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Radiosurgery of vestibular schwannomas: summary of experience in 829 cases

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Object. Management options for vestibular schwannomas (VSs) have greatly expanded since the introduction of stereotactic radiosurgery. Optimal outcomes reflect long-term tumor control, preservation of cranial nerve function, and retention of quality of life. The authors review their 15-year experience.

Methods. Between 1987 and 2002, some 829 patients with VSs underwent gamma knife surgery (GKS). Dose selection, imaging, and dose planning techniques evolved between 1987 and 1992 but thereafter remained stable for 10 years. The average tumor volume was 2.5 cm^3. The median margin dose to the tumor was 13 Gy (range 10–20 Gy).

No patient sustained significant perioperative morbidity. The average duration of hospital stay was less than 1 day. Unchanged hearing preservation was possible in 50 to 77% of patients (up to 90% in those with intracanalicular tumors). Facial neuropathy risks were reduced to less than 1%. Trigeminal symptoms were detected in less than 3% of patients whose tumors reached the level of the trigeminal nerve. Tumor control rates at 10 years were 97% (no additional treatment needed).

Conclusions. Superior imaging, multiple isocenter volumetric conformal dose planning, and optimal precision and dose delivery contributed to the long-term success of GKS, including in those patients in whom initial microsurgery had failed. Gamma knife surgery provides a low risk, minimally invasive treatment option for patients with newly diagnosed or residual VS. Cranial nerve preservation and quality of life maintenance are possible in long-term follow up.

Key Words • **radiosurgery** • **gamma knife surgery** • **vestibular schwannoma**

Vestibular schwannomas are relatively rare primary brain tumors accounting for approximately 10% of newly diagnosed intracranial tumors; they are estimated to occur at a frequency of 2000 to 2500 new cases per year in the United States. Therapeutic options include microsurgical removal, radiosurgery, or possibly fractionated radiation therapy. In recent years VSs have come to be diagnosed more frequently and at earlier stages of presentation because of the widespread availability of MR imaging. Advances in microsurgical technique have greatly improved the outcomes after surgical removal by one of several routes.[32,33] Recently, fractionated radiation therapy has been reintroduced as a treatment option.[35,36,39,41] Both patients and surgeons agree that long-term tumor control, preservation of cranial nerve function, and maintenance of a high quality of life represent desirable outcome goals. It is surprising that no consensus exists regarding the selection of candidates for therapeutic intervention.

Abbreviations used in this paper: GKS = gamma knife surgery; MR = magnetic resonance; VS = vestibular schwannoma.

To assess the long-term experience of the management of VS by GKS, we performed a retrospective review of our 15-year patient database (1987–2002).

Clinical Material and Methods

During this 15-year interval, 829 patients with VS (418 female and 411 male patients) underwent GKS with a Leksell model U, B, or C unit (Elekta Instrument AB, Stockholm, Sweden) (Table 1). A prior gross-total resection was performed in 35 (4.2%), and a subtotal resection was performed in 130 (15.7%). Neurofibromatosis Type 2 was noted in 62 (7.5%) of patients. Evolution in the technique included improved dose selection, remarkable advances in the quality and reliability of imaging, dramatic improvements in computer dose planning techniques, and improved patient selection. Although dose planning and dose selection concepts evolved between 1987 and 1992, margin dose prescriptions have remained stable for more than 10 years. The average tumor volume was 2.5 cm^3. The median margin tumor dose was 13 Gy (range 10–20 Gy).

TABLE 1
Demographics in patients undergoing GKS of VS

Parameter	No. (%)
sex	
female	417 (50.4)
male	412 (49.6)
side of op	
lt	416 (50.2)
rt	413 (49.8)
prior op	
gross-total resection	35 (4.2)
subtotal resection	130 (15.7)
cranial nerve signs	
imbalance/ataxia	423 (51)
hearing loss	754 (91)
tinnitus	368 (44.4)
facial nerve symptoms	
Grade I	646 (78)
Grade II–VI	183 (22)

TABLE 2
Results of 12- to 13-Gy GKS at 6 years (1991–2001)

Result	6-Yr Outcome
tumor control rate*	98.6 ± 1.1%
facial nerve function preservation	100%
normal trigeminal function	95.6 ± 1.8%
unchanged hearing level	70.3 ± 5.8%
useful hearing preservation	78.6 ± 5.1%

* Two patients underwent delayed resection of their tumor.

Pre-GKS Evaluation

All eligible patients with suspected VSs are evaluated with high-resolution MR imaging, undergo clinical evaluation, and have audiometric tests that include pure tone average and speech discrimination score tests.[2–5] Hearing is graded using the Gardner–Robertson modification of the Silverstein and Norell classification. Facial nerve function is assessed according to the House–Brackmann grading system. Serviceable hearing, Classes I and II, was defined as a pure tone average or speech reception threshold lower than 50 dB and speech discrimination score higher than 50%. Hearing loss of some degree was noted in 91% of patients, imbalance and/or ataxia in 51%, and tinnitus in 44%. Facial sensory loss was detected in 15% preoperatively; 22% had between Grade II and VI facial weakness before GKSs.

Radiosurgical Technique

The surgical procedure begins with the patient's head undergoing rigid fixation in an MR imaging–compatible Leksell stereotactic frame (model G; Elekta Instrument) after application of a local anesthetic supplemented by mild intravenous sedation. High-resolution 1.5-tesla MR images are obtained with an appropriate fiducial system. Volume acquisition studies require 1- to 1.5-mm axial slice thicknesses that are subsequently reformatted in coronal and sagittal projections. Conformal dose planning optimization requires multiple isocenter techniques. The prescription isodose, maximum dose, and dose to the margin are determined jointly by a neurosurgeon, radiation oncologist, and medical physicist. Dose fall off to the brainstem and the cochlea are evaluated. Since 1992, a dose of 12.5 to 13 Gy has been prescribed at the 50% isodose level, which conforms to the irregular geometry of the tumor volume.[2] Gamma knife surgery was performed using the 201-source Cobalt-60 U, B, or robotic C gamma knife models.[8]

Dose Prescription

The success of GKS for VS depends on high conformity between the prescription dose and the tumor margin. During the first 5-year experience at our center, higher tumor margin doses (average 16 Gy) were prescribed.[16–19] Since 1992, we have selected 12.5 to 13 Gy as the usual tumor margin dose. We have been reluctant to prescribe lower margin doses for fear that the tumor control rate may suffer over additional years. No difference in tumor control rates was noted between patients receiving 12.5 to 13 Gy at the margin and those patients who received higher doses.[2,18]

Postoperative Care and Evaluations

At the conclusion of the procedure, patients receive intravenously administered methylprednisolone (40 mg). Patients are observed for a few hours in the same-day surgical unit and are discharged within 24 hours after the procedure. Patients are followed with serial contrast-enhanced MR imaging studies, which are requested at 6 months, 12 months, 2 years, 4 years, 8 years, and 16 years. All patients who have preserved hearing are advised to obtain appropriate audiometric testing at the time of their MR imaging follow up.

Results

Tumor Growth Control

The goal of GKS is tumor growth control (prevention of additional volumetric growth). Long-term (≥10 years) follow-up data were available in 252 patients. We have identified a 98% long-term tumor control rate (absence of the need for further surgical or radiosurgical intervention). Six percent of tumors initially enlarged 1 to 2 mm during the first 6 to 12 months after GKS as they lost central intravenous contrast enhancement. Most such tumors thereafter regressed in comparison to the pre-GKS volume. In this experience, fewer than 2% of patients required subsequent tumor resection after GKS. One hundred fifty-seven patients have been evaluated between 10 and 15 years after GKS for a benign tumor. Seventy-three percent showed a reduction in tumor volume, and 25.5% showed no further change in their tumors. Three patients underwent delayed tumor resection. Seven patients (0.8%) required management of hydrocephalus.

No patient developed a radiation-associated malignant or other benign tumor (defined as a histologically confirmed and distinct neoplasm arising within the initial radiation field after at least 2 years had elapsed). Table 2 provides a summary of outcomes in patients who received 12 to 13 Gy tumor margin doses between 1991 and 2001.

Hearing Preservation

At 5 to 10 years, 51% of patients had no change in their hearing status. For patients with intracanalicular tumors, hearing preservation rates in those treated with 12.5 to 14

TABLE 3

Hearing preservation after 12- to 13-Gy GKS to the tumor margin

Parameter	Value
preservation of preop Class I–IV	84.2%
5-yr actuarial preservation rate	70.3 ± 5.8%
serviceable hearing (Class I–II)	78.6 ± 5.1%
hearing improved by 1 class	1.5 ± 0.9%
preservation of any testable hearing	97 ± 1.5%

TABLE 4

Significant long-term complications after GKS

Complication	No.	
hydrocephalus	7 (0.8%)	
trigeminal neuralgia	2 (0.2%)	exceedingly rare
disabling tinnitus	2 (0.2%)	exceedingly rare
tumor apoplexy	1 (0.1%)	
delayed peritumoral cyst enlargement	3 (3.6%)	
death from delayed progression	1 (0.1%)	
radiation-related neoplasm	0 (0.0%)	compare to micro-sx

Gy at the margin showed 90% preservation of serviceable hearing.[22] The 5-year actuarial rates of hearing level preservation and speech preservation were 69% and 86%, respectively, for 103 patients treated with less than 14 Gy at the tumor margin.[21] Early hearing loss is rare after GKS. Hearing impairment, if it occurs, tends to be gradual over 6 to 24 months. Early hearing loss (within 3 months) was rare, perhaps caused by local neural edema or demyelination. Table 3 provides outcome data in 267 patients who received 12 to 13 Gy at the tumor margin between 1991 and 2001.

Facial and Trigeminal Nerve Preservation Rates

In our early experience, normal facial function was preserved in 79% of patients after 5 years. Trigeminal nerve function was preserved in 73%. These preservation rates (as often quoted in the literature) reflect the higher tumor margin doses of 18 to 20 Gy used during the computerized tomography–based planning area before 1991. For patients who received 13 Gy to the tumor margin, the risk of any new facial weakness of any degree was less than 1%, and the risk of trigeminal sensory loss was 3.1%. A margin dose of more than 14 Gy was associated with a 2.5% risk of new but temporary facial weakness. None of the patients who underwent GKS for intracanalicular tumors developed either facial or trigeminal neuropathies. Other long-term complication rates are noted in Table 4.

Results With Present Techniques

We recently completed our review of 313 patients with unilateral VSs treated between 1991 and 2001 with our present doses of 12 to 13 Gy.[2] The actuarial 6-year resection-free tumor control rate was 98.6 ± 1.1%. Two patients underwent resection, and facial nerve function was maintained in 100%, trigeminal nerve function in 96%, unchanged hearing level in 70.3 ± 5.8%, and useful hearing preservation in 78.6 ± 5.1%.

Discussion

Perhaps because of the relative rarity of this tumor, controversies are endemic and often polemic relative to therapeutic options for VSs. A wide variety of practitioners remain eager to perform skilled microsurgical resection despite the excellent functional outcomes documented after stereotactic radiosurgery. Patients leave the hospital within 1 day and are able to return to their role in life almost immediately. Duration of hospital stay and total charges are less in patients who undergo radiosurgery.[27]

Microsurgery after failed radiosurgery has been reported to be more difficult.[26,33] Most studies failed to differentiate between prior fractionated radiation therapy, truly conformal stereotactic radiosurgery, proton radiation,[7] and other linear–accelerator based techniques for the management of VSs with fractionated radiation. In our experience, microsurgical resection in patients who have undergone GKS is more challenging only in those patients in whom initial microsurgery had failed before GKS.[28] In our experience, identification of the true target volume (separation of residual postoperative scar changes from tumor volumes) may lead to underassessment of tumor volumes and thus undertreatment, but it is unclear whether the prior microsurgical treatment or the radiosurgical treatment produces a tumor that is more difficult to resect a second time.[26,28]

Delayed Oncogenesis

Although we have not encountered such a case, delayed malignant transformation of a histologically benign VS to a more aggressive neoplasm is potentially possible. We have reported on a patient originally thought to have a VS who eventually died of a malignant cerebellopontine angle triton tumor (mesenchymal sarcoma) despite initial GKS without tissue diagnosis and subsequent microsurgery after tumor progression.[1] Other centers have reported at least three cases of a secondary malignant neoplasm.[15,34] The risk of oncogenesis over a 5- to 30-year period (fitting the description of a radiation-related cancer) is estimated to be approximately 1:1000. Such a case has not been confirmed in our total radiosurgical experience of more than 6200 procedures. The outcome of this potential problem related to single-fraction exposure of a small volume of radiation could be compared with the estimated surgical mortality rates at centers of excellence in patients undergoing microsurgery for VSs (0.5% or 1 in 200 in the 1st postoperative month). Interestingly, we have also seen one patient who developed a VS after previously undergoing fractionated radiation therapy for a malignant glial tumor and another who developed a glioblastoma multiforme after resection of a VS (without any radiation).

The current results of this experience suggest that in the vast majority of newly diagnosed VSs enhanced outcomes can be obtained in patients who undergo GKS as the primary management strategy.[2–14,16–25,27,29,30,31,37,38,40] Tumor control is achieved in 98% of patients, cranial nerve preservation is possible in the vast majority of patients, and patients are able to return to their normal lifestyle almost immediately. It is likely that the role of GKS will expand in the management of this benign tumor.[29] Abundant disinformation exists in the medical literature, on the Internet, and in the minds of both physicians and patients. Such disinformation includes the concept that patients who undergo radiosurgery do not have improvement or in fact have wors-

ening of vestibular function (vertigo or imbalance). We have no data to substantiate this allegation based on our experience in more than 800 patients.

In our experience tinnitus is usually unchanged after GKS. In fact, tinnitus almost certainly represents a deafferentation phenomenon similar to chronic pain. We have noted a number of patients who are deaf after microsurgery who have residual tinnitus. There are very few cases of exacerbation of tinnitus in our patients, including those who have long-term preservation of hearing. No doubt a properly case-matched study in which the outcomes of microsurgery and radiosurgery are compared in terms of the control of tinnitus, dizziness, or ataxia would be valuable. As tumors are being recognized in modern times more frequently and at earlier stages because of the widespread availability of MR imaging units and because hearing and facial nerve preservation rates are quite high, it is likely that the majority of patients with small- to medium-sized VSs in the United States are candidates for GKS. To obtain significant improvement by converting to local field conformal fractionated radiation therapy techniques, a very large experience would be required to detect any significant difference in the hearing or facial nerve preservation rates at the current level.

Thirty-three years have elapsed since Leksell first reported GKS for VS.[14] Most patients are willing to accept tumor growth control coupled with enhanced hearing and cranial nerve preservation rates.[9,] The goals of VS management should be prevention of further tumor growth, preservation of neurological function, and maintenance of a high quality of life in long-term follow up. The technologies and results are currently available.

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