.

Patient Survey

All patients were surveyed 5 to 10 years following radiosurgery. This mail-in survey included questions regarding preradiosurgery management, patient employment or retirement status, and change in level of activity after radiosurgery. Patients were asked to describe whether they had sustained a “complication” after radiosurgery and to describe that complication. Additionally, patients were asked three questions. 1) Did gamma knife radiosurgery meet your expectations? 2) As you look back, was radio-
Results

Imaging Response and Tumor Control After Radiosurgery

The majority of irradiated meningiomas decreased in size over time (Fig. 2). Imaging studies performed 2 to 4 years after radiosurgery revealed that 58.8% of tumors were reduced in size. At Years 4 to 6, 6 to 8, and 8 to 10, the rates of tumor reduction were 69%, 73%, and 88%, respectively. Six older patients refused further follow-up imaging after the first 2 years because they were doing well clinically and had no new symptoms. Their status is reflected only in the clinical outcome data. Seven patients underwent delayed surgical resection of their tumors, five within the first 4 years after radiosurgery. Although the tumor had not grown, resection was performed within 6 months after radiosurgery in two patients because of continued symptoms. Only two patients underwent later resections. One surgery was performed in a patient who had undergone prior resection of a petroclival tumor that showed initial regression within 2 years after radiosurgery, stable tumor for the next 6 years, and then enlargement. Resection was performed in another patient 8 years after radiosurgery because the patient experienced visual symptoms related to a cavernous sinus meningioma (Table 3).

We characterized the pattern of failure on imaging studies according to growth of the treated tumor and/or growth of a new separate or adjacent tumor. The failure rate from radiosurgery of the treated tumor mass was 4.9 ± 2.8% at 53 to 120 months. The total failure rate for any subsequent tumor growth in any location was 11.3 ± 4.2% at 63 to 120 months. Local tumor progression after radiosurgery was related to a history of prior resection (p = 0.02) and history of multiple meningiomas (p < 0.00001). No patient experienced tumor growth after radiosurgery if no prior resection had been performed (42 patients). In univariate testing, patient age, margin dose, isodose, and tumor volume were not important factors for the tumor response.

Of the 99 patients in this series, 10 were known to have died from unrelated causes, three were elderly at the time of radiosurgery and eventually were lost to follow-up review (they were presumed to have died), and six refused further imaging but were well and had no new symptoms. In two patients, no follow-up imaging could be obtained. Twenty patients had a change of address after their initial imaging reviews and could not be found either by us or by their referring physician for later reviews.

Clinical Response After Radiosurgery

All patients were discharged within 24 hours after radiosurgery. Occasionally patients experienced a headache lasting several hours after removal of the stereotactic headframe. There were no infections or systemic complications. Patients were allowed to resume their activities and daily routine immediately after discharge.

Neurological function evaluations showed that new or worsened deficits occurred in five patients from 3 to 31 months after radiosurgery. No patient described a radiation-related neurological complication between the 4th and 10th years. The actuarial rate of postradiosurgery complications that were believed to be related to irradiation was 4.85 ± 2.4% at 31 to 120 months. These new or worsened neurological deficits included visual acuity deterioration (at 6 months, recovered), hemianopsia (at 31 months, permanent), hemiparesis (at 12 months, recovered), and abduction nerve palsy (at 18 months, recovered) in the same patient; worsening of a preexistent oculomotor palsy (at 3 months, persisted); and hemianopsia from occipital lobe edema (at 30 months, permanent). Complete resolution of symptoms was observed in two of five patients (40% resolution rate at 8 months). Postradiosurgery complications were not related to tumor volume, margin dose, maximum dose, prior surgery, or skull base location (all factors had a probability value > 0.3). Two patients underwent placement of a ventriculoperitoneal shunt for progressive symptoms of hydrocephalus that were present at the time of radiosurgery. When we combined the incidence of new or worsened neurological problems related to irradiation or tumor growth, we found a rate of 8.8 ± 3.2% at 38 to 120 months.

### Table 3

Response on imaging after meningioma radiosurgery in 97 patients

<table>
<thead>
<tr>
<th>Years Postop (no. of patients)</th>
<th>Tumor Response</th>
<th>0-2</th>
<th>2-4</th>
<th>4-6</th>
<th>6-8</th>
<th>8-10</th>
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<td>3</td>
<td>10</td>
<td>22</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>no change</td>
<td></td>
<td>10</td>
<td>4</td>
<td>10</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>increased size</td>
<td></td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

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Patient Survey After Radiosurgery

A survey was returned by 70 patients or their relatives (79% of 89 survivors). Sixty-five patients answered questions regarding employment. Twenty-seven patients (42%) were employed at the time of radiosurgery and 20 (74%) remained so afterward. Three active patients who had retired before radiosurgery continued to maintain an unchanged functional level. Of 35 patients who were not employed at the time of radiosurgery, five (14%) resumed employment. Patients described their overall level of activity as remaining unchanged in 65%, being increased in 8%, or decreased in 27%. When asked whether gamma knife radiosurgery met their initial expectations, 61 patients (91%) responded in the affirmative. Two patients who answered “no” had tumors that regressed after radiosurgery and required no further treatment. Complications were described by nine patients (13%) and in four of these the complications resolved. The complications included hydrocephalus, problems in performing mathematics, transient disorientation, unspecified infection, visual blurring (two cases), double vision (two cases), and a transient unspecified problem. Radiosurgery was described as a “successful” treatment by 67 (96%) of 70 patients. When asked if they would recommend the procedure to a friend or family member, 68 patients (97%) responded “yes,” none responded “no,” and two replied that they “did not know.”

Discussion

Surgical resection of a meningioma and its dural base is the preferred treatment for most patients. Complete resection may not be feasible in some patients when the tumor is closely associated with critical vascular, cranial nerve, and parenchymal brain structures. Advanced microsurgical cranial base techniques have reduced the incidence of morbidity associated with resections of smaller tumors that are now more readily detected using high-resolution imaging studies. Supratentorial tumors close to venous sinuses may not be amenable to complete resection without significant risk for new neurological deficits resulting from venous infarction. Because complete resection of some meningiomas may not be possible, consideration of alternative or adjuvant strategies is important. Currently, these include stereotactic radiosurgery or fractionated external-beam radiation therapy. To date, hormonal therapies or chemotherapy have played only a limited and investigational role in the management of meningiomas.

In his hallmark paper, Simpson described meningioma recurrence rates based on the type of resection. The recurrence rates discussed by Simpson may have been an underestimation because his data preceded the development of computerized imaging techniques. He reported a 9% recurrence rate after “complete resection” of the tumor and its neoplastic dural base (Grade 1), a 19% recurrence rate when the tumor was “resected” and the dural base was only coagulated (Grade 2), a 29% recurrence rate when the tumor itself was removed but the dura could not be excised (Grade 3), and approximately a 40% recurrence rate when only a subtotal resection was performed (Grade 4).

In a recent long-term analysis, Conдра, et al. found a 70% rate of tumor progression after subtotal resection alone and concluded that incomplete removal in a young or middle-aged patient was incomplete tumor treatment. Better long-term control was achieved when radiation therapy was administered. Mathiesen and colleagues identified symptomatic recurrence rates of 16% and 20% after Grade 1 and 2 resections, respectively, with follow-up periods lasting past 5 years. Even Simpson’s anticipated recurrence rates after resection of the tumor mass but incomplete management of the neoplastic dura only approaches the reported rates after stereotactic radiosurgery. It may be that, for smaller meningiomas suitable for radiosurgery, the biological effect of radiosurgery on the tumor mass provides just as good a response as tumor removal (100% tumor control for patients in this series with no prior surgery and 94% overall). The response in the neoplastic dural base after radiosurgery may be better than dural coagulation (Simpson Grade 2) because we identified only an 11% long-term intracranial progression rate (this rate includes remote tumor growth).

Comparison of Radiosurgery and Radiation Therapy

Until the beginning of this decade, fractionated external-beam radiation therapy was a controversial treatment for patients with meningiomas. Some reports showed no evidence of therapeutic benefit, whereas others suggested a positive effect. Because of the relatively infrequent finding of tumor regression after radiotherapy, meningiomas were believed to be relatively radioresistant tumors. The increased radiobiological effect of delivering radiation in a single fraction (radiosurgery) was thought to be one way to overcome this element of radioresistance. However, several recent studies substantiated the role of radiation therapy for meningiomas after a subtotal resection. For this reason, we recommend that radiation therapy be considered for patients with larger tumors (> 3 cm in average diameter), tumors that compress the optic chiasm, and tumors with irregular and diffuse borders.

The fact that radiation cannot be conformed to the imaging-defined tumor margins remains the major drawback of radiation therapy, but one of the advantages of radiosurgery (Fig. 3). Stereotactic fractionated radiation therapy, a combination of techniques using relocatable frames, has been used in the last several years. Although this confines the radiation more than conventional fractionated techniques, it is not a conformal irradiation approach. The volume of the regional brain that is irradiated still exceeds that irradiated in radiosurgery, although the effect of this irradiation may be lessened by the number of fractions. A recent review from McGill University of stereotactic fractionated radiation therapy for skull base tumors that included meningiomas showed that four of 20 patients who underwent a six-fraction regimen experienced significant complications. Irradiation of the brainstem surrounding a petrous apex tumor led to neurological deficits that likely would have been avoided if conformal radiosurgery had been performed. Finally, the radiobiological effect of single-fraction delivery remains an additional advantage of radiosurgery. In a slowly dividing tumor or in late responding tissue such as a meningioma, vestibular schwann-
noma, or arteriovenous malformation, there may be no biological reason to fractionate \( 17 \), and little reason to irradiate larger volumes of normal brain.

**Indications for Radiosurgery**

We believe that current indications for meningioma radiosurgery include newly diagnosed, recurrent, or residual tumors after prior resection (Fig. 4). In many patients, the imaging findings are typical and can be used to make the diagnosis of a meningioma. Patients with atypical imaging findings should have histological confirmation of their tumor. For small or medium-sized tumors consistent with meningiomas, radiosurgery may be an option. At this time we do not believe that radiosurgery should be a first-line approach for patients with convexity meningiomas, in whom the likelihood of postresection cure is high. Radiosurgery is not often performed for optic nerve sheath tumors and current systems are not designed to approach

spinal meningiomas. However, for skull-base tumors or parasagittal tumors, radiosurgery may be an excellent management alternative. Although some surgeons believe in resecting as much of the tumor as possible and following the residual tumor using serial imaging studies, this subtotal approach may be inadequate for younger patients. It may be better to manage the entire neoplasm in some way that might include complete resection, resection plus radiosurgery, or radiosurgery alone. This may provide better long-term outcomes than an approach of “watchful waiting.”

In our initial experience, we advocated that a distance of at least 5 mm be present between the tumor margin and the optic nerve or chiasm. This distance was necessary to allow a falloff in radiation dose to maintain preservation of vision. Since 1992, for patients treated after those reported herein, current high-resolution imaging techniques and sophisticated high-speed workstations have facilitated the creation of gamma knife radiosurgery dose plans so that only 1 mm between tumor margin and the chiasm may be necessary if this proximity occurs only at one point. An extremely steep falloff in dose can be created at this point and the radiation shifted elsewhere (such as into the skull base). This has allowed the use of radiosurgery for tumors more closely related to the optic chiasm. The use of volume-acquisition stereotactic MR imaging (divided into 1-mm imaging intervals) provided graphic definition of tumor borders and regional structures including cranial nerves. In our 11-year experience, which includes 203 patients with cavernous sinus region tumors (including petrous apex lesions), only two patients developed visual complications after undergoing radiosurgery. Both patients were treated in our early experience using CT guidance and received optic chiasm doses of 11.5 and 12 Gy (discussed earlier). Since we began restricting the dose delivered to the optic chiasm below 8 Gy and conforming the radiosurgery plan with more sophisticated planning software, no subsequent patient has developed a delayed visual deficit.

Rarely do we perform radiosurgery in patients with larger tumors (> 3 cm in average diameter) because the...
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dose reduction necessary to minimize adverse radiation-related tissue effects decreases the efficacy of the procedure. There is no evidence that 3 cm is an absolute limit, but rather a relative one that must be used as one of many factors included in the management decision. In 1987, our initial inclusion criteria consisted of elderly patients, those with concomitant medical problems that argued against resection, and patients with residual or recurrent tumors after resection. Until 1990 we recommended surgical resection to most younger patients, but some refused and underwent radiosurgery. Our early analysis of results in these younger patients showed findings similar to those obtained from older patients. Thus, by 1991 we began to offer radiosurgery to all patients with nonconvexity meningiomas regardless of age or prior surgical history. The outcomes obtained in this 5 to 10-year analysis did not differ between younger and older patients. The role of conservative management in patients with small, asymptomatic tumors remains important. We continued to observe older patients (> 70 years) with small and minimal symptomatic tumors. These patients undergo annual imaging studies and receive treatment only when tumor growth or progressive symptoms are documented.

Long-Term Expectations After Radiosurgery

Although longer-term results (> 10 years) will be necessary to substantiate the potentially curative effects of radiosurgery, we believe that the present analysis highlights several points. First, radiosurgery is a well-tolerated surgical procedure that meets most patients’ expectations. Second, the rate of tumor volume reduction is significant and higher than previously believed. Early reports noted a 30 to 40% rate of tumor regression, whereas 73% of the patients in this study who underwent imaging 5 or more years postradiosurgery had smaller tumors. With extended follow-up observation most patients have tumors that have regressed in size and are not merely unchanged. Third, when tumor growth does occur, it usually does so early after radiosurgery. We still advocate periodic late follow-up imaging, perhaps every 3 years, which is what we recommend for any patient after subtotal resection of a meningioma. Fourth, post radiosurgery cranial neuropathy or other neurological symptoms occur within the first 3 years and may be transient. Finally, over the long term, the vast majority of patients describe radiosurgery as a successful treatment for their meningioma and would recommend it to friends or family. Levels of satisfaction and continued employment were similar to results from our survey of patients who had vestibular schwannoma radiosurgery. As we refine methods to analyze results and make therapeutic recommendations, we must understand the foundations of patient decision making. This includes information on medically defined treatment outcomes as well as data on employability, functional status, and satisfaction.

Conclusions

The optimum treatment for an intracranial meningioma is complete surgical resection of the tumor and neoplastic dural base. This can be achieved frequently in patients with convexity meningiomas and in selected meningiomas in other locations. Most cranial base meningiomas and those attached to patent venous sinuses cannot be completely removed without a high risk for new or additional neurological deficits. It is in this large patient group that radiosurgery may play a significant role. The role of radiosurgery in the management of meningiomas is limited by tumor size and, to some degree, by location. Long-term outcomes have substantiated the safety of this technique and the high rate of tumor growth control.

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