LONG-TERM RESULTS AFTER RADIOSURGERY FOR BENIGN INTRACRANIAL TUMORS

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BACKGROUND: Stereotactic radiosurgery is the principal therapeutic alternative to resecting benign intracranial tumors. The goals of radiosurgery are the long-term prevention of tumor growth, the maintenance of patient function, and the prevention of new neurological deficits or adverse radiation effects. Evaluation of long-term outcomes more than 10 years after radiosurgery is needed.

METHODS: We evaluated 285 consecutive patients who underwent radiosurgery for benign intracranial tumors between 1987 and 1992. Serial imaging studies were obtained, and clinical evaluations were performed. Our series included 157 patients with vestibular schwannomas, 85 patients with meningiomas, 28 patients with pituitary adenomas, 10 patients with other cranial nerve schwannomas, and 5 patients with craniopharyngiomas. Prior surgical resection had been performed in 44% of these patients, and prior radiotherapy had been administered in 5%. The median follow-up period was 10 years.

RESULTS: Overall, 95% of the 285 patients in this series had imaging-defined local tumor control (63% had tumor regression, and 32% had no further tumor growth). The actuarial tumor control rate at 15 years was 93.7%. In 5% of the patients, delayed tumor growth was identified. Resection was performed after radiosurgery in 13 patients (5%). No patient developed a radiation-induced tumor. Eighty-one percent of the patients were still alive at the time of this analysis. Normal facial nerve function was maintained in 95% of patients who had normal function before undergoing treatment for acoustic neuromas.

CONCLUSION: Stereotactic radiosurgery provided high rates of tumor growth control, often with tumor regression, and low morbidity rates in patients with benign intracranial tumors when evaluated over the long term. This study supports radiosurgery as a reliable alternative to surgical resection for selected patients with benign intracranial tumors.

KEY WORDS: Acoustic neuroma, Gamma knife, Meningioma, Radiosurgery, Schwannoma

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A lthough histologically benign, tumors of the cranial base and the coverings of the brain can cause significant neurological morbidity and mortality. Stereotactic radiosurgery has become an important treatment for patients with brain tumors. Little information exists regarding long-term clinical and imaging results in patients who choose such a management strategy. Published longterm results after surgical resection also are uncommon. Few studies have systematically used serial imaging studies in clinical assessments to determine treatment results more than 10 years after intervention. Early results after radiosurgery for patients with pituitary

tumors, cranial base schwannomas, and craniopharyngiomas and longer-term assessments in patients with vestibular schwannomas and meningiomas have been reported (1, 5, 10–14, 21–26, 28, 32–39, 41, 42, 45). Because the tumor is not removed during radiosurgery, only further long-term follow-up can determine treatment effectiveness. To assess the results after radiosurgery in patients with benign extraaxial tumors, we studied all patients who underwent treatment at a single center between 1987 and 1992. Results up to 15 years after radiosurgery were determined on the basis of serial imaging studies and clinical evaluations.

PATIENTS AND METHODS

Patient Characteristics

The University of Pittsburgh Institutional Review Board approved this study. Stereotactic radiosurgery was performed in 157 patients with vestibular schwannomas. The mean patient age was 60 years. Forty patients with vestibular schwannomas had undergone previous surgery (8 total and 32 subtotal). The most common presenting symptoms were hearing loss (n = 60) and tinnitus (n = 35). We used the Gardner-Robertson (15) classification to assess hearing. Seventy-six patients had serviceable hearing before undergoing radiosurgery. Eighty-five patients with meningiomas whose mean age was 59 years were treated. Prior surgery had been performed in 50 patients (10 total and 40 subtotal). Ten patients with a mean age of 47 years had schwannomas of other cranial nerves; six had undergone prior surgery. Twenty-eight patients had pituitary tumors treated at a mean age of 44 years. Prior surgery was performed in 24 of these patients. Five patients had craniopharyngiomas that were treated at a mean age of 24 years. All five had undergone prior subtotal resection.

Radiosurgical Technique

All patients underwent stereotactic radiosurgery with the Leksell gamma knife unit (Elekta Instruments, Atlanta GA). Patients were selected for radiosurgery if they had tumors less than 3.5 cm in maximum diameter (less than 3 cm diameter for vestibular schwannomas), if the tumor edge maintained a distance of at least 3 mm from the optic chiasm, and if the imaging characteristics were typical of the tumor type (for those without a prior histological diagnosis). Radiosurgery was performed while the patients were under local anesthesia supplemented with mild intravenous sedation when necessary. Between 1987 and 1991, radiosurgery was performed with computed tomographic imaging guidance. Patients managed in 1991 and 1992 underwent radiosurgery with magnetic resonance imaging guidance. Multiple irradiation isocenters were used to create radiosurgical plans as necessary (vestibular schwannoma, 99%; meningioma, 97%; other schwannoma, 95%; pituitary tumor, 90%; craniopharyngioma, 80%). An initial tumor margin dose of 18 to 20 Gy was selected for patients with schwannomas or meningiomas, but by 1989 this dose was reduced to 13 to 18 Gy on the basis of tumor volume, irradiation history, and tumor location in the brain (9) (mean tumor margin doses were vestibular schwannoma, 16.7 Gy; meningioma, 16.5 Gy; other schwannoma, 16.8 Gy; pituitary tumor, 20.8 Gy; craniopharyngioma, 18.5 Gy). In addition, the proximity of the optic nerves and the chiasm was important in patients with pituitary tumors or craniopharyngiomas. In 1990, we instituted a policy of limiting the dose administered to those structures to a maximum of 8 Gy (46). After radiosurgery, all patients were administered a single 40-mg dose of intravenous methylprednisolone and were discharged from the hospital the next morning.

Follow-up Evaluations

Serial imaging studies (magnetic resonance imaging, or computed tomography if magnetic resonance imaging was contraindicated) were requested every 6 months for the first 2 years, annually for the next 2 years, and then once every 2 to 3 years thereafter. Patients who lived far from Pittsburgh underwent imaging and clinical evaluations at locations near their homes and were evaluated clinically by their referring physicians. All imaging studies were sent to our center for detailed review. Patients in our region returned to our center for evaluation. Each patient underwent a detailed examination that included a neurological examination and specific tests for hearing, visual, or endocrinological function when appropriate. Contrast-enhanced imaging studies were obtained to identify the tumor response, assess the appearance of the regional brain, and check for remote changes such as hydrocephalus. Before and after radiosurgery, caliper measurements of each tumor were taken from the images as described previously (29). Tumor enlargement or regression was defined as a change of ± 2 mm in one dimension. We also noted whether patients developed any other tumors in the brain or in any other body location. Univariate analysis of factors potentially affecting tumor recurrence was performed with the Cox proportional hazards model using continuous variables for factors such as age, tumor volume, and marginal and maximum radiation dose.

RESULTS

Vestibular Schwannomas

The median follow-up period was 9.1 years, and it was 10.2 years in patients who were still living at the time of this analysis (n = 136). This includes 54 patients whose last assessment was 10 to 15 years after treatment, 65 patients who were last examined 5 to 10 years after treatment, and 17 who were last seen 1 to 5 years after treatment. Normal facial nerve function (House-Brackmann Grade 1) was present in 124 patients before radiosurgery, and 118 of these patients maintained normal facial nerve function after radiosurgery (95%) (20). Facial nerve function worsened in 26 patients (not below House-Brackmann Grade 3) who were treated early in our experience. Five patients had improvement in facial movement. One hundred twenty-four patients had normal facial sensation, and this was maintained in 115 patients. Reduced sensation followed by resolution of the deficit was found in 25 patients. Six patients had improvement in facial sensation. Hearing remained unchanged in 25% of patients (n = 19) and at serviceable levels (Grades 1 or 2) in 50% of patients. An additional 38 patients (50%) remained at House-Brackmann Grade 3 level.

Two patients had a surgical procedure after radiosurgery (at 33 and 40 mo). One had documented growth of the extracanalicular portion of the tumor, and one had a cystic recurrence that initially was drained and then was partially resected. Ten patients with vestibular schwannomas later developed other intracranial tumors, including two who had pituitary tumors, five who had distant meningiomas, two who had brain metastases, and one who had another schwannoma. All of these tumors were in remote brain locations. No patient developed a radiation-associated malignant or benign tumor (defined as a histologically confirmed and distinct neoplasm arising in the initial radiation field after at least 2 years had passed). Serial imaging studies obtained after radiosurgery (n = 157) showed a decrease in tumor size in 114 patients (73%) (*Fig. 1*), no change in 40 patients (25.5%), and an increase in 3 patients who later underwent resection (1.9%). An additional patient had surgery for an adjacent arachnoid cyst, even though the tumor had not enlarged.

Pituitary Tumors

Previous surgery was performed in 24 patients, and radiation had been administered previously in 6 patients. Two patients with Cushing's disease had undergone adrenalectomy. Cavernous sinus invasion was present in 10 patients. Hormone hypersecretion normalized in five of eight patients with acromegaly and improved in another two. Hypersecretion improved in 7 of 11 patients with Cushing's disease. A reduction in pituitary function was seen in two patients with Cushing's disease and in one patient with a nonsecreting tumor. Normal vision was preserved in 23 of 28 patients. Two patients with nonsecreting tumors developed impaired vision. Both of these patients had undergone prior surgery. Three patients underwent resection at 1, 2, and 8 years after radiosurgery, respectively. Surgery was performed because of increasing acromegalic symptoms in one patient and because of increased visual field deficits due to tumor compression in two patients. One patient had repeat radiosurgery for an



FIGURE 1. Axial contrast-enhanced magnetic resonance images showing right acoustic neuroma at the time of radiosurgery in 1990 (A) and tumor regression 12 years later (B).

increase in the cavernous sinus component in the setting of acromegaly. Serial imaging studies showed a decrease in tumor volume in 14 patients (50%), no change in 10 patients (36%), and an increase in 4 patients (14%). No patient developed a radiation-associated tumor.

Meningiomas

Meningioma radiosurgery was performed in 85 patients. Thirty had presented with multiple cranial nerve deficits and an additional 12 had a single cranial nerve deficit. Two patients had cavernous sinus meningiomas, and 15 patients had visual acuity or visual field impairments. Decreased hearing was present before radiosurgery in 11 patients. Twelve patients had evidence of trigeminal nerve dysfunction, and two had trigeminal neuralgia. This constellation of symptoms reflected a tendency toward a tumor location at the base of the cranium (90% of the patients in this study). In 36 patients (42%), the tumor involved the cavernous sinus region. After radiosurgery, 45 patients (53%) had a decrease in the size of their tumor (2-15 mm in the maximum tumor diameter), with most of the reduction occurring within the first 2 years (Fig. 2). Thirty-four patients (40%) had no change in tumor size during extended follow-up, and six patients (7%) had an increase in tumor volume. Tumor resection was performed in five patients 3, 3, 50, 54, and 95 months, respectively, after radiosurgery because of delayed tumor growth (n = 3) or persistent symptoms (n = 2). The patient who had surgery 95 months after radiosurgery did not have a growing tumor but complained of persistent visual symptoms. The tumor was partially removed, and she developed a small brainstem infarction. Another patient underwent removal of multiple new meningiomas 12 years after radiosurgery. No patient developed a radiation-associated tumor at or near the irradiated site. During follow-up, three patients developed breast cancer, four had benign breast tumors, and one each developed lym-



FIGURE 2. Axial contrast-enhanced magnetic resonance images showing tentorial meningioma at the time of radiosurgery in 1992 (A) and tumor regression 10 years later (B).

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phoma, oncocytoma, thyroid cancer, cranial tumor, multiple myeloma, and basal cell carcinoma of the forehead.

New or worsened neurological deficits developed in five patients from 3 to 31 months after radiosurgery, two of whom experienced complete resolution. These deficits included decreased visual acuity in a young man who was treated for a radiation-induced meningioma, hemianopsia in two patients with cavernous sinus tumors who were administered 11 to 12 Gy to the optic chiasm, transient hemiparesis and abducens deficit in a patients with a petroclival meningioma who was treated with 20 Gy delivered to the tumor margin, and worsened oculomotor deficit in a patient with a complex petroclival meningioma after undergoing prior partial resection. There were no infections or systemic complications.

Craniopharyngiomas

Five patients had radiosurgery for craniopharyngiomas (age range, 10–66 yr). All had undergone prior resection, and four had undergone prior radiotherapy. The median follow-up period after radiosurgery was 9 years, and it was 11.5 years in the four surviving patients. Three patients did not have any new hormonal deficits, but two patients, both of whom had undergone prior radiotherapy, developed further hormonal losses. Four patients had impaired vision before radiosurgery; after treatment, four remained without change in their vision, and one had deterioration. Repeat radiosurgery was performed for one patient who developed a recurrent tumor in another brain location, and one developed a cystic recurrence 12.5 years after their first procedure. In the other patients, imaging studies showed stable tumors in three patients and a regressed tumor in one patient.

Other Cranial Nerve Schwannomas

Radiosurgery was performed in 10 patients who had tumors that arose from the trigeminal nerve (n = 5), the jugular foramen region, or the glossopharyngeal-vagal nerve complex (n = 5). The age range of these patients was 26 to 72 years. No patient had undergone prior radiotherapy. The median survival was 9.1 year. All patients with trigeminal nerve tumors presented with trigeminal nerve symptoms, and two patients had additional oculomotor, abducens, and cochlear nerve deficits. All patients with jugular foramen tumors presented with combinations of dysphagia or vocal changes. One patient had a facial palsy and a spastic hemiparesis. Serial imaging studies showed stable tumors in five patients, regressed tumors in four patients, and increased tumor size in one patient (*Fig. 3*). No patient developed a secondary tumor.

Univariate proportional hazards analysis of factors potentially affecting tumor recurrence correlated tumor recurrence with a history of radiotherapy (P = 0.0038; hazard rate ratio = 6.46; 95% confidence interval, 1.83–22.83) and the type of tumor (P = 0.0024; hazard rate ratio = 2.47; 95% confidence interval, 1.33–4.59). The 10-year actuarial tumor control rates were 94.4 ± 1.6% for tumors in patients who had undergone no prior radiotherapy (260 of 270 controlled), 69.2 ± 15.6% in



FIGURE 3. Kaplan-Meier plot showing imaging-defined tumor control of benign brain tumors during a 15-year period.

patients who had undergone prior radiotherapy (10 of 13 controlled), 96.9 \pm 1.4% in patients with schwannomas (162 of 167 controlled), 91.5 \pm 3.4% in patients with meningiomas (79 of 85 controlled), and 81.1 \pm 7.9% in patients with other benign tumors (29 of 34 controlled). Tumor volume, radiation dose, patient age or sex, and prior surgery were not related to the tumor response.

DISCUSSION

Intracranial tumors cause tremendous disability in many patients who harbor them. Whereas malignant brain tumors often lead to disability and death, histologically benign intracranial tumors can lead to functional deficits that may persist for many years. Such clinical problems can lead to loss of personal independence, loss of employment, depressed mood, and the need for additional medical care, all of which represent a significant cost to society (31, 47, 48). During the past century, patients found to have tumors such as vestibular or other cranial nerve schwannomas, intracranial meningiomas, pituitary adenomas, or craniopharyngiomas were managed with surgical resection, some form of radiotherapy, or simple observation (2–4, 7, 8, 17, 18, 30, 40, 44, 49). No treatment was a choice for patients with minimal symptoms, those with concomitant medical illnesses, and those with tumors in particularly high-risk locations. For patients who underwent surgical resection, either a complete tumor resection was performed, if feasible, or a planned partial removal was performed to improve the patients' symptoms by reducing the amount of brain compression. For tumors that later recurred, repeat resection was considered. Selected patients were administered some form of radiotherapy using external beam coned-down techniques, whole-brain irradiation, or, rarely, surgical placement of radioactive seeds into the tumor. Longterm clinical outcome studies after any of these treatments

have been reported infrequently (4, 7, 40). Thus, it has been difficult for patients and their physicians to choose between available management strategies, particularly when the long-term results of each approach are being compared. When a new treatment is introduced, physicians often state appropriately that such a treatment should be chosen cautiously because no long-term outcome data are available.

In the late 1980s and early 1990s, stereotactic radiosurgery became the new therapeutic option for many patients with benign or malignant intracranial tumors, as well as selected patients with cerebral vascular malformations and functional disorders. Radiosurgery was introduced at our center in 1987, and a program of prospective data collection in all patients was introduced. Our plan was to study the imaging and clinical responses of patients after radiosurgery, determine the need for subsequent resection of the tumor or the need for other treatments, identify the risk of delayed malignant transformation, and predict whether other unsuspected complications might occur over time. Each tumor type posed unique clinical challenges, with a variety of issues related to tumor location in the brain, tumor volume, radiosurgical dose planning and selection, postradiosurgical imaging assessments, and cranial nerve and brain tissue morbidities. We thought that linking these tumor types would allow us to learn more about the role of radiosurgery in the treatment of patients with benign intracranial tumors.

The results of this study reflect a tendency to perform radiosurgery if the patient had undergone prior resection and had either residual or recurrent tumor, if the patient was elderly or had significant concomitant medical problems, or had a tumor that posed excessive surgical risks (i.e., cavernous sinus location). As our experience grew, an increasing number of younger or healthier patients chose radiosurgery as an alternative to resection. This occurred because early published data identified results that appeared similar in younger or older patients or after the use of radiosurgery as the primary or adjuvant management modality. Forty-four percent of patients in this study had undergone one or more resections before having radiosurgery, and prior radiotherapy had failed in 5%.

In this study, we found that radiosurgery provided a high rate of tumor growth cessation. Overall, 95% of tumors either remained without further growth or decreased in volume during long-term follow-up. Tumor volume reduction usually occurred slowly, beginning as early as 6 months after the procedure but continuing even years later. The majority (63%) of tumors eventually became reduced in size. Some tumors that had decreased in size by 5 years after radiosurgery were even smaller 7 and 10 years later. In rare patients, particularly patients with schwannomas, an early effect of irradiation led to marked loss of central contrast enhancement associated with slight (1–2 mm) expansion of the tumor capsule diameter. Some of these patients developed local (i.e., retroauricular), transient, sharp pain, perhaps as a result of dural inflammation. Most such tumors eventually regressed. Delayed regression in tumor volume was not associated with symptoms.

The tumor response rate after radiosurgery seemed to be equal to or better than that found by others who administered fractionated radiotherapy, particularly compared with longterm results. Maire et al. (30) managed 20 patients with vestibular schwannomas at a total dose of 51.4 Gy and found tumor control in 85% in median follow-up of 30 months. Andrews et al. (1) found high tumor control rates for both radiosurgery and radiotherapy in their comparison study (98 and 97%), but the mean follow-up period in their study was short (10 mo). A long-term (median, 9 yr) assessment at the University of Pittsburgh in patients with nonfunctional pituitary adenomas who underwent radiotherapy found actuarial tumor control rates of 87.5% at 10 years and 77.6% at 20 years (4). The rate of new radiation-induced neoplasms was 2.7% at 10 years. In a study of the response of meningiomas to radiotherapy, Goldsmith et al. (17) reported a 5-year progressionfree survival rate of 98% in patients who were treated after 1980 with the use of modern techniques. The 10-year control rate for their entire series was 77%. Condra et al. (7) found that subtotal excision alone was associated with a lower 15-year control rate (30%) compared with partial resection followed by radiotherapy (87%). No long-term studies that evaluate the efficacy of radiotherapy as the primary treatment for meningiomas have been reported.

No patient in our study developed a delayed, radiationassociated malignant tumor. Malignant transformation after large-field radiotherapy is reported to occur with an incidence of approximately 1 to 3% (4). Data obtained in patients who underwent pituitary tumor radiotherapy during the past 4 decades indicates that a wide variety of new tumor types could develop in the treatment field 5 to 30 years after irradiation. In a stereotactic radiosurgical procedure, the steep decrease in the radiation dose delivered outside the tumor allows the regional irradiation volume to be greatly reduced. Correspondingly, the risk for delayed malignant transformation should be much less after stereotactic radiosurgery than after radiotherapy (27). Two case reports described in detail the development of glioblastomas multiforme after radiosurgery was performed to treat a meningioma and a vestibular schwannoma that met the criteria for radiation-associated tumors (43, 50). We reported the case of a patient who had radiosurgery for a presumed vestibular schwannoma in whom the tumor was later resected and found to be a malignant triton tumor (6). Although the risk of a radiationassociated neoplasm after radiosurgery may be approximately 1:1,000 to 1:20,000, this risk is significantly less than the 1:200 risk of death in patients who undergo cranial base craniotomy.

Brain Tolerance

Knowledge of the tolerance of normal brain structures is crucial to performing a successful radiosurgical procedure. This point is particularly important, given that we did not find evidence of a tumor dose-response correlation in this study. It seems that within the dose range that we have used to date, the tumor margin dose (i.e., the minimum dose received by

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the tumor) was adequate to halt tumor growth. We continue to search for radiosurgical doses that are safe, lead to tumor growth arrest, provide a reasonable rate of tumor volume regression, and, we hope, improve patients' symptoms. Early experimental studies found that doses far above those used in human tumor radiosurgery would cause focal brain necrosis or vascular injury (100–400 Gy). Within the dose range of this study, brain, cranial nerve, or vascular injury was rare. We found no evidence of large-artery occlusion or stenosis (e.g., the carotid artery within the cavernous sinus) or small-vessel occlusion (e.g., lacunar infarction in the brainstem adjacent to the tumor). We did find evidence of new-onset cranial neuropathy or adverse radiation effects in the brain, which we attributed to radiation in the absence of tumor growth. Such effects were delayed in onset (3-31 mo later) and usually were transient (16, 28). This time until symptom onset is similar to that reported by other groups (19). However, symptoms often took weeks to months to resolve. Corticosteroid therapy was administered in patients whose deficits caused functional disabilities.

Stereotactic radiosurgery seems to be curative for many patients with small or medium-sized benign brain tumors. We found that it was rare for a tumor to enlarge after 4 years of follow-up had passed. Similarly, radiation-related morbidity usually occurred early, within 3 years. Although it would be rare for a tumor to show growth 10 or more years after radiosurgery, we continue to recommend that imaging studies be obtained every 4 years once 10 years of follow-up have been completed. Radiosurgery is the best choice for patients with tumors that do not cause significant symptoms due to brain compression. For that reason, we recommend it not only for patients who have residual or recurrent tumors after resection but also as an important choice for patients with newly diagnosed tumors.

DISCLOSURE

DK and LDL serve as consultants to Elekta Instruments, Inc.

REFERENCES

- Andrews DW, Suarez O, Goldman HW, Downes MB, Bednarz G, Corn BW, Werner-Wasik M, Rosenstock J, Curran WJ Jr: Stereotactic radiosurgery and fractionated stereotactic radiotherapy for the treatment of acoustic schwannomas: Comparative observations of 125 patients treated at one institution. Int J Radiat Oncol Biol Phys 50:1265–1278, 2001.
- 2. Bederson JB, von Ammon K, Wichmann WW, Yaşargil MG: Conservative treatment of patients with acoustic tumors. **Neurosurgery** 28:646–651, 1991.
- 3. Borovich B, Doron Y: Recurrence of intracranial meningiomas: The role played by regional multicentricity. **J Neurosurg** 64:58–63, 1986.
- Breen P, Flickinger JC, Kondziolka D, Martinez AJ: Radiotherapy for nonfunctional pituitary adenoma: Analysis of long-term tumor control. J Neurosurg 89:933–938, 1998.
- Chang SD, Adler JR Jr: Treatment of cranial base meningiomas with linear accelerator radiosurgery. Neurosurgery 41:1019–1027, 1997.
- Comey CH, McLaughlin MR, Jho HD, Martinez AJ, Lunsford LD: Death from a malignant cerebellopontine angle triton tumor despite stereotactic radiosurgery: Case report. J Neurosurg 89:653–658, 1998.

- Condra KS, Buatti JM, Mendenhall WM, Friedman WA, Marcus RB Jr, Rhoton AL Jr: Benign meningiomas: Primary treatment selection affects survival. Int J Radiat Oncol Biol Phys 39:427–436, 1997.
- Day JD, Fukushima T: The surgical management of trigeminal neuromas. Neurosurgery 42:233–241, 1998.
- 9. Flickinger JC: An integrated logistic formula for prediction of complications from radiosurgery. Int J Radiat Oncol Biol Phys 17:879–885, 1989.
- Flickinger JC, Kondziolka D, Lunsford LD: Dose and diameter relationships for facial, trigeminal, and acoustic neuropathies following acoustic neuroma radiosurgery. Radiother Oncol 41:215–219, 1996.
- Flickinger JC, Kondziolka D, Niranjan A, Lunsford LD: Results of acoustic neuroma radiosurgery: An analysis of 5 years' experience using current methods. J Neurosurg 94:1–6, 2001.
- Flickinger JC, Kondziolka D, Pollock BE, Lunsford LD: Evolution in technique for vestibular schwannoma radiosurgery and effect on outcome. Int J Radiat Oncol Biol Phys 36:275–280, 1996.
- Flickinger JC, Lunsford LD, Linskey ME, Duma CM, Kondziolka D: Gamma knife radiosurgery for acoustic tumors: Multivariate analysis of four year results. Radiother Oncol 27:91–98, 1993.
- Foote KD, Friedman WA, Buatti JM, Meeks SL, Bova FJ, Kubilis PS: Analysis of risk factors associated with radiosurgery for vestibular schwannoma. J Neurosurg 95:440–449, 2001.
- Gardner G, Robertson JH: Hearing preservation in unilateral acoustic neuroma surgery. Ann Otol Rhinol Laryngol 97:55–66, 1988.
- Girkin CA, Comey CH, Lunsford LD, Goodman ML, Kline LB: Radiation optic neuropathy after stereotactic radiosurgery. **Ophthalmology** 104:1634– 1643, 1997.
- Goldsmith BJ, Wara WM, Wilson CB, Larson DA: Postoperative irradiation for subtotally resected meningiomas: A retrospective analysis of 140 patients treated from 1967 to 1990. J Neurosurg 80:195–201, 1994.
- Gormley WB, Sekhar LN, Wright DC, Kamerer D, Schessel D: Acoustic neuromas: Results of current surgical management. Neurosurgery 41:50–60, 1997.
- Hakim R, Alexander E III, Loeffler JS, Shrieve DC, Wen P, Fallon MP, Stieg PE, Black PMcL: Results of linear accelerator-based radiosurgery for intracranial meningiomas. Neurosurgery 42:446–454, 1998.
- House JW, Brackmann DE: Facial nerve grading system. Otolaryngol Head Neck Surg 93:146–147, 1985.
- Huang CF, Kondziolka D, Flickinger JC, Lunsford LD: Stereotactic radiosurgery for trigeminal schwannomas. Neurosurgery 45:11–16, 1999.
- Kida Y, Kobayashi T, Tanaka T: Gamma knife radiosurgery of intracranial neuroma other than acoustic tumors. Neuroradiology 37:599, 1995 (abstr).
- Kondziolka D, Flickinger JC, Perez B: Judicious resection and/or radiosurgery for parasagittal meningiomas: Outcomes from a multicenter review— Gamma Knife Meningioma Study Group. Neurosurgery 43:405–414, 1998.
- Kondziolka D, Levy EI, Niranjan A, Flickinger JC, Lunsford LD: Long-term outcomes after meningioma radiosurgery: Physician and patient perspectives. J Neurosurg 91:44–50, 1999.
- Kondziolka D, Lunsford LD, Coffey RJ, Flickinger JC: Stereotactic radiosurgery of meningiomas. J Neurosurg 74:552–559, 1991.
- Kondziolka D, Lunsford LD, McLaughlin MR, Flickinger JC: Long-term outcomes after radiosurgery for acoustic neuromas. N Engl J Med 339:1426– 1433, 1998.
- Laws ER Jr, Vance ML: Radiosurgery for pituitary tumors and craniopharyngiomas. Neurosurg Clin N Am 10:327–336, 1999.
- Lee JY, Niranjan A, McInerney J, Kondziolka D, Flickinger JC, Lunsford LD: Stereotactic radiosurgery providing long-term tumor control of cavernous sinus meningiomas. J Neurosurg 97:65–72, 2002.
- Linskey ME, Lunsford LD, Flickinger JC: Neuroimaging of acoustic nerve sheath tumors after stereotaxic radiosurgery. AJNR Am J Neuroradiol 12:1165–1175, 1991.
- Maire JP, Caudry M, Guerin J, Celerier D, San Galli F, Causse N, Trouette R, Dautheribes M: Fractionated radiation therapy in the treatment of intracranial meningiomas: Local control, functional efficacy, and tolerance in 91 patients. Int J Radiat Oncol Biol Phys 33:315–321, 1995.
- Martin HC, Sethi J, Lang D, Neil-Dwyer G, Lutman ME, Yardley L: Patientassessed outcomes after excision of acoustic neuroma: Postoperative symptoms and quality of life. J Neurosurg 94:211–216, 2001.

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- Muthukumar N, Kondziolka D, Lunsford LD, Flickinger JC: Stereotactic radiosurgery for jugular foramen schwannomas. Surg Neurol 52:172–179, 1999.
- Ogunrinde OK, Lunsford LD, Flickinger JC, Kondziolka D: Stereotactic radiosurgery for acoustic nerve tumors in patients with useful preoperative hearing: Results at 2-year follow-up examination. J Neurosurg 80:1011–1017, 1994.
- Pendl G, Schrottner O, Eustacchio S, Feichtinger K, Ganz J: Stereotactic radiosurgery of skull base meningiomas. Minim Invasive Neurosurg 40: 87–90, 1997.
- Petit JH, Hudes RS, Chen TT, Eisenberg HM, Simard JM, Chin LS: Reduceddose radiosurgery for vestibular schwannomas. Neurosurgery 49:1299–1307, 2001.
- Pollock BE, Kondziolka D, Flickinger JC, Maitz A, Lunsford LD: Preservation of cranial nerve function after radiosurgery for nonacoustic schwannomas. Neurosurgery 33:597–601, 1993.
- Pollock BE, Lunsford LD, Flickinger JC, Clyde BL, Kondziolka D: Vestibular schwannoma management: Part I—Failed microsurgery and the role of delayed stereotactic radiosurgery. J Neurosurg 89:944–948, 1998.
- Pollock BE, Lunsford LD, Kondziolka D, Flickinger JC, Bissonette DJ, Kelsey SF, Jannetta PJ: Outcome analysis of acoustic neuroma management: A comparison of microsurgery and stereotactic radiosurgery. Neurosurgery 36:215–229, 1995.
- Pollock BE, Lunsford LD, Kondziolka D, Sekula R, Subach BR, Foote RL, Flickinger JC: Vestibular schwannoma management: Part II—Failed radiosurgery and the role of delayed microsurgery. J Neurosurg 89:949–955, 1998.
- 40. Samii M, Matthies C: Management of 1000 vestibular schwannomas (acoustic neuromas): Surgical management and results with an emphasis on complications and how to avoid them. Neurosurgery 40:11–23, 1997.
- Sheehan JM, Vance ML, Sheehan JP, Ellegala DB, Laws ER Jr: Radiosurgery for Cushing's disease after failed transsphenoidal surgery. J Neurosurg 93:738–742, 2000.
- Shin M, Kurita H, Sasaki T, Tago M, Morita A, Ueki K, Kirino T: Stereotactic radiosurgery for pituitary adenoma invading the cavernous sinus. J Neurosurg 93[Suppl 3]:2–5, 2000.
- Shin M, Ueki K, Kurita H, Kirino T: Malignant transformation of a vestibular schwannoma after gamma knife radiosurgery. Lancet 360:309–310, 2002.
- Simpson D: The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry 20:22–39, 1957.
- Subach BR, Lunsford LD, Kondziolka D, Maitz AH, Flickinger JC: Management of petroclival meningiomas by stereotactic radiosurgery. Neurosurgery 42:437–445, 1998.
- Tishler RB, Loeffler JS, Lunsford LD, Duma C, Alexander E III, Kooy HM, Flickinger JC: Tolerance of cranial nerves of the cavernous sinus to radiosurgery. Int J Radiat Oncol Biol Phys 27:215–221, 1993.
- Wiegand DA, Fickel V: Acoustic neuroma: The patient's perspective—Subjective assessment of symptoms, diagnosis, therapy, and outcome in 541 patients. Laryngoscope 99:179–187, 1989.
- Wiegand DA, Ojemann RG, Fickel V: Surgical treatment of acoustic neuroma (vestibular schwannoma) in the United States: Report from the Acoustic Neuroma Registry. Laryngoscope 106:58–66, 1996.
- Yamamoto M, Hagiwara S, Ide M, Jimbo M, Arai Y, Ono Y: Conservative management of acoustic neurinomas: Prospective study of long-term changes in tumor volume and auditory function. Minim Invasive Neurosurg 41:86–92, 1998.
- Yu JS, Yong WH, Wilson D, Black KL: Glioblastoma induction after radiosurgery for meningioma. Lancet 356:1576–1577, 2000 (letter).

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COMMENTS

This article seems to report the largest series and the longest follow-up period for patients with selected benign tumors treated with gamma knife radiosurgery. The authors carefully demonstrate that tumor control is durable and can be achieved in the majority of patients. The absence of a dose response is surprising. Does this mean that the dosing of these tumors should be reconsidered and reduced? Also, because these are benign lesions, long-term "control" also can be achieved with observation in some patients. The presence of a control group would have been helpful. Regardless, the natural history of these lesions is to grow, and one can assume that would be the case in this population. The authors have been leading advocates for the use of gamma knife radiosurgery, and these data support their strategy.

Joseph M. Piepmeier New Haven, Connecticut

he authors present their experience with stereotactic radiosurgery for the treatment of benign or slow-growing intracranial tumors. They conducted long-term follow-up, in many instances more than 10 years after the radiosurgery was performed. In the nearly 300 patients evaluated, the control rates were quite impressive. In particular, and as expected on the basis of the available literature, patients with vestibular schwannomas and meningiomas fared quite well, and most important, the morbidity associated with the use of this technique was rather low. It is also important to know that in patients with these types of tumors, for whom standard radiotherapeutic therapy was administered initially, there is a salvage rate with good tumor control of approximately 70%. This pales in comparison to the nearly 95% tumor control rate in those patients who have not undergone prior radiotherapy. Notwithstanding that point, this is an excellent salvage rate for patients with these tumors.

Thus, one should consider performing stereotactic radiosurgery in situations in which a benign intracranial tumor such as a meningioma or a schwannoma cannot be resected completely because of morbidity. Often radiosurgical morbidity is significantly less than it would have been if complete resection had been attempted. This strategy tends to bring most neurosurgeons full circle, from the time when radical attempts were made to achieve complete resection of tumors despite the morbidity profile to a stage at which tumors can be resected aggressively but incompletely and patients can be salvaged with less morbidity by performing stereotactic radiosurgery. This approach should be advocated more routinely when the operative morbidity profile is unacceptable.

> Mitchel S. Berger San Francisco, California

The authors describe a large series of patients (perhaps the largest reported to date) who underwent radiosurgery for benign tumors. The majority of patients had acoustic neuromas; the next largest subgroup had meningiomas, followed by patients with pituitary adenomas and 15 patients with tumors a variety of other benign histologies. The results indicate tumor control in 95% of the patients, with few patients experiencing permanent complications of treatment. With long-

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term follow-up, a couple of interesting facts emerged. One is that there were no second tumors. Second is that patients with biologically more aggressive tumors who had received prior radiation did not fare as well as other patients. Also, patients with tumors with certain histologies, such as acoustic neuromas, fared better than patients with tumors with other histologies, such as meningiomas. The analysis of factors associated with success and complications is well done. I am not sure what is the advantage of combining the various histologies into one article; however, I do not consider that a drawback.

> **Jay S. Loeffler** *Radiation Oncologist Boston, Massachusetts*

This article provides a compelling look at the long-term results of one of our busiest and most expert sterotactic radiosurgery centers. In years past, it was possible to convince oneself and then one's patient that the results were not in with regard to radiosurgery for the long-term control of benign tumors such as acoustic neuromas and meningiomas and that microsurgery was the only certain way of dealing with these lesions. As time goes by, more radiosurgical groups will publish radiosurgical data with longer follow-up in patients with these benign tumors. The median follow-up of the diverse patient group presented in this article is 10 years. The treatment in experienced hands seems to have been not just effective but also reasonably safe during this time span. Patient selection seems to be an important part of both efficacy and safety. Obviously, in young patients, 10-year median follow-up is not completely reassuring, but some of the patients in this series are 15 years from treatment, and I know that the Pittsburgh group will provide further updates on their patients at intervals.

> Philip H. Gutin New York, New York



A last-minute field goal kicked by "Automatic Jack" Manders wins the game for the Chicago Bears against the New York Giants at the Polo Grounds; this kick preserved a perfect 13–0 regular season for the Bears in 1934. Helmets were not mandatory at that time, but they were worn by some players. In the 1934 NFL title game, the Giants defeated the Bears 30–13. (From, private collection of Richard Whittingham.)

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